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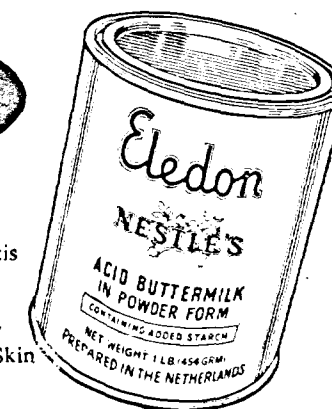
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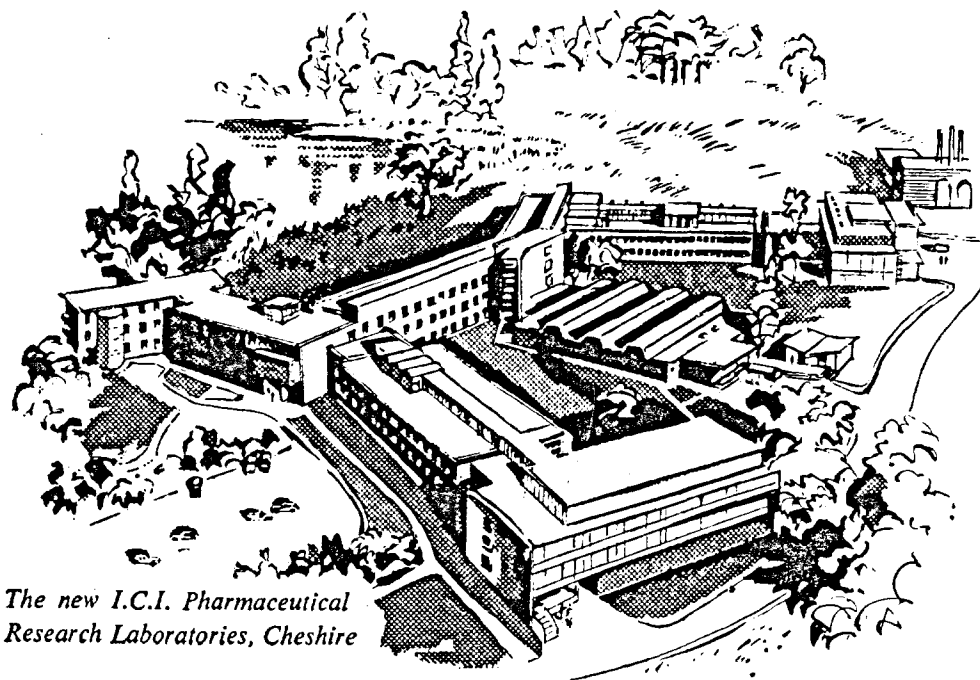


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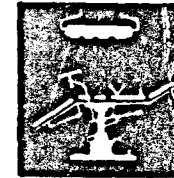
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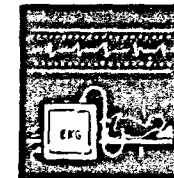
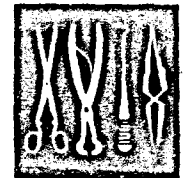
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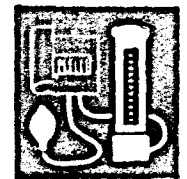
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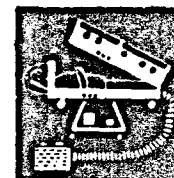
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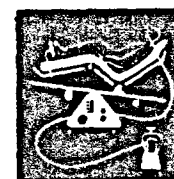
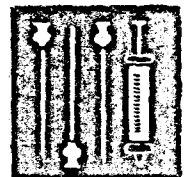
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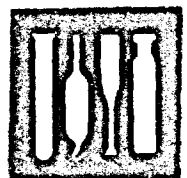
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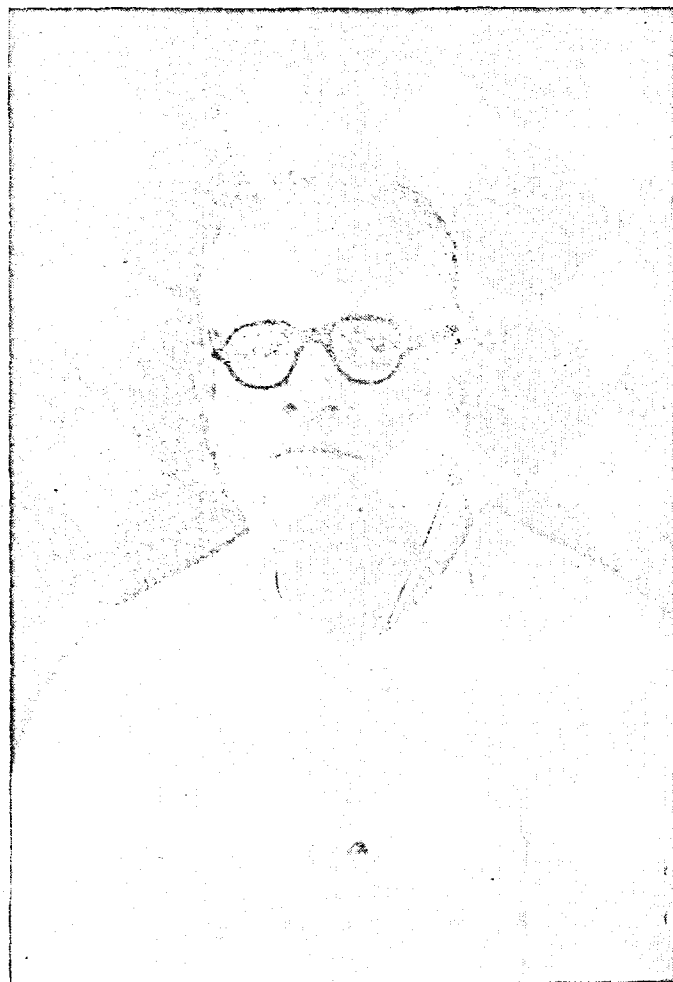
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Scientific Research—in Theory and in Practice

"COULDN'T the teaching hospital with all the resources at its command spare you one single x-ray film to satisfy your academic curiosity?" said the private Radiologist having taken an x-ray of a specimen for a person I know. He refused to accept any payment—not even for the cost of the film. Breaking into a ripple of derisive laughter, he said "It is a pleasure to me to assist some one who is interested. It is indeed a tragic state of affairs when unofficial research has to be pursued in this manner without encouragement or support in a large teaching institute."

When the same person went up to the Research Chief and requested permission to pursue in his own small way a research problem, although he was not being paid to do so the official reaction was quite noteworthy. The Chief leaned back on his cosy chair. "Research" he said magnanimously "is team work. We will have to consider carefully the subject one which research needs to be done. Then we have to formulate a plan and a policy. This we will have to put on paper. We will have to estimate the approximate cost of the research project. We will have to have specialized workers on it. All this we have to put before the local research committee. We can proceed only when it has received their official sanction and approval. I would like to tell you this. Even if it does receive sanction you are not qualified to do any work because you have first to be *selected* for research." The Candidate pleaded with him "May I not have facilities at least to take an occasional x-ray of an interesting specimen?" "I will see what I can do in this matter" said the Chief and immediately issued verbal instructions to the Radiologist not to co-operate in any way or to take x-ray pictures or give any facilities for research work.

What a sad story! Yet it is true! The tragedy is this. We do not care to practice what we preach. Yet when a responsible individual behaves in this fashion, the Scientists of India, Vice-Chancellors and Educationists who met at a big conference recently passed resolutions like this. "Adequate facilities should be given to research workers by way of equipment, apparatus and other assistance such as laboratory, library and clerical facilities. Adequate financial aid should be guaranteed to research workers and schools of research in Universities and elsewhere, and greater freedom to choose his subject and publish his results should be given to the research worker in Universities and elsewhere, specially to the *younger worker*. Financial and other procedures should be simplified and *conditions of academic freedom ensured*."

In this particular case no special equipment was asked for; no scholarship requested; no library and special clerical facilities wanted. Yet such a simple request could not be met! When genuine interest is not encouraged what may we expect for the future?

To do research one has to be selected, and quite often aptitude or interest in academic study is not the criterion on which selections are made. Very often a research post is something designed to provide the candidate his daily bread and butter as well as

a little pocket money while he looks round for a better job. When this is the basis on which people are selected for research, it follows that in a state institution it is not difficult for a candidate to discover reasons why a particular research project has to be temporarily abandoned. There may be no glass slides. The stains may be out of supply. A technician who has been given to render assistance may be absent. The expert who has to help in the interpretation of the slides may be too busy to do so. The work comes to an end and the research worker idles his time drinking coffee in the canteen.

There is another great drawback. This is a general reluctance on the part of a research worker to take off his coat and get down to work. He prefers to give orders, rather than to use his own hands. What else can one expect when the chief of research himself considers it undignified to remove his coat and soil his hands on a laboratory bench? Sitting under a fan in the cool comfort of an air-conditioned room on a comfortable chair may be conducive to formulate extravagant research schemes. He can grasp desperately at fleeting ideas like a drowning man at straw. Sitting on a peacock throne studded with the diamonds of authority and wearing the mantle of administrative power and commanding people to do this and that does not help in getting great ideas translated into hard facts. One day the Chief may become possessed of the notion that an electron-microscope is an important tool for advanced research, much modern scientific work having been done with its aid. It may be within his power and possible to purchase such a microscope but often interest wanes and the microscope is soon abandoned to lie in some dusty cupboard to be brought out into the light of the day only on occasions such as for an annual verifications of stock.

Another great drawback for a research worker is the lack of freedom to select a subject on which he wishes to work. The person in charge of research may thrust his own ideas or may allot subjects in such a way that what is done will be of considerable advantage to himself in his own field of work whatever that may be. In the circumstances which prevail at least in certain institutions today it is unlikely that at any time scientific research of note will be done at all.

Let us be optimistic and hope that the spirit of enquiry may thrive. It should theoretically be possible to plant a seed in the scorching sands of a barren desert and hope that it will blossom forth into a big tree. Such an event should be possible provided certain conditions are fulfilled. There should be a protective canopy of eternal shade. A liberal supply of water should be at hand. The soil should be cooled by some air-conditioning device and fertilizers should be provided; and above all the seed must be a potential healthy one. Similarly in the circumstances and conditions which prevail today research could flourish and yield results provided such extraordinary conditions are forth-coming;—and that you will agree will be a fluke!

It should be our constant endeavour to create a totally different environment in which some measure academic freedom may prevail un-fettered by the ambitions of those who believe that once they have risen to the administrative summit they can do what they please. It is my contention that as things are today even a person with private

financial backing, cannot readily command the opportunities or facilities so necessary to do research.

There are so many other good, great and noble things which were formulated at the conference of Indian Scientists, Vice-Chancellors and Educationists. Here are some of their resolutions "Salaries and conditions of service should be rationalised and improved in relation to the superior administrative services to attract and retain a fair proportion of the ablest men and women in various scientific professions, and specially in teaching and research."

"The initial salary should be adequate to attract the best, and in each faculty of a University there should be a number of national professors whose salary could be comparable with the highest administrative posts to ensure that they continue in the teaching profession."

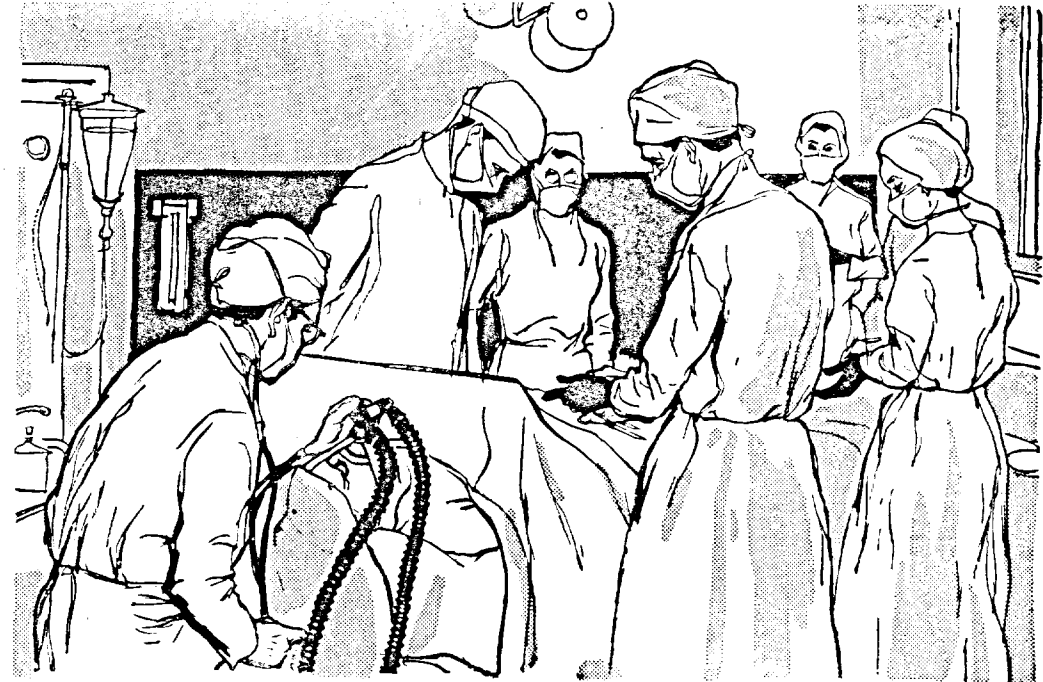
"To encourage talented young men to remain in research, a great number of research fellowships of adequate value at the Masters and Doctors levels should be instituted. Machinery should be set up to ensure that these trained men are subsequently absorbed in suitable employment."

As though to complete the pious and wonderful things which they have formulated they have declared further "A pool of scientists and technologists should be created by recruiting outstanding young men available in the country and by recalling young Indian scientists and technologists working abroad. Until such time as they are found suitable employment, they should be given fellowships and employed in research in Universities, national laboratories and institutions of higher learning and industry."

I believe most emphatically that if only we look around in our own country we will find innumerable instances of people who are well qualified who are not being utilised; of instances in which those who have qualified for one thing are being utilised for something totally different; of people who are on the verge of emigrating to other countries because their own country has denied them opportunities; of those who have become despondent and frustrated without having access to the facilities for research for which they are pre-eminently qualified and clamour for.

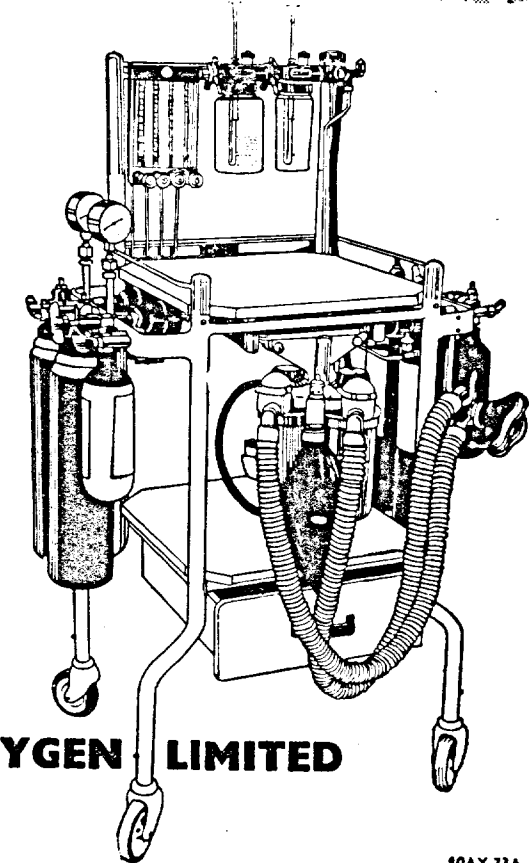
Until we have made a sincere effort to remedy this sad state of affairs it would be a tragedy of the very greatest magnitude to recall young Indian scientists and technologists working in other countries, because I am sure that these men have found in Universities and learned institutions outside the country a true spirit of academic freedom. Such facilities they will be denied in our country when they return. Those who are at work abroad enjoy an experience which is intellectually valuable to them and besides they are on financially sound ground. What object, then, is there in bringing them back only to make embittered men of them? They will only acquire a gloomy outlook for the future and feel unwanted.

So first let us put things right in our own country before we bring back our qualified nationals from abroad to frustrate them, and to destroy their spirit.



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No ante-natal examination of a pregnant woman is complete without getting her blood examined for the presence of this serious disease, whether there are any obvious clinical signs or not. Only by making serological examination of pregnant women a routine, may the presence of syphilis be diagnosed and effective treatment begun without delay. In this part of the country about 8 women out of 100 who have had their blood examined in the ante-natal department are found to have a positive serological reading (Rajam 1954). It does not mean however that all those who have a positive reaction necessarily suffer from this disease, because ailments such as eosinophilia, malaria, leprosy or even a virus disease such as a common cold may be the cause for a false positive reaction. A positive reaction in the absence of clinical evidence of syphilis deserves that the test be repeated. Even if a test is negative it is advised that it should be carried out at the second, fifth and eighth months of pregnancy.

Syphilis was so prevalent at one time and was such an important cause of maceration of the foetus that most of such cases were thought to be due to this disease. The position has changed considerably because of public health measures and the extensive and possibly indiscriminate use of antibiotics such as penicillin, that syphilis is only a minor cause for still births. Nevertheless, it is important that in cases where a dead child is expelled both the foetus and the placenta should invariably be sent for histo-pathological scrutiny.

PATHOLOGICAL FEATURES

In untreated cases an examination of the foetus and the placenta may be of help. In the typical case the placenta is heavy and looks pale. The weight of a normal placenta is approximately one sixth of the weight of the foetus. If the placenta is more than one fourth of the weight of the foetus after the 36th week of pregnancy it is very suggestive of syphilis. When examined microscopically the villi are enlarged, relatively avascular and cellular. Endarteritis may be present. The placenta in erythroblastosis does not show endarteritis. If the umbilical cord is sectioned and examined round cell infiltration may be found around the vein. When it is possible to obtain cord blood serological investigations may yield positive results. In approximately a third of the cases the syphilitic foetus tends to be macerated. When a patient who has not taken advantage of ante-natal care gives birth to a macerated foetus syphilis should always

be excluded. A foetus which looks perfectly normal on inspection may turn out to be infected with syphilis. The internal organs especially the liver, spleen and the bony epiphyses should be examined for evidence of infection. The liver tends to be heavy and may show the presence of peri-cellular cirrhosis. Sometimes the treponema pallida may be demonstrated. The spleen is often enlarged. It may be enlarged in erythroblastosis as well, but in this condition the serological tests on the blood will be negative.

THE MANAGEMENT OF LABOUR

Syphilis rarely gives rise to any complications in labour. Lesions on the vulva are apt to be infectious and great care should be taken in performing a vaginal examination. It should be remembered that secondary sepsis may occur and infection in the puerperium should be guarded against. Occasionally the danger of introducing infection is magnified when obstetric procedures requiring internal manipulations become necessary. It should be remembered that the child may become infected in its passage through the birth canal.

CONGENITAL SYPHILIS

The obstetrician should be familiar with the clinical picture of early congenital syphilis. This is adequately described in the standard text books. In the great majority of cases (90%) the child may appear to be quite healthy and clinical signs of infection may appear only 6 to 8 weeks after birth. When the disease is suspected the child should be carefully followed up. If a blood test is positive in a new-born child it does not mean that it is infected. It may be due to the passive transfer of anti-bodies. If there are external lesions or there is radiological proof that congenital syphilis is present the child should be treated. If the blood test alone is positive the child may be watched and the test repeated. If the titre rises steadily or if the child which at first had a negative reading subsequently showed a positive reaction, infection may be suspected. The passive anti-bodies usually disappear within three months. An useful and important sign is changes in the long bones which may be detected by radiology. (Fig. 4). Osteochondritis is the most common manifestation of congenital syphilis in infants (Jones and Lovett 1933). If the x-ray demonstrates this saw-toothed line a positive diagnosis of syphilis may be made. (Fig. 5). It should be remembered that congenital syphilis can be present without radiological evidence in the bones being necessarily present.



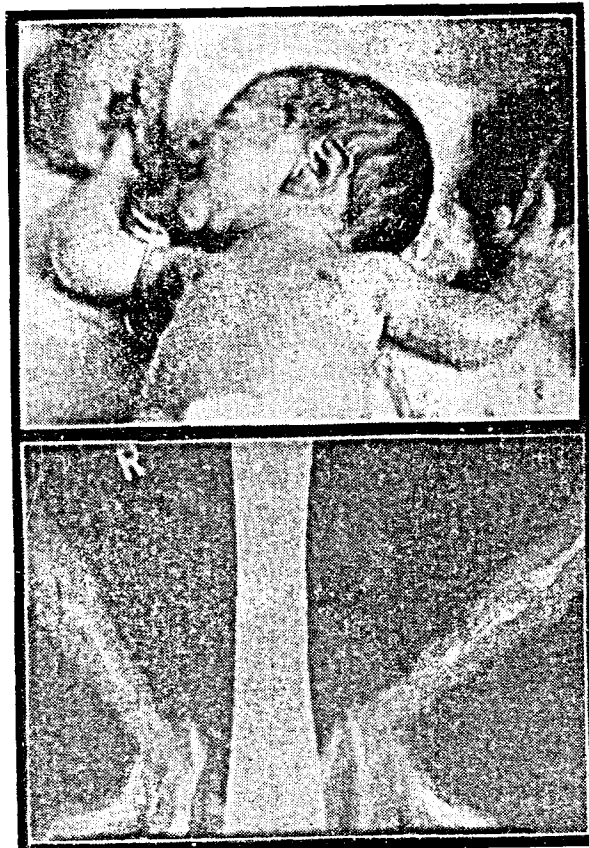
(Courtesy: The Govt. Women and Children's Hospital, Egmore, Madras)

Fig. 4. These X-rays demonstrate certain of the radiological features of congenital syphilis. Bone growth is delayed and the epiphyses take a long time to appear. The ends of the bones show a transverse line of increased density and directly adjoining this there is a transverse band of rarefaction.

TREATMENT

Today we have in penicillin a most effective antibiotic drug which has made it unnecessary to use potentially toxic metallic drugs such as bismuth and the arsenicals. Yet there was a time when the toxic properties of these metallic drugs discouraged practitioners from using them at all when a patient was pregnant.

Francois Mauriceau (1637—1709) the great French Obstetrician wrote in his book *The diseases of Woman with Child and in Childbed*. "In the year 1660, when I practis'd Midwifery in the Hostel de Dieu at Paris, a young wench not above twenty years old, came thither to lie-in of her second child, that had had the Pox before ever she conceived the first time, and after miscarried of a dead child, rotten with the Pox; therefore being big this second time, and perceiving the accidents of her disease to augment more and more, she concluded there was no hopes this great-belly would succeed any better than the first, because she had all over her body, especially upon both her breasts, very many malignant ulcers, which encreased daily: and fearing it might turn to a Cancer before her reckoning was compleat, being but three Months gone, she resolved to submit to a through cure then, and to hazard her life in that condition to save her child's, having no other hopes to effect it, nor being able herself to resist the growing disease. She acquainted three or four chirurgeons both with her disease and design, not at all concealing her great-belly; who for that cause would not under-take



(Courtesy: The Govt. Women and Children's Hospital, Egmore, Madras)

Fig. 5. An 18 year old patient having her third child was admitted at full term with labour pains. A diagnosis of poly-hydramnios complicating pregnancy was made. The foetal heart sounds were barely audible. A high rupture of the membranes showed the liquor to be stained with meconium. She gave birth to a premature male child weighing 4½ pounds. The child seemed to be normal except that both the elbows appeared uniformly enlarged. The surface of the skin over them was slightly discoloured. Crepitus was elicited on movement at the joint. An X-ray was taken. This showed some of the characteristic features of congenital syphilis. When she was interrogated it transpired that she was the second wife of a man, whose first wife had borne him a child which also had swellings on the elbows at birth. A subsequent serological test on the mother showed her to have active syphilis.

This case is of special interest because one usually associates some type of congenital malformation of the foetus with polyhydramnios. Instead the correct diagnosis in this case turned out to be 'congenital syphilis'!

her, (altho' she was fully resolved upon it, and promised to pay them well) telling her that their conscience would not suffer them to do it in the condition she was in, and that it would be better she would patiently submit to it as well as she could, till

as brought to bed, and then they would very willingly undertake her: But when she found none would undertake her, unless she concealed her great-belly, which was not hard to be done, being but 3 months gone, and believing there was no better an expedient; she met with another (to whom she mentioned nothing of her great-belly,) that put her into the ordinary course, as if there had been no conception; and besides the common remedies used in this disease, he gave her a Salivation by five or six reiterated frictions of the ointment, which followed her very plentifully five whole weeks, so that she was behind of her disease. When she was almost recovered, and that all had succeeded well, she told her chirurgeon she was 4 months and a half gone with child, (for she was 3 months when she came to him, where she lodged six weeks intire, without having it in the least perceived) which at first he could hardly believe, but perceiving her belly rather grown he was immediately assured of the truth of it: She informed him, that the reason why she had concealed her great-belly, was the refusal four chirurgeons (to whom she confest it) made to take her in hand. From the time she was cured she suffered not the least inconvenience during the remainder of her time, except a little want, because all the money she had was given the chirurgeon for her cure, which made her come to the Hostel de Dieu to lie in, where I delivered her of a child at the full time, as big, fat and healthy, as if the mother never had had the least touch of that disease in her whole body; and which was very remarkable, the burden (which is a part very susceptible of the least impression of a woman's corrupt humours) was as neat, fair and ruddy as could be imagined."

Once a diagnosis of syphilis has been made modern treatment is fairly simple and straight-forward. That a cure has been obtained may be determined by serial serological examination of the blood as well as the clinical progress.

The following schedule of treatment is widely recommended and used with good results:

600,000 units of penicillin in oil with 2% aluminium monostearate daily for 8 to 10 days intra-muscularly (a total dose of 4.5—6 Mega-units). An alternative form of treatment is to use Benzyl Diamine a long acting penicillin preparation in a watery suspension (2.4 million units is made up in 8 cc. of water and this quantity is injected at one sitting in divided doses in each thigh). The injection is painful.

(Continued on page 14)

In addition to specific treatment attention should be directed to improve the general health of the patient.

There appears to be no contra-indication to breast-feeding. A syphilitic child may be suckled with impunity by its own mother as she already has the disease.

In congenital syphilis the dose customarily employed is 150,000 units of penicillin with 2% aluminium mono-stearate injected daily intra-muscularly for infants below four months of age. The dose may be increased to 300,000 units daily for the same period of time for children above 4 months and up to the age of 2 years.

CONCLUSION

Syphilis is an instance of a disease which can do serious harm to the child and yet with adequate treatment employing modern anti-biotics it can be completely cured. Congenital syphilis is a preventible disease.

ACKNOWLEDGMENT

I wish to acknowledge my gratitude to Dr. Mrs. S. Abraham, M. D., Professor of Obstetrics and Gynaecology, Madras University, and Superintendent, The Govt. Women and Children's Hospital, Egmore, Madras, not only for her unfailing encouragement, but to her generosity in permitting me to make use of clinical material from the hospital. (All the photographs including x-ray reduction prints were taken by me—V. S.).

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Ten Years of W.H.O. in South-east Asia

By A SPECIAL MEDICAL CORRESPONDENT

THE creation of the World Health Organization, in 1948, was the culmination of a long series of efforts made over the centuries to prevent the spread of disease from one continent to another and to achieve international co-operation for better health throughout the world.

Today the Organization derives its authority from 88 Member Countries which have, since its inception, ratified its Constitution. These are grouped under six Regions: South-east Asia, Eastern Mediterranean, Americas (Pan American Sanitary Bureau); Western Pacific, Africa, Europe.

The Regional Office for South-east Asia was the first of WHO's Regional Offices to come into being. It may be said to have started with the first session of its Regional Committee, which was held in New Delhi on October 1948.

The original Member States were Afghanistan, Burma, Ceylon, India, Thailand and two metropolitan powers—France and Portugal, in respect of Pondicherry and Goa. Later Indonesia, Nepal and the United Kingdom (in respect of the Maldives Islands) joined, making a total of ten Member States.

During 1949 and 1950 the Regional Committee was still in the formative stage, and programme proposals were of necessity mainly formulated in the Regional Office. In the ensuing years, however, the programme began to be developed with the active participation of the Regional Committee and even more so of the national health administrations working in close, daily co-operation with WHO staff at the country level.

The position today is that the Regional Office is accepted as an organic part of the health set-up in

the Region in the planning and development of national health programmes.

All the countries represented in the Regional Committee, with similar socio-economic backgrounds, had almost the same health needs and problems.

They were predominantly rural: eighty per cent of the population of the Region lived in rural areas with extremely low living standards bordering often on almost bare subsistence. Public health services, poor in the few urban centres, were almost non-existent in rural areas.

Communicable diseases due to wide-spread insanitary environment were widely prevalent. Malaria was claiming about 100 million victims each year, with about a million deaths. Also, serious malnutrition was wide-spread and the rate of maternal and infant deaths alarmingly high.

In the health services the bias was on clinical medicine, and there was an acute shortage of technical personnel and essential resources. Many of the countries had recently become independent of foreign rule, however, and the new popular governments were determined to improve the lot of their people as rapidly as possible. Hence WHO became a part of a wide-spread move to improve social services.

As the expansion of basic public health services for such large populations required tremendous resources, a beginning had to be made with immediate short-term programmes, especially those relating to the control of communicable diseases, which contributed so predominantly to the heavy toll of morbidity and mortality.

Quite naturally, it became the first task of the

Regional Office to supplement these heroic efforts to bring wide-spread endemic diseases under control.

The major WHO programmes during the first two to three years consisted, therefore, of the provision of international teams, with some supplies, for the control of malaria, tuberculosis, venereal diseases, yaws and filariasis.

Most countries in the Region started off with some form of assistance in controlling one or more of these diseases. The method of work, in all cases, consisted of (1) establishing so-called demonstration and training projects in well-defined geographical areas, (2) with the support of national counterparts and other local resources, demonstrating modern methods of control, and (3) training the local staff in these techniques for a fixed period of time, after which WHO assistance was withdrawn.

While assistance in the control of communicable diseases was being actively pursued, pilot activities were started, almost simultaneously, towards positive health. A beginning was made programmes for improving maternal and child health, which also took the form of demonstration and training projects.

From the outset, the training of counterpart physicians also received major attention; that of nurses started very early (even in 1949 seven nurses were working with WHO demonstration teams), and this was soon followed by the training of auxiliary staff and other technicians. The emphasis, however, in the earlier years remained on training the local personnel that were working with the WHO staff in particular projects.

While 1949 saw 16 WHO-assisted projects with about twenty-five field staff, costing about \$ 340,000 the programme in 1952 jumped to an estimated expenditure of more than four million dollars (including over 2½ million under "Other Extra-Budgetary Funds") covering 55 projects and utilizing about 125 field staff. By 1956 there were 120 projects, 143 field staff, and a field expenditure of \$ 4,213,487 (including \$ 1,902,866 under "Other Extra-Budgetary Funds"). The corresponding figures for 1958 (budgeted) are 141 projects, 276 field staff, and a field budget of \$ 8,960,022. These include 7 projects (including one fellowship) with 48 staff and a budget of \$ 2,056,371 under the Malaria Eradication Special Account. This is a new feature of the

1958 budget since malaria eradication programme have or are likely to start in most of the countries of the Region during the year. The number of fellowships (including those financed by Unicef funds) also rose from 46 in 1949 to 69 in 1952 to 114 in 1956-57 and to 133 in 1957-58.

Altogether, in the first ten years, WHO in South-east Asia has assisted with 14 malaria control projects, 11 projects for the control of venereal diseases and yaws, 25 for the control of tuberculosis (including BCG vaccination), 24 for the promotion of maternal and child health (frequently combined with the training of nurses), and with 27 additional nursing projects, as well as with many programmes in other fields.

The shortage of equipment and supplies formed a major obstacle from the very beginning as most of the necessary medical supplies were not produced within the countries of the Region and had to be imported and paid for in foreign currency. It is noteworthy that UNICEF joined hands with the Regional Office of South-east Asia from the very beginning, by providing much needed supplies and equipment, for the demonstration and training project.

Major achievements of WHO and UNICEF in this field were the joint development of a penicillin-producing factory and DDT factory in India, yaws programmes, maternal and child health projects and assistance to 3,000 rural health centres.

From 1952 onwards, as a result of experience in the field, it became clear that the control of communicable diseases needed to be developed by means of nation-wide mass attacks, employing a large number of auxiliary health workers under the supervision of qualified physicians. Therefore, demonstration and training projects in communicable diseases gradually gave place to mass programmes, such as those for BCG vaccination, malaria control, and yaws control, in all of which WHO assisted.

Today (mid-1958) the situation is that out of 450 million people exposed to malaria, roughly 50% have been protected, and in the BCG campaign against tuberculosis, 134 million people have been tested and 46 million vaccinated. As regards yaws, by the end of

(Continued from page 13)

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1957, in the endemic areas of India, Indonesia and Thailand, 39.93 million were examined and 4.33 million treated during initial treatment surveys; during re-surveys 45.7 million was again examined and 2.31 million treated.

Pilot projects in plague, leprosy and trachoma, on the basis of which large campaigns are being planned, are also under way.

The achievements in the fight against malaria is perhaps the most spectacular example of health progress in the Region. In 1948 the vast population of this essentially rural region had virtually no protection against malaria. To-day antimalaria programmes have made sufficient headway for all countries in the Region to adopt a change in the strategy from control to eradication on the verge of becoming eradication programmes. Venereal-disease control projects are now also being carried on largely by national personnel.

It is of interest to note that today tuberculosis, which is the most important communicable disease of the Region after malaria, is no longer being tackled through demonstration and training projects but by the extensive development of domiciliary and ambulant therapy with modern drugs.

The large-scale isolation of individual cases at institutions was found completely beyond the financial and technical resources of the countries in this Region. Similarly, in leprosy control the emphasis has shifted to active case-finding and non-institutional treatment.

* * *

The training of counterpart personnel alone proved insufficient and had to be expanded to assist in training the very large numbers of workers required for mass programmes.

Simultaneously, the promotion of maternal and child health services led to the need for training nurses, midwives, health visitors and nursing auxiliaries—training in which WHO has given large-scale and increasing assistance.

The Regional Director's Annual Report in 1953 lists courses assisted by WHO staff giving training to about 1,850 nurses, midwives and nursing auxiliaries during the period under review; according to his

report for 1957-58, similar courses were given to over 3,000 such workers.

Substantial assistance has also been directed towards developing, promoting and expanding nursing and midwifery schools as well as toward providing adequate field experience for the trainees.

All these expanding programmes also needed highly qualified medical personnel in large numbers. The number available was shockingly small: for example, it is estimated that Afghanistan and Indonesia had one doctor to about 60,000 people; India, one to 6,000, and Thailand, one to 7,000.

Because of the scarcity of qualified teachers as well as the costliness of modern medical schools, progress in this vital field has remained slow, although there has been steady improvement during the past two to three years.

WHO has helped by providing professors to set up various departments in medical schools and to train counterpart staff, as well as by furnishing teaching equipment and supplies. Some help has also been given in the preparation and translation of text-books.

With the world-wide shortage of highly trained personnel, the assistance which the Regional Office has been able to render in this field has not been adequate in quantity, although much has been done to improve the quality of teaching through promoting revisions of the medical curriculum and providing field experience in urban as well as rural areas.

* * *

Recently the Regional Office has particularly promoted the establishment of full-time departments of preventive medicine and of paediatrics.

Owing to the absence of qualified teachers in preventive medicine, a special arrangement was made with the Harvard School of Public Health to train young national teachers in a specially organized public-health teachers' course lasting two years.

In addition to the assistance given to medical schools, an important project was developed jointly with UNICEF to expand and improve the activities at the All-India Institute of Hygiene and Public Health, Calcutta, for providing training in general public health, maternal and child health, public health nursing, sanitary engineering and health education.

In the past four years WHO's role has been directed more and more towards these training programmes. In 1956, in addition to training counterpart teams and organizing a very large number of training courses in different subjects, the Regional Office assisted in conducting 40 refresher courses for about 700 trainees consisting of medical officers, nurses, technicians, sanitarians and other auxiliary workers; in 1957-58, there were 50 refresher courses for 932 trainees.

The emphasis has also been shifting from individual communicable disease control towards meeting the more basic needs of the Region—for rural health services, for improvement in sanitation and for health education—and towards integrating specialized programmes into the general public health services.

During the same period, some countries of the Region, particularly India, have undertaken very large national community development programmes, for the strengthening of which assistance is being increasingly provided, especially through the development of rural health centres.

* * *

The need for reliable vital and health statistics in the Region (even today, for three out of the seven countries, it is not possible to give birth and death rates) is recognized by governments, and WHO has helped during the last few years in efforts to improve and develop statistical services.

The absence of such statistics makes it very difficult to give any pronouncement on the health of the people. Speaking generally, however, it may be said that during recent years there has been an upward trend in the birth rate and a downward trend in the death rate, while the infant mortality rate has not shown much improvement in most countries.

It is generally assumed that while death rates keep declining, morbidity continues almost unchanged. This picture is changing somewhat, as a result of the extensive malaria control programmes.

Any further substantial reduction, however, is not likely until the programme for environmental sanitation takes hold. This will still take many years.

* * *

As the awareness of positive health has increased among the populations and large amounts of

international and bilateral assistance have become available, governments are being compelled to expand their health services, to the utmost of their resources. Quantity is very often provided at the sacrifice of some quality, and the lack of adequate supervision at all levels has become a matter of grave concern.

Provision of counterpart personnel by governments has much too often been inadequate so that full use has not been made of the training possibilities provided by highly skilled WHO experts. Sometimes no counterparts at all have been provided, and in other cases, they have proved too poor to make suitable leaders.

Apart from WHO, there have been other important organizations working in the field of health in South-east Asia. Of the United Nations family, the chief one with whom WHO has worked very closely indeed is, of course, UNICEF.

Through the bilateral programme of the USA, much public health support has also been made available, of which the assistance being given to malaria control (and more recently malaria eradication) is the most noteworthy.

A large number of fellowships and a variety of experts as well as some equipment and supplies have been provided through Colombo Plan arrangements. The Rockefeller Foundation and the Ford Foundation have also substantially assisted in medical education and training.

With all these organizations the Regional Office has worked very closely in order that each should supplement the other in the promotion of the common objective of improving health in South-east Asia.

* * *

The most important achievements in the first ten years of WHO assistance may be summarized as follows:

- (1) Expansion of programmes for the control of major communicable diseases; their development into mass programmes and their gradual integration into the concurrently expanding general public health services.
- (2) Improvement of medical education generally.
- (3) Emphasis on paediatrics, especially paediatric

education, as well as the promotion of maternal and child health services, and—what is more important—the integration of these specialized services into general public health.

- (4) The establishment of departments of public health and preventive medicine, and the integration of the teaching of preventive medicine into the general curricula of medical schools.
- (5) Tremendous strides in the training of personnel, especially nursing personnel and health

auxiliaries.

- (6) Active promotion of vital and health statistics.
- (7) Promotion of health education by the training of key personnel and the demonstration of field techniques at the country level.

Perhaps the most important achievement of all, however, has been the fact that the governments in this region now look upon WHO as their natural collaborator and partner in all efforts to improve the national health services.

Orthodontists finding Teamwork is Essential

A working partnership between the orthodontist, the pediatrician and other health specialists was recommended as in "the best interests of the public" at a conference.

The proposal for closer co-operation among these groups was included in a program drawn up at the workshop in orthodontics sponsored by the University of Michigan School of Dentistry and the W. K. Kellogg Institute.

The education committee of the American Association of Orthodontics acted as adviser to the workshop, which was headed by Dr. Robert E. Moyers, Professor of Dentistry at the University.

Relationship of orthodontics to other health services was explored at the meeting panel moderated by Dr. Maynard K. Hine, Dean of the Indiana University School of Dentistry.

Participants agreed that the orthodontist, periodontist, oral surgeon, pediatrician and physician must work together more closely to insure proper care for the patients.

They recommended that medical schools institute adequate courses on the growth and development of the dento-facial complex, "with special references as to the role orthodontics plays in the physical and mental well-being of the individual."

Other recommendations included :

- Dental schools should provide a greater range of medical education ;

- Editors of journals for pediatricians and orthodontists should combine to publish articles of common interest ;

- There should be a greater exchange of information on orthodontic problems in hospitals, with orthodontists brought in for consultation on facial injuries and similar problems.

The workshop underscored the extent of the need for orthodontic services by pointing out that in the mid-west alone 60% of the children have crooked teeth or improperly formed jaws which interfere with health, speech or appearance.

For the nation as a whole, it was noted, there is a ratio of one orthodontist per 12,400 children under 18. In some areas, the ratio is one in 78,300, with no orthodontists available within a radius of 100 to 300 miles.

Of 47 dental schools, only 22 offer graduate courses in orthodontics, the workshop disclosed.

A discussion on educating the undergraduate in orthodontics brought a proposal that dental schools reconsider their teaching programs. The panel said the graduate should be able "to provide complete dental service for the child as well as the adult" and understand "the possibilities of orthodontic treatment."

Another panel recommended that the general practitioner be "adequately informed in the interception of malocclusion" and be trained to "make an appraisal of orderly growth and development."



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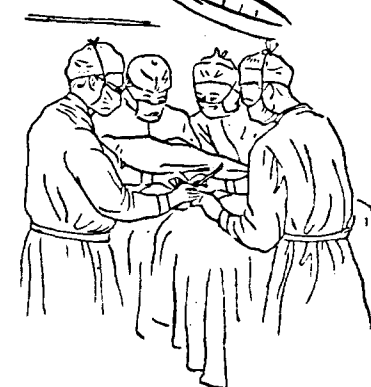
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TOM & BAY

Gastroileostomy : A Surgical pitfall : A case report

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GASTROILEOSTOMY is an erroneous, inadvertent, and an accidental surgical mistake that might have happened or may happen even in good hands, while doing gastrojejunostomy or partial gastrectomy.

Between 1915 and 1932 about 25 cases were reported in literature. Since then upto 1953 about 8 cases were reported. The first reported case was by Martin and Carroll in 1915. The last one was in 1956 by Deaver and Hopkins. Their case was 58 year old man on whom partial gastrectomy was done in May 1953. He had persistent diarrhoea, and rapid loss in weight. He lost weight heavily and was again operated in February 1954, when gastroileostomy was found, short circuiting many feet of jejunum and ileum. This was undone, end-to-end ileoileostomy and gastrojejunostomy were done. Their patient developed attacks of hypoglycemic collapse during postoperative period, and dramatically rallied round on intravenous glucose saline. He explains these postoperative hypoglycemic states due to depletion of liver glycogen or to sudden over-activity of pancreatic islet-cells on removing the gastroileal shunt.

The most recent in the literature is a case report by Haas and Ritter reported in February 1958. Their patient was a man of 63, who was done subtotal gastrectomy, and inadvertent gastroileostomy for duodenal ulcer in September 1954. He started passing loose, bulky and frequent motions, containing lot of undigested food material. He was rapidly losing in weight. Barium meal X-ray series showed rapid entry of Barium into the terminal ileum, and colon within few minutes after taking. He undid the anastomosis and did ileoileostomy, and gastrojejunostomy. Their patient recovered uneventfully.

SYMPTOMS AND SIGNS

- (1) Diarrhoea: The surgical slip may happen while doing a gastrojejunostomy, partial

gastrectomy or jejunojejunostomy after gastrojejunostomy with partial gastrectomy. The symptoms will follow operation and more marked if it is a gastrectomy. Diarrhoea may be less marked or it appears late if it is plain gastroileostomy without stomach resection. Then diarrhoea will be as marked in plain gastroileostomy as after partial gastrectomy if subsequently duodenal stenosis occurs in the ulcer. Diarrhoea is due to undigested irritating food passing almost directly into the colon.

- (2) Vomiting: has not been stressed as a prominent sign by the previous authors. It may be bilious, faecal or may contain undigested food.
- (3) Malnutrition: will rapidly develop and he begins to lose weight because of erroneous exclusion of much of the small intestine, its digestive juices, and absorption.
- (4) Dehydration: results from diarrhoea, non-absorption, vomiting, and inability to take enough by mouth.
- (5) Secondary anaemia: of hypochromic type results.
- (6) Hypoproteinaemia: results from lack of digestion, and absorption. This will be more marked after operation, as he begins to take well by mouth and digest well, after operation fluid content increases faster than protein build up. So there is relative hypoproteinaemia after operation.
- (7) Oedema: round ankles and dependent parts appears. Even though this is not present before corrective operation, will develop after operation because of relatively increased hypoproteinaemia.

- (8) Giddiness: is not at all mentioned by previous authors. May be very marked in some cases as ours.
- (9) Motion will be frequent, bulky, and contains particles of undigested food. In simple gastroileostomy the content of undigested food will be less in motion than in gastroileostomy after gastrectomy, and gastrojejunocolic fistula. In addition in gastroileostomy, and gastrojejunocolic fistula there may be air in the stomach.
- (10) Mental apathy: There will be very dull look of the patient, and he will be quite inactive.
- (11) X-ray findings: Barium rapidly appears in the terminal ileum and colon. In gastroileostomy after gastrectomy, and in gastrojejunocolic fistula there may be air in the stomach.

DIFFERENTIAL DIAGNOSIS

- (1) Gastrojejunocolic fistula: This takes some time after operation to appear as a complication. It is only this point that will help to exclude the fistula. The Barium meal X-ray will show Barium in the stomach, jejunum, and colon almost simultaneously, where as in gastroileostomy it enters the terminal ileum from the stomach, and then only proceeds to the ascending colon.
- (2) Reversed loop anastomosis (antiperistaltic anastomosis): This will have vomiting, dehydration, malnutrition, but will not have diarrhoea and X-ray findings.
- (3) Very long loop of jejunum: may produce some vomiting and may subside after some time. There will not be diarrhoea, and X-ray findings.
- (4) Very short loop: Can happen rarely after subtotal resections under general anaesthesia. Every thing including diaphragm are in a state of relaxation, and anastomosis may be made under stretch of a segment of jejunum from duodenojejunal flexure, and its mesentery. After recovery from anaesthesia it may be short producing kink at the duodenojejunal flexure, and tension on the mesentery. This may produce constant pain and vomit-

ing on taking food. This can be ruled out by the absence of characteristic diarrhoea, and X-ray findings.

- (5) Obstruction at the stoma: The girth of the jejunum is not much. People not blessed with dexterity in handling may use the whole diameter of the jejunum in invaginating with deeper bites during anastomosis. There may be pain, dyspepsia, and vomiting. Diarrhoea and X-ray findings can rule out this.
- (6) (Retrograde) jejuno gastric intus-susception: will produce pain, and vomiting. Can be excluded by the absence of diarrhoea, and characteristic X-ray findings.
- (7) Antecolic anterior gastric anastomosis: This is chosen in cases with short mesocolon, and more because of fixation of the posterior wall of the stomach either by adhesions or neoplastic infiltration. When doing an anterior gastrojejunostomy there is an inadvertent and unmindful attitude among surgeons in not sticking to the principle of keeping the loop with proximal segment towards lesser curvature, and distal arm of the loop towards the greater curvature. This may produce discomfort, fullness, and delayed emptying. Vomiting may appear in some cases.
- (8) Diarrhoea resulting after resection of long segment of small intestine must be excluded by Barium meal findings.
- (9) Diarrhoea from pancreatic disease has to be excluded by motion analysis and Barium series.

The longest history of gastroileostomy was thirty-six years, when the patient died of subsequent transurethral prostatectomy, postmortem revealed the gastroileostomy. This was the case reported by McKenzie and Robertson.

The diagnosis of gastroileostomy is made fairly easily provided it is known to happen. The characteristic diarrhoea containing undigested food particles, and X-ray appearance of Barium reaching the terminal ileum from the stomach.

Assessment of preoperative condition of the patient has to be made. Pulse, blood pressure, Red cell

count, white cell count, Serum protein, chloride, Sodium in milliequivalents, potassium in milliequivalents, Blood sugar, Blood urea, urine examination, and motion analysis are to be done.

Preoperative treatment is directed towards anaemia, hypoproteinemia, and dehydration with oral hæmatinics, proteins, blood transfusion, and intravenous glucose saline infusion.

Operation is to undo gastroileostomy, do end-to-end anastomosis of the ileum, and gastrojejunostomy.

Postoperative management is directed towards operative shock, hypoglycemic states, relative hypoproteinemia, and anasarca which may be temporary, and localised.

CASE

K. S. 40 a married male having a grown up daughter. He came to us in December 1956 with vomiting of bile and that which was taken, anorexia, diarrhoea containing particles of undigested food, and giddiness on standing.

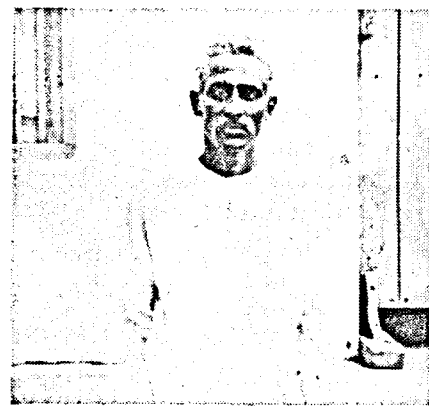


Fig. 1. Showing the patient before operation.

He was operated for what was suspected to be gastric dyspepsia in September 1955. Since then he was having these symptoms and losing in weight.

On examination we could not find anything positive to indicate an exploration. Though the Barium pictures showed Barium within few minutes in the terminal portion of the ileum, and ascending colon, it did not attract our attention. While we

were thinking all the while about gastrojejunocolic fistula, out of inability to read the appearance of pictures, and to understand the significance of the symptoms, we sent him away with medical advice much against his appreciation. He came back with all symptoms not in the least relieved, and in great desperation for an operation whatever the need, inconvenience, and risk may be.



Fig. 2. X-ray damaged by bad keeping showing Barium in the stomach, terminal ileum and colon, taken few minutes after giving Barium.



Fig. 3. X-ray (spoiled in keeping) taken 1½ hours after Barium, stomach empty, and Barium passage in the colon.

Barium meal series showed Barium in few minutes after giving in the terminal ileum, and ascending colon. The picture of gastrojejunocolic fistula was before us and we excluded other possibilities like (1) Long loop. (2) Reversed loop anastomosis, (3) Very short loop with tension on the duodenojejunal flexure, and the ligament of Trietz, (4) Stomal stenosis

by deep stitch anastomosis, (5) Jejunogastric intussusception, and (6) anterior gastrojejunostomy with proximal loop towards the greater curvature. It never occurred to us that there was a possibility of gastroileostomy because there was no previous experience of having seen it or memory of having read it.

13-9-'58. Seconal, Largactil, Pethidine and heavy spinal. Abdomen opened through upper right paramedian muscle sliding incision. There was an anastomosis. There was no gastroduodenal pathology, and rest viscera were normal to look, and feel. For a time we were puzzled when appendix and ileocaecal junction were very near the anastomosis. To confirm what we saw, we started looking down from the duodenojejunal flexure. We realised it was gastroileostomy only nine inches proximal to the ileocaecal junction. As there was no pathology active or cicatrising in the gastroduodenal area, we sectioned the ileum at the stoma, did end-to-end anastomosis of the ileum, closed the defects on the stomach with two layers of invaginating stitches, and closed the defect in the transverse mesocolon.

Postoperatively he had glucose saline for two days, and intermittent gastric aspiration for three days. With usual management it went well with him. The

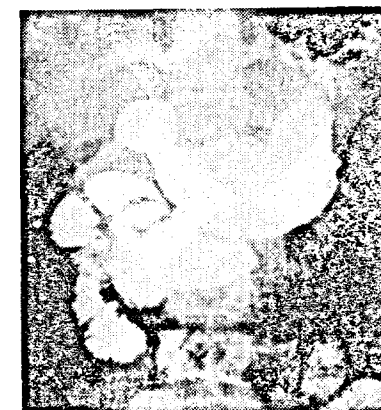


Fig. 4. X-ray taken 45 minutes after Barium showing usual passage in the gastrointestinal tract.

diet was slowly built up starting with fluids. Appetite and digestion improved; Giddiness, vomiting, and undigested food particles in motion disappeared. He developed oedema round ankles which subsided within a week with oral protein hydrolysate. He went home well.

There was no recurrence after corrective operation of either the complaints preoperative or the complications postoperative of the original operation. He joined his work as an agriculturist and is well till today. It is probably the latest in the series reported so far.

Comment: In our case the patient though could not stand up unassisted, did not lose much weight. The giddiness and vomiting were more prominent than characteristic diarrhoea, malnutrition, and dehydration. This may be due to the presence of healthy gastroduodenum. The hypoproteinemia temporarily might have increased after operation, and produced oedema round ankles. This would subside in less than a fortnight. After an operation for gastric dyspepsia if the patient develops diarrhoea, vomiting, malnutrition, and gradual loss in weight should indicate for an exploration with prior consultation with Barium X-ray series.

We thank M/S. Neptune Studio, Guntur-2 for their ungrudging and ever-ready co-operation in clinical photography.

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2. Deaver, J. M.: Gastroileostomy and its Prevention, Surg., Gynec. & Obst. 100 : 621, 1955.
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STUDY YOUNGSTERS

A pilot study of orthodontics in Burlington, Ontario, involving 1,200 children, aged three to 12 years, was described to the University of Michigan School of Dentistry workshop by Dr. Robert M. Grainger, Chief of Dental Statistics and Research, Ontario Department of Health.

The study, under the direction of Dr. Frank Popovich, was launched in 1952 with a \$125,000 grant from the Canadian government and is now half completed. It is exploring the role of heredity, congenital abnormalities, diet and disease in producing changes in facial and tooth structure.

TISSUE INCOMPATIBILITY CAN BE OVERCOME

By DR. E. DOSKACH

Moscow - U.S.S.R.

THE first All-Union Conference on Overcoming Tissue Incompatibility was held in Moscow under the auspices of the Institute of Experimental Biology of the USSR Academy of Medical Sciences. As is known, this is one of the most vital problems of medical science today which still remains unsolved.

Among the numerous reports made at the conference several of them can be united into a special group because in them are outlined the practicable means of overcoming tissue incompatibility in surgical practice.

In transplanting organs or skin from one person to another, i. e. from donor to recipient, each time the same obstacle arises: the transplanted strip of skin (or organ) takes root only temporarily and after a definite period either falls off or is resolved. It has been established long ago that this phenomenon is due to the negative reaction of the organism to the intrusion of alien protein. In response to this intrusion the recipient organism begins to produce anti-bodies. The process is similar to that which takes place in an organism subjected to morbid infection.

Some interesting experimental work was accomplished in the biology department of the Kirghiz Medical Institute headed by Prof. I. Yefimov. Although its beginning was not original, it nevertheless disclosed a definite regularity in the immunity of the recipient to the tissue of the donor, namely, the closer the relation between donor and recipient and the younger they are, the weaker is the degree of immunity. In Prof. Yefimov's experiments the greatest resistance was observed in cases of skin transplantation and the least resistance in transplanting ovaries. But even in the latter case the best results were observed when donor and recipient were in some degree related. As to skin transplantations, coalescence was observed only in the cases when the kinship between donor and recipient was very close. For instance, the ideal donors for the mother rat were its newborn young.

But the most interesting data were supplied by the second series of Prof. Yefimov's experiments because they dealt with the methods of overcoming tissue incompatibility in practice. In these experiments rats

were taken at an age when their immunity to alien tissue is particularly great (from 3 months to 2 years of age). The donors were 3 or 4 week old rats.

The recipient rat was at first narcotized, then it was injected with protein taken from the tissue of the donor. This was done with the aim of inducing tolerance to the tissue of the future donor in an organism whose reactivity is weakened during sleep. After a certain time the skin was transplanted. The strip of skin was first subjected to conservation in the cold. After the operation the recipient rat was again narcotized for the entire period during which the transplant took root. These three conditions—prolonged sleep, conservation of the transplant in the cold and preliminary introduction of the donor's protein exerted an exceptionally good influence in some of the cases. In 50 per cent of the animals the transplanted skin healed in; while in the control group the transplant altogether failed to take root.

Evidently, further improvement of this method will make it possible to utilize it successfully in the clinic.

The influence exerted by the nervous system and external conditions on the results of transplantation of organs was shown in the experiments conducted at the Medical Institute of Gorky (headed by Prof. N. P. Sinitsin). The investigators successfully solved the problem of transplanting the heart in anurans. The best effect was produced by the following method. The heart of the donor frog was extracted and kept for 5 days in an artificial nutritive medium at a low temperature (from 6 to 8°C). Before and after the operation the recipient frog was also kept in a state of prolonged narcotic sleep. As a result the donor's heart took root in 75 per cent of the cases while under ordinary conditions coalescence occurs only in 15 per cent of the cases. Prof. Sinitsin, like Prof. Yefimov, came to the conclusion that sleep therapy considerably reduces the immunity of the organism to alien tissue; besides that, it protects the central nervous system of the recipient against pathological impulses coming from the site of the operation which interfere with its successful outcome.

A new effective method of transplanting endocrine glands has been worked out in the surgical clinic of the Dnepropetrovsk Medical Institute. Prof. T. E. Gnilyorbov, Honoured Scientist of the Ukrainian SSR in the course of 10 years performed 104 homoplastic operations of this type in man.

In order to overcome tissue incompatibility he prepared the tissue for transplantation in the following way. At first all the vessels of the extracted donor's gland are washed twice with a 5 per cent solution of sodium citrate and an 0.85 per cent solution of sodium chloride. Then when the recipient's and the donor's vessels are joined the central section of the recipient's vessel, the surrounding tissues, the instruments, suturing material and the hands of the operators are also washed with sodium citrate. The observation of this rule alone, i. e. the complete sterilization of the transplant considerably increased the percentage of coalescence. The results were still better when sterility was combined with the conservation of donor's tissue in the cold at a temperature of from 2 to 4°C. (in a special conserve with the addition of glucose and penicillin solutions). Immediately

before transplanting the gland the vessels are once again washed.

Prof. Gnilyorbov's observations show that if the transplantation of the gland by means of vascular connections is repeated in the same patient good results are obtained in 100 per cent of the cases, that is, the transplanted gland always takes root well. This can be explained only by the fact that the first transplantation evidently plays the same role as the injection of the donor's protein to the recipient in Prof. Yefimov's experiments.

Thus, Gnilyorbov's methods are based on the transplantation of endocrine organs on a vascular stem only (instead of simple subcutaneous or intramuscular implantation), absolute sterility of the transplant, and preliminary conservation of the donor's tissue at temperatures of from 2 to 4°C.

The points that these three reports have in common to some extent throw light on the more promising paths along which searches for means of overcoming tissue incompatibility in surgical practice should be conducted.

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FAMILY PLANNING

BY DR. B. B. RAI, M.B., B.S., O.B., St. J.

Medical Officer, Incharge Government T. B. Clinic, Bareilly, U. P. (India)

INTRODUCTION

THE day is long behind us when the traditional sentimentalism of grand-pas and grannies in India measured the blessings of Providence in terms of the number of children in a family. The old Biblical injunction 'increase and multiply' or the benediction on him 'who hath his quiver full of arrows' have lost their value and validity in the complex and strained economy of the modern world. The accelerated pace of the growth of population without proportionate development in the means and resources to sustain it have ushered in an era of ration and controls. India is no exception.

Family Planning is today an imperative necessity in our country—particularly in view of the economic poverty of the lower and middle income groups. The Secretary General of the Indian Census Commission 1951, stated that more than three children in a house constituted improvident maternity. The situation has, if anything, worsened since then, and plethora of children in present conditions economic and physical, are not only a heavy drain on a family but a national liability. Indeed today the cruel paradox is that the poorer families breed larger number of children and in consequence suffer the greater misfortune.

To censure the continued virility and happiness of the nation, rationalisation of family life in the sphere of maternity, through effective checks and control of child-birth by scientific and other methods, has become essential. Family Planning is intended to achieve this end.

The Planning Commission of the Government of India formulated a family planning programme, the main object of which have been laid down as follows:—

1. To obtain an accurate picture of factors contributory to the rapid increase of population in India.
2. To discover suitable techniques of family

planning and devise methods by which knowledge of these techniques can be widely disseminated.

3. To make advice on Family Planning an integral part of service in Government Hospitals and Public Health Agencies.

Out of Rs. 497 lakh, Rs. 400 lakh in the Central Sector and Rs. 97 lakh in the States Sector—provided for family planning in the Second Plan, Rs. 373.25 lakh are for family planning clinics, Rs. 15.75 lakh for training, Rs. 50 lakh for education, Rs. 50 lakh for research and Rs. 8 lakh for Central Organisations. About 2500 family planning clinics—2000 in rural and 500 in urban areas will be opened during the Plan period. Out of the Plan target of family planning clinics, 300 in rural and urban areas were to have been opened by the State Government by March 1958.

Besides, a high power Family Planning Board has been set up at the Centre to formulate comprehensive Planning Programmes. Family Planning Boards are also functioning in no less than 10 States of India, including U. P. The States of Andhra, Assam, Bihar, Madras, Mysore, Punjab, Rajasthan maintain full-time Family Planning Officers. Training in the technique of Family Planning is imparted at the Family Planning and Research Centre at Bombay, the Family Planning, Training Demonstration and Experimental Centre at Ramnagar (Mysore), and the All India Institute of Hygiene and Public Health at Calcutta. Public Education on the subject is being carried on with the help of pamphlets, posters, films, exhibitions etc.

RESEARCH

Important Research on contraceptives is being carried on at the Contraceptive Testing Unit, Indian Cancer Research Centre, Bombay, The All India Institute of Hygiene and Public Health, Calcutta and Pharmacology Department, University of Lucknow. Suitable contraceptives are recommended for use in the Family Planning Clinics after being

properly tested at the contraceptive Testing Unit of the Indian Cancer Research Institute, Bombay.

PRACTICAL ASPECTS OF FAMILY PLANNING

Not many people, understand the full connotation of Family Planning. It means how a husband with his wife should plan his family, so that maximum food and other necessities are obtained not only for the family but also for the Society and the Country. The subject includes such questions as when should the first child be born, when should the next come, what should be the age of differences and how many children should there be altogether, upto what age should children be born, and what should be done to restrict the number and what should be done if no child is born to a pair within 2, 3 years of the married life.

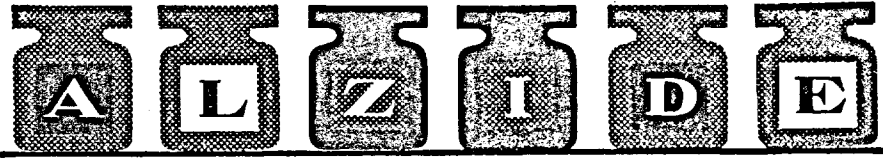
WHEN SHOULD THE FIRST CHILD BE BORN?

It is very difficult question to answer. Much depends on individual circumstances but certain principles can be laid down. Economical, social,

Physical and other circumstances being normal it would be desirable to have the first child within a very short space of time after the marriage. This would infuse new life of love between the husband and wife, because the child becomes the centre of attraction for both. This will also be a great economic help to the family, as the child will become an earning member of the family long before the father gets too old to earn. If the first child is not born within 2 or 3 years of the marriage or it takes a longer time, the birth becomes very trouble-some and even dangerous when the age advances. It is desirable therefore to have the first child soon after the marriage. If a pair is unable to produce a child within 2 or 3 years of the marriage the reasons should be found out with the help of an expert Physician, so that proper treatment can be given to remedy the defects.

HOW MANY CHILDREN SHOULD BE BORN?

Taking into consideration the present difficulties, including the high cost of food and education, it would be enough to have not more than 3 or 4 children altogether for a couple.



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EVEREST

WHEN SHOULD THE LAST CHILD BE BORN ?

This is a very important question.

It is often seen that children are born to parents of 50 or 60 years of age. This results in the father/mother dying when the child is only a few years old and he has to be looked after by the elder brothers making them economically decrepit to bear the burden. It is desirable, therefore, that the last child be born at such an age that he is fully grown up, when the parents are 50 or 60 years of age. This means that the last child should be born when the parents are about 35 or 40 years. Moreover, if children are to be born when the parents are say, 25 years, there will be about 4 children by the time they reach the age of 35 or 40 years. Therefore, attempts should then be made to avoid child birth, by all possible means.

UNDER WHAT CONDITIONS SHOULD CONTROL BE EXERCISED ON CHILD BIRTH ?

This question hardly arises in cases where the couple is healthy of course, when one or both of them suffer from diseases such as heart, high blood pressure, kidney, T. B. It is extremely important that child birth should be restricted. However, this restriction must be enforced in cases where pregnancy is a danger to the life of the mother. In cases where one of the couple suffers from a disease which is likely to effect the child, it is necessary not to produce any child. It is always better to have no child, rather than to have a child suffering such a disease as syphilis, etc. which are hereditary.

NON-PRODUCTIVITY OF CHILDREN

This is a cognate subject with family planning. If a child is not produced within a reasonable period after marriage, attempts must be made to find out the causes and to have proper medical treatment. Production of children is a necessity, in the same way as the restriction of the number of children which are both in the interest of the family and society.

METHODS OF FAMILY PLANNING

While people in general agree that there is need for family planning, there is a difference of opinion as to the methods which should be used. Some people advocate marriage at an advanced age while others

consider that celibacy is the only sure way, and that tax should be imposed by the Government on persons having a larger number of children over a legally prescribed quota. Scientists and medical men regard the various artificial methods, quite sufficient. It is therefore difficult for an average person to decide for himself what is the best course to follow :—

MARRIAGE AT ADVANCED AGE

The protagonists of this theory consider that ability of a woman to produce children decreases with the advancing age. The rate of child-birth between the age of 20 or 25 decreases afterwards and this has been corroborated from the available statistics. We have, however, to see whether this practice can solve the problem of Family Planning of each individual. It is possible that the statistics produced may not be quite correct because apart from the age factor, there may be other which may be responsible for a decrease in birth rate as the age of female advances. There are certain other factors, which make this method totally unsuitable. It is accepted all round that the rate of mortality among mothers is higher in cases where the first child is born at an advanced age or at least labour pains are severe and sometimes act not only dangerous but also fatal. Moreover to delay marriages beyond 20 or 25 years of age, may produce undesirable results, mental and physical, and thus the practice of advanced age marriage may delay production of children for sometime but certainly cannot solve the problem of spacing 'Family Planning'. It is desirable that normally a pair should produce the first and second child with a proper spacing of at least 2 years as soon as possible. There after they should plan future 'child births' according to their views and necessity.

BRAHMACHARYA

Leaders of thought, Social or religious reformers in India preach this as the most effective method of preventing over-production. While in theory this is the surest method, from the practical point of view it is not only difficult but also well nigh impossible to observe strict celibacy as even one meeting in a year, may result in conception. While Brahmacharya is very desirable for the satisfaction of Physical and mental needs it cannot from the practical point of view serve as the only means of successful family planning.

LEGAL ASPECT

Some people suggest that some sort of a tax or penal punishment on production of children over a fixed maximum should be imposed by law. We do not regard it as desirable because there is hell of trouble against such a tax or punishment without taking the public in confidence or even without educating the public on this subject.

SCIENTIFIC CONTRACEPTIVES

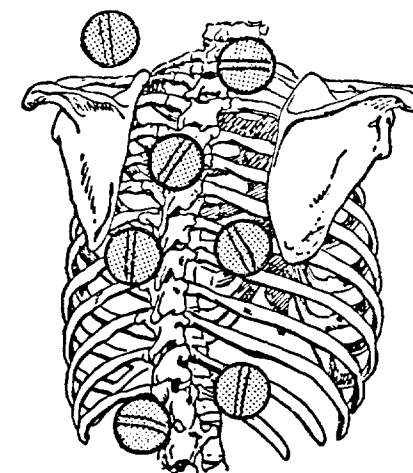
There are at least 2 or 3 methods by which conception can be checked, without either effecting adversely, the health of the couple or producing any other 'after effects.' One is the use of chemical preparation which kills the spermatozoa before entering the ova, and the other is the use of scientific rubber appliances. Another largely successful method is the strict observance of the 'Safer Period.' These methods appear to be dependable, successful and easy and we are of the opinion that they should be used until other methods have been found to be more

(Continued on page 30)

successful by the scientists.

OBJECTIONS AGAINST THE USE OF CONTRACEPTIVES

Opposition to contraceptives is based on irrational prejudice of conservative elements of Society or on religious grounds. The man of religion, who can still powerfully appeal to the religious susceptibilities of the superstitious and gullible masses of India, brands the use of contraceptive methods of birth control as an act of sin which is tabooed by the ancient scriptures. But the Passage of time ultimately sanctifies the usages and customs which arise in response to the challenge of a new age and so the heresy of one generation becomes the orthodoxy of the other. The exigencies of life in modern conditions require a reorientation in our attitude and approach to this problem in order to ensure our survival. Contraception and other scientific devices may appear heterodox today but the blessings they will confer will sanctify them in due course. Religious dogmas and creeds have to be redefined, revalued in the context of the



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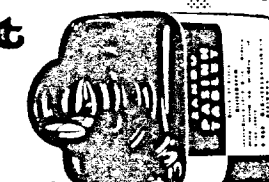
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Graphic 224

Recent Developments in the Surgical Treatment of Carpal Scaphoid Fractures

BY DR. HENRY BURLINGTON, M.D.

Bethlehem, Pennsylvania
from
St. Luke's Hospital, Bethlehem, Pennsylvania

FRACTURES of the carpal scaphoid continue to present, rather frequently, somewhat difficult problems in management. Three rather recently developed new surgical techniques appear to be quite promising, apparently representing fairly definite improvements over previous methods.

There are many reasons why the carpal scaphoid fracture ranks second only to the femoral neck fracture as a common problem in management. To begin with, the fracture frequently gives rise to rather minimal symptoms at the time of the original injury, so that it is not unusual for it to be considered as a minor sprain by the patient, and even by his physician. The injury commonly is not felt worth the trouble of x-ray investigation, and in fact the fracture is not at all

uncommonly missed even when x-rays have been taken. Diagnosis is therefore frequently made rather late, understandably leading to unsatisfactory end results in many cases.

In addition, even the promptly treated fracture can be quite difficult. A good many of these fractures are completely undisplaced, and if immobilized early will go on to prompt union within a matter of four to six weeks. More often, however, the fracture is displaced, in which case ordinary plaster immobilization frequently must be continued for many weeks, often twelve or sixteen, before there is definite evidence of union. It is difficult to secure complete immobilization of the scaphoid with plaster, and this undoubtedly is one reason for slow healing in displaced unstable fractures.

(Continued from page 29)

changing pattern of society and a rigid interpretation or an adherence to them results in stagnation or decay. Dharma must sustain society and the use of scientific methods of birth control is our 'Dharma' today.

FINALLY A FEW WORDS ABOUT 'CONTRACEPTIVES'

An ideal contraceptive is one that is safe, reliable, easily available, acceptable (from the asthetic, cultural, moral and religious point of view) and cheap.

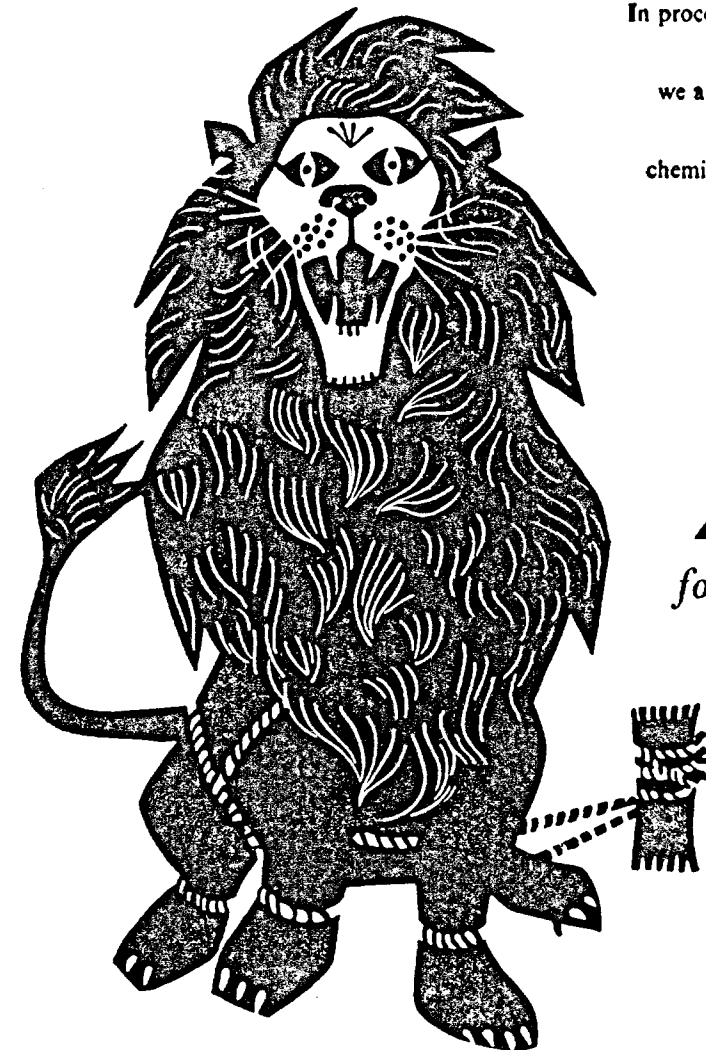
Under this sponge and foam powder (foam tablets) are commonly used. Previously sponge with gingelly oil was used, but unfortunately this was found not very favourable and acceptable. The foam powder has been found more popular. The sponge is made of very soft scrap rubber, about 2" square with eighth-inch long thin silk thread at one end. It is easily inserted (before retiring or before intimacy) and pulled out with the aid of the string after 8 hours' intimacy. The sponge can be washed with soap and warm water and is usually good for many exposures. It is given

free and mothers can have as many as they want. The foam powder which is sprinkled on it, keeps over long periods under air-tight containers.

It is absolutely necessary to find out an ideal contraceptive which should be something simpler and when used once only will be effective for enormous exposures over a period of weeks or months. Majority of women are keen to have an injection, a mixture or a pill which could be easily taken to provide immunity over a longer period of time. If a much talked of oral contraceptive is perfected, "The Family Planning Programme" will be a success.

The final conclusion is submitted with considerable reserve. Under Socio-Economic and cultural conditions prevailing in India, especially in its villages, the easier and more effective way out of the problems seems to be either vasectomy or salpingectomy. Of these two surgical methods of permanent 'conception control', the first is rather easy and handy and should be given widest publicity and promoted on a large scale.

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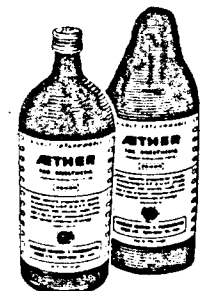
Prior to the middle of the 19th Century the fully conscious patient was either tied securely with ropes to prevent his escaping the surgeon's knife or made unconscious with blows on the head or deadened with harmful narcotics.

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In addition, this is one of the commoner sites of avascular necrosis following fracture. The proximal fragment frequently has a meager blood supply, and if the fragment be small, the blood supply may be completely interrupted at the time of fracture. This is particularly prone to occur in cases which are treated late, or treated inadequately, but happens also even with prompt, proper, prolonged immobilization in a distressingly frequent number of cases.

The patients very commonly are young, often either athletes or young manual workers, and a chronically painful wrist in such a person represents a fairly serious disability.

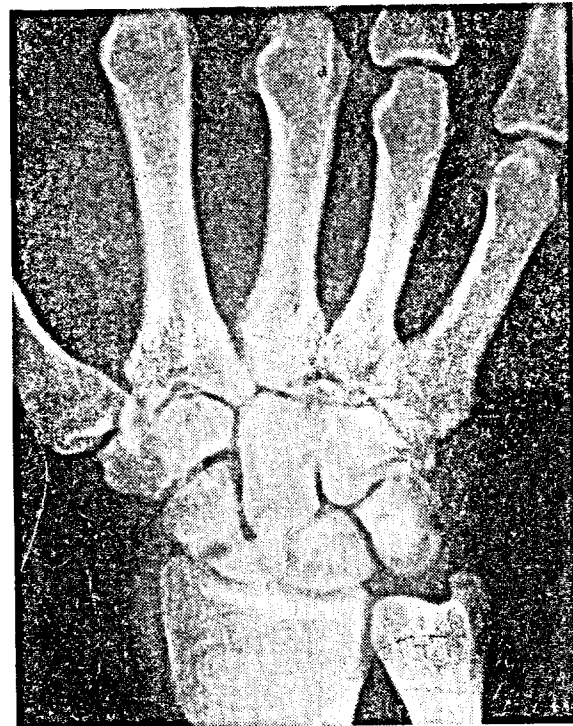
STANDARD SURGICAL PROCEDURES

In the past, it has been considered that surgical intervention was indicated when there was clearcut evidence of either established non-union, or avascular necrosis of the proximal fragment. Many procedures have been attempted in the past for the correction of either or both of these complications, but only a few have stood the test of time.

Insertion of a bone graft across the fracture site is a recognised and acceptable surgical procedure, which has been used with a fair amount of success in the treatment of non-union. It is frequently a technically difficult procedure. It requires a minimum period of post-operative plaster immobilization of approximately two and one-half months, and frequently longer. It is of no value in cases of avascular necrosis. Complete failure of the procedure is not uncommon, probably only about eighty per cent of cases going on to satisfactory clinical results.

In cases of avascular necrosis of the proximal fragment, it has been common surgical practice to simply excise the necrotic fragment. If this represents a relatively small fraction of the mass of the bone, and particularly if it carries with it only a small fraction of the proximal articulating surface, simple excision of the avascular fragment may be extremely successful. If however the fragment comprises one-third or more of the bone, simple excision usually does not give a completely asymptomatic wrist.

Excision of the entire navicular has been attempted, and is sometimes successful. However, many authors have become discouraged with it, and report nearly fifty per cent of these cases as being completely unsatisfactory.



Patient L.W., delayed diagnosis. Displaced, unstable fracture, several weeks old at time of treatment.



Patient L.W., following open reduction and internal fixation with McLaughlin screw.

Excision of the entire proximal row of carpal bones has been used occasionally for non-union of the scaphoid, or for avascular necrosis. It is a procedure which probably is sometimes indicated, especially if the navicular injury is associated with dislocation or other injury to the lunate. Following proximal carpal row excision, the wrist usually is pain-free, but unfortunately there is usually some considerable weakness in the grip, and function is imperfect.

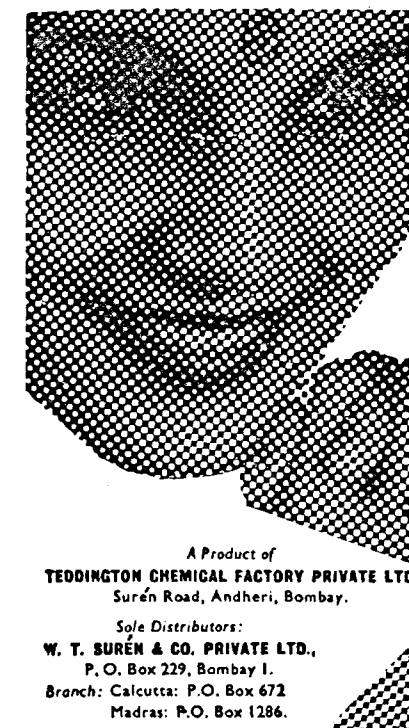
An older procedure of simply drilling across the site of non-union has been largely abandoned, due to the extremely high rate of unsatisfactory results.

NEWER SURGICAL PROCEDURES

McLaughlin (1) in 1954 reported on the use of an especially designed lag screw used for open reduction and internal fixation of scaphoid fractures. He reported the use of this device in a fairly large series of cases, with a very satisfactory incidence of prompt union. He considered the screw to be indicated in fresh displaced unstable fractures, and in cases of delayed union without avascular necrosis. It can be

argued that fresh displaced unstable fractures will go on to union with simple plaster immobilization if this is continued over a prolonged period of time, and that surgery is not indicated for such cases. However, the screw obviates the need for plaster immobilization, which in these cases can frequently keep a working man away from his job over a rather prolonged period of time. A person who does relatively light work with his hands can return to work within a matter of two to three weeks after surgery if good firm internal fixation has been secured.

This procedure has now been used in a large number of cases by a great many men, and is generally accepted as being a very useful means of treatment. Technically, it is not an easy procedure, since proper placement of the screw is essential and complete visualization of the fracture undesirable. It is important not to strip away soft tissues, particularly from the proximal fragment, any more than absolutely necessary, so that good x-ray control is essential. With the single drawback of technical difficulty, the procedure will almost certainly become a standard one.



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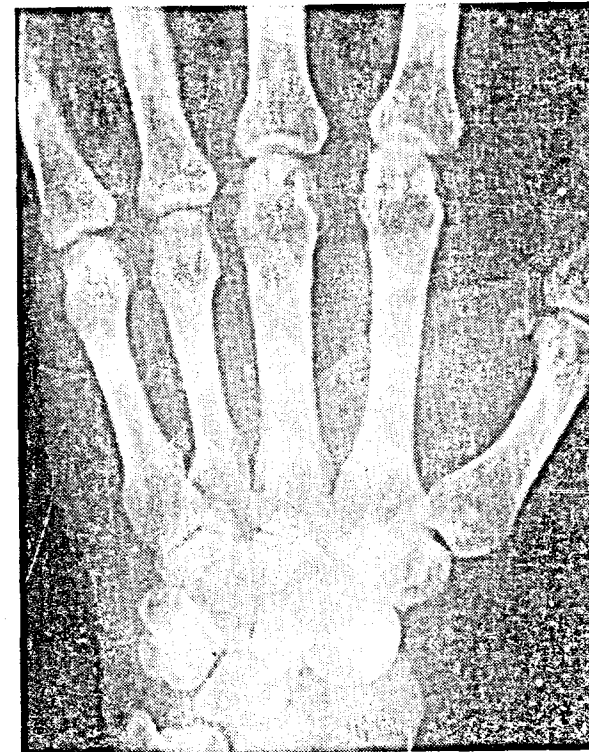
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Patient L.B., Avascular necrosis of both the proximal and distal fragments, following unsuccessful attempt at internal fixation.

Legge (2), in 1951 reported on the use of a spherical vitallium replacement prosthesis for the carpal navicular. The device is a simple polished vitallium sphere, available in an assortment of sizes, which can be used to replace the entire navicular, and forms a very stable prosthesis between the radio-carpal joint and the proximal surface of the greater multangular bone. We have used the device several times, always for the treatment of avascular necrosis. The entire navicular, both proximal and distal fragments, is excised, and the prosthesis inserted. The wound is closed, and the wrist immobilized for a period of two to three weeks for soft tissue healing. We have been impressed with the procedure as being a technically relatively easy one, and one which appears to produce uniformly very satisfactory results. We do not feel that its use is indicated in the treatment of non-union, but it seems to be the most satisfactory approach that we have in the treatment of avascular necrosis. We have not been too greatly impressed with the use of prosthetic replacement in other areas, especially in so-called replacement arthroplasty of the hip. We feel that in the hip, prosthetic devices have a very limited legitimate use. Few hips so treated



Patient L.B., following excision of both fragments, and replacement with spherical vitallium prosthesis. Patient returned to work four weeks post-operatively, as a railroad brakeman. Three years post-operatively, he reports the wrist completely free of symptoms. There is about thirty-five per cent restriction of motion in extension, other motions being full and free.

become asymptomatic. The navicular prosthesis, on the other hand, has in our hands always yielded a wrist that was strong, completely pain-free, and abnormal only because of moderate limitation of motion in extension. This latter factor is rarely considered by the patient to be of any importance.

In 1952, Helfet (3) submitted a preliminary report on a new procedure for the treatment of non-union. His operation consists of arthrodesing both the proximal and distal fragments of the scaphoid to the adjacent capitate. This, in effect, amounts to the use of the capitate bone as an onlay graft in treating the fracture. This procedure may obviate some of the difficulties previously encountered in the usual inlay type of peg grafting. The procedure is an interesting one, and may prove to be very valuable. It has not been used in a great number of cases, and has not yet been used by very many men, so that it is as yet too early to assess it as a routine procedure. It would seem likely, however, that a procedure of this type

can be expected to give at least as good results as the somewhat more difficult procedure of inlay grafting. Should this procedure prove to yield a higher percentage of satisfactory cases, then it may very well become a standard item in the treatment of non-union.

It would be well to mention also the use of radio-carpal arthrodesis as a salvage procedure in difficult cases. This is of course not a new procedure, but it is one that can be resorted to when everything else seems to fail. In addition, it is especially useful in old delayed cases in which considerable destructive arthritis of the radio-carpal articulation has developed. The arthrodesis is a relatively easy one technically, and yields a high percentage of cases with solid union. It does of course produce a completely stiff wrist, which in certain occupations would be somewhat disabling.

The most important factor in the handling of this problem remains early diagnosis and treatment, with

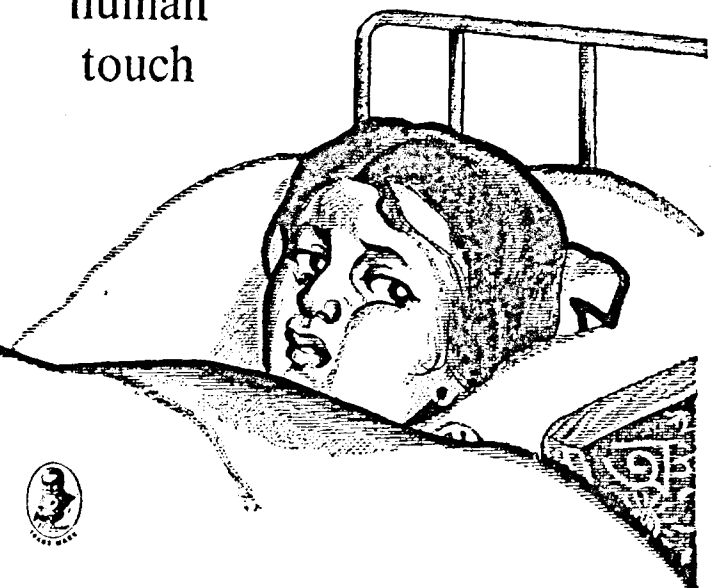
plaster immobilization being satisfactory in the overwhelming majority of cases treated early. "Sprained" wrists should routinely be x-rayed, even if the symptoms and physical findings are rather minimal. A high index of suspicion will lead to earlier diagnosis, and will obviate in large part the need for surgical intervention.

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SURGERY OF BRAIN TUMOURS

(From the Practice of the Leningrad Surgical Institute)

BY DR. I. S. BABCHIN

Leningrad, U.S.S.R.

PRACTICAL experience of the A. L. Polenov Neurosurgical Institute of Leningrad in surgery of the brain tumours is based upon analysis and generalization of statistical data, concerning clinical treatment of 2,836 patients during 30 years of the Institute's work.

Surgery of brain tumours at the Institute, as well as in neurosurgery in general, developed unevenly. It started with operations of tumours which are easily recognized, i. e. with those of the posterior cranial fossa and hypophyseal portion of the brain. Tumours of the cerebral hemispheres which are the most difficult for diagnosis and approach were the last in which surgical treatment was applied.

In the development of surgery of brain tumours the Leningrad school of neurosurgery went through the following periods: I period—the search of independent routes of its development (during the early twenties, the period after the revolution and the civil war); II period—the process of its setting up and stabilization on the basis of personal experience and the study of practical experience of world neurosurgery (the thirties, pre-war period); and the III period of wide development of the modern neurooncology with more profound study of previously almost inaccessible brain portions, those located deeply in the brain tissue, in the ventricles and stem tumours (post-war period).

In surgical treatment of 869 patients with tumours of the posterior cranial fossa, the Institute has acquired experience in surgical skill which was difficult to gain, but very useful. The Institute was one of the first in our country (A. L. Polenov since 1921) to commence systematic operations of tumours of pontocerebellar angle, of cerebellum and of the fourth ventricle. The first period (before 1925) was characterized by primitive pre-Cushing technique. The operation was carried out in 2 stages under general anaesthesia and with maximal radicalism (extracapsular enucleation of neurinomas of the VIII

nerve), associated with extremely high mortality rate. The II period (which began in 1926) was characterized by the study and spread of the classical Cushing's single-staged operative technique with puncture of the lateral ventricle during the operation and by refusal from surgical dangerous radicalism (intracapsular excochleation of neurinoma) with the following improvement and simplification of his cross-bow incision (aponeurotic muscular border and festoon according to Polenov in 1931, semicross-bow and small cross-bow incisions in 1938) which reduced the mortality rate by almost 66.7 per cent. The III period is characterized by gradual simplification of operative approach, development of rational radicalism with prophylaxis of post-operative complications.

The median vertical incision which is recommended by the Institute for the past 15 years, was improved by creation of muscular-aponeurotic rhombus (1941) and advanced surgery of tumours of the posterior cranial fossa to the periphery. Thus, this fossa became approachable for practising neurosurgeons of the Soviet Union.

Further contribution of the Institute to the surgery of tumours of the posterior cranial fossa consisted in the following: a) description of the new röntgenological symptom of the occipital bone (1941), b) introduction of tension relieving ventricular punctures with prolonged drainage of the lateral ventricle by a blunt needle during 24—48 hours (1941). These punctures were performed in patients in serious condition before the operation for combating hypertensional-hydrocephalic crises, c) development of an operative technique of subtotal removal of neurinoma of acoustic nerve, including a part of the capsule (1949), d) improvement of diagnosis and surgery of the arachnoidendotheliomas of the posterior cranial fossa (1953).

In view of surgical treatment of 265 patients with tumours of hypophysis the Institute deserves the merit of introduction of systematic operations of

such tumours in our country. The Institute, likewise, showed the advantages of intracranial method and intradural approach to adenomas of hypophysis (1931), developed the operative approaches to the area of cella turcica and chiasma (frontal, frontal-temporal). Luminous spatula was introduced into practice for the first time in the Soviet Union also by the Institute. The method of aspiration of adenomas of hypophysis and cystic craniopharyngiomas (1932), the technique of partial resection of the frontal lobe in large olfactory meningiomas and those above the cella (1937) and surgical treatment of craniopharyngiomas in conjunction with X-ray therapy (1952)—all these surgical interventions were developed at the Institute. The diagnosis and surgery of basal arachnoidendotheliomas were particularly studied after the war.

Tumours of the cerebral hemispheres constitute more than one half of all the tumours of the brain and were revealed in 1450 patients at the Institute. Retarded development of surgical treatment of these tumours is due to: a) unfavourable intrahemispheric and intraventricular localization of these tumours (in 2/3 of the cases) with prevalence of infiltrative malignant gliomas, angioreticulomas and cancer metastases, b) difficult approach in basal and parasagittal localization of most of the extrahemispheric meningiomas (arachnoidendotheliomas), which are intimately connected with the venous meningeal sinuses, c) late diagnosis with grave general state of inoperable patients with large tumours, which it is impossible to remove.

At the Institute the fundamental stages of development of surgery of tumours of cerebral hemispheres were intimately connected with improvement of the methods of their diagnosis (M. P. Mikitin, L. V. Blumenau, M. I. Astvatsaturov, I. Ya. Razdolsky) and pathomorphology (V. M. Gakkal, A. A. Vasiliev). These stages were manifested by: a) the gradual transfer from general anaesthesia during the first period to the local anaesthesia during the second period and to different combinations of these methods during the third period; b) by continuous search of operative techniques with minimal haemorrhage; by combating haemorrhage during operation (biological swabs, electro-coagulation, clamps); c) by introduction and improvement of prophylactic measures during surgical operations by intravenous drop

injections of anti-shock, tonic, dehydrating solutions or blood; d) by choosing larger and less traumatic operative approaches instead of narrow and tight; e) in individual decision in each case, whether to perform one or two stage operation; f) in gradual development of radicalism in antitlastic surgery; in further development of indications and technique of radical and subtotal excision of tumours; g) in constant provision of sufficient decompression of the brain even in comparatively radical removal of tumours. Surgeons gradually gained proficiency in fundamental and principal operative methods of removing tumours of cerebral hemispheres. The results of treatment correspondingly improved and the lethality rate went down.

The problem which is awaiting solution next, still remains to be the surgery of intrahemispheric and intraventricular tumours with infiltrative, malignant and recurring growth, including cancer metastases. The factors which will aid in the successful solution of

(Continued on page 38)

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The Patient's Reaction To Pulmonary Tuberculosis

By DR. L. C. BHANDARI, M.A., Ph.D.(Lond.)

Associate Member, British Psycho-analytical Society ; Associate British Psychological Society ;
Foreign Affiliate American Psychological Association.

NOTWITHSTANDING the fact that Pulmonary tuberculosis has been so far to all intents and purposes regarded as a truly organic disease, brought about by the infection caused by the specific micro-organism—tubercle bacillus—the reaction of the patients who suffer from this disease is by no means uniform. From the psychological viewpoint, the patient's reaction to any illness, whether organic or emotional, is determined by his personality make-up formed by his constitution and emotional experiences. In view of this each patient reacts to the onset of illness in a characteristic manner, on the basis of his particular personality constellation.

Taking a broad sampling of the tuberculous patients, it may be possible to choose three representative personality types, which may be classed as, (1) The Complaining—Insecure Type; (2) The Rebellious Type; (3) The Self-driving Type. A study of these three types in relation to their reaction to illness shows the fact that how greatly the previous personality of the patients determine the reaction they have to their disease.

(1) *The Complaining—Insecure Type* :— The

patients belonging to this type may be further subdivided into three categories, namely, i) The Over—dependent type; ii) The Leaning type; iii) The Asserters of independence type.

(i) *The Over-dependent type*. Lacking in their personality resources of self-reliance and personal initiative, when this type of patients fall ill they like to be pampered and spoilt by others. Notwithstanding the terrific shock which they receive on learning that they suffer from tuberculosis, greatest measure of frustration comes to them from the curtailment of pleasures of everyday living which this disease inevitably entails. On the basis of their personality characteristics of passive dependence self-centredness and exaggerated self-love, they either show a reaction of hypochondriacal anxiety or hysterical emotionalism. In whatever activity they engage themselves, they always have the harrassing fear that it might have an aggravating effect on their health. Thus they become excessively introspective and ruminative. A patient belonging to this type remarked "Every pleasure is a bitter sweet. When you are playing a game, having a drink or kissing a girl you wonder whether that is right." Illness in this way becomes a

(Continued from page 37)

this problem are: a) further improvement of the methods of early diagnosis and more precise localization of these tumours with employment of modern auxiliary methods, such as X-ray diagnosis, electrophysiological methods and isotopodiagnosis; b) to distinguish among the intrahemispheric tumours those which can be approached for radical or subtotal removal; c) further development of trans-cerebral approaches to intrahemispheric and intraventricular tumours; d) improvement and wider use of combined methods, i. e. of antiblastic surgery with radiation, hormonal and drug-therapy.

The Institute deserves the merit of commencing the systematic operations of brain tumours in children since 1929. Specific features and difficulty of children's neurooncology were taken into consideration and systematic analysis of data, concerning these

operations is carried out since 1941. Achievements in surgical treatment of 508 children with brain tumours are due to: a) the study of characteristic features of the growing child's organism, his brain and cranium; b) the careful operative technique, without blood loss; d) rational radicalism; e) wide use of X-ray therapy in inoperable malignant gliomas and tumours of the circulatory system (1941, 1955).

Recently the surgery of brain tumours entered the fourth period of its development. This period is characterized by the introduction of modern auxiliary methods of diagnosis and by radical antiblastic surgery in connection with modern therapy. Combined method of anaesthesia with employment of artificial vascular hypotonia reveals tempting perspectives in this most complex field of brain surgery.

plausible excuse for these patients for avoiding any form of physical and mental exertion, thereby surrendering to complete dependence. When they are admitted to the sanatorium its environment becomes a safe haven and refuge from the cares and worries of the world, where all their primary wants to be protected and looked after shall be attended to by the doctors and nurses. In other words, psychologically, they begin to show behaviour characteristics of helpless and dependent children, who seek protection and love from their parents in the persons of the members of the staff of the sanatorium. As long as they remain in the protective shell of the sanatorium they take life easily and do not seem to be particularly disturbed by the fact that they suffer from a grave disease like tuberculosis. They take the gravity or seriousness of their illness with a child-like naivete and feeling of unconcern so long as they can be comfortably spoonfed by others.

The initial reaction to illness of these patients is usually one of great emotional shock and mental perturbation, but they soon settle down when all the requirements of their personality to be indulged in and

fussed about are met by others.

We may quote here the case of a patient for whom to suffer from tuberculosis was not so disturbing so long as she was sure of the support and love of her relations. She remarked at the time her illness started "When I knew 'this', I screamed at my mother 'you told me I was all right'. At the same time I cried around my aunt's neck. I did not know how serious it was.... They think you die of it and I got out of my business, I was glad in that way. When my husband came home he took it very well. Then I was all right and it did not worry me any more."

(ii) *The Leaning type*.

The patients belonging to this category usually show close affinity in their personality make-up to the over-dependent individuals. They too feel the curtailment in the pleasures and the enjoyment of living as the most serious effect of the illness. They bemoan the sense of loss they feel by becoming tuberculous; for no longer they think they will be able to lead the type

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of lives they used to prior to the onset of their illness. Thus one patient conveyed his strong feeling of frustration and bitterness, since his illness started, by remarking that "I feel like a dog on a chain; Chained down, I am determined to get well."

Since the motives of pleasure and enjoyment remain uppermost in the minds of these patients, they take to bed at the earliest opportunity when things go wrong, and do not protest against staying in hospital so long they can entertain the hope that medical regimentation and discipline enforced upon them would ultimately enable them to lead lives of ease and freedom.

In their reaction to illness these patients show the same type of exaggerated self-concern and hypochondriacal anxiety, which characterize the over-dependent patients.

In one respect, however, they show a particular personality reaction, which distinguishes them from the over-dependent type, namely, their over-whelming fear of social ostracism and danger of infecting others.

Psychodynamically speaking, this anxiety becomes understandable, because these patients owing to their overwhelming need for love and support think that to suffer from tuberculosis involves the risk of being rejected and discarded by others. They usually voice their feelings of insecurity in such phrases as "No one seems to want you with this illness", "You do not want to look different."

(iii) The Asserters of Independence Type

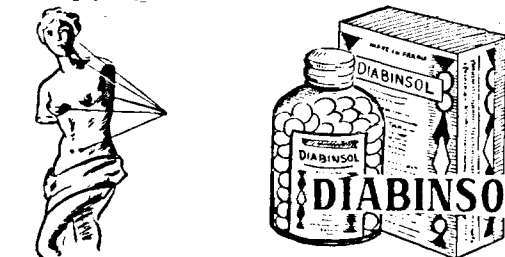
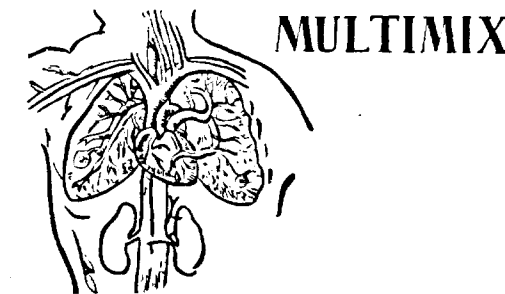
While studying the reaction to illness of these patients, who pose themselves as self-sufficient and independent of the support of others, one is particularly struck by the fact that outwardly, though they make a determined effort to get well and not to worry about their illness, inwardly they remain passive and dependent like the previous two types. The initial reaction of these patients, too, like that of other patients is one of anxiety and depression, but they attempt to put up a bold face to this anxiety provoking situation, and show a facade of resignation and unconcern. In order to ward off the underlying anxiety and depression they keep themselves continually busy and put up a barrier of defensive over-activity. To some, however, illness comes as an

undisguised blessing, for it solves for them problem with which they had previously remained pre-occupied, but for which they could not find any solution. It caters to their inward need to be dependent and loved which they do not wish to outwardly admit, while it serves as a face-saving device in a situation in which they rely on the help and attention of others.

II. The Rebellious Type

The patients belonging to this type are generally defiant of all forms of external restriction and authority, for they take the view that their illness is their own affair. They feel confident that they are able to take care of themselves, and have not to depend upon others. They usually say that illness does not worry them and hence they do not much think about it. Thus they seem to maintain a casual and carefree attitude towards the disease. Behind this front of lack of concern and defensive cheerfulness, they continue to be critical and hostile to their environment. They do not put much faith in the treatment and intention to help on the part of the doctors and nurses. Rather they evolve their own theories as to what would suit them best in the treatment of the disease; and that authorities should follow a specific therapeutic regimen as dictated by them. A patient of this type said, "I used to get medical dictionaries. I got knowledge about X-Ray. Read medical books. I found that surgical treatment for this complaint is hopeless. I believe that fresh air, light nourishing food, about two years' good conditions, no worry, a trained staff—knowing that we are pernickety—that is the treatment I would like to have." He further added, "I do not mind drugs; but no surgical treatment. I believe that once the lungs are touched with surgical treatment, there are always complications, even death. I saw about 300 die with this complaint, mostly 'a. P.' (artificial pneumothorax). I have never seen a good 'a. P.'"

In conformity with their personality traits of suspiciousness and latent hostility against the Sanatorium staff, they misconstrue all medical help as an attempt to do them harm, or as leading to a harmful effect on the process of their recovery to health. They become aggressive and quarrelsome when the treatment does not seem to show the speedy results which they expect from it. In keeping with their unmitigated egotism and lack of adaptability to discipline and rules of conduct, they present a



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most challenging problem to deal with at the Sanatorium. They soon get fed up with their surroundings and wish to leave for home on a slight pretext, without waiting to be cured. Even when the things are done in their own interest they still remain pig-headed and intransigent. Like sullem and irritable children they wish to be left alone; and even when seriously ill, out of sheer stubbornness they minimise the gravity of their illness. They continue to make, however, vigorous attempts to fidget out against their environment and their disease, toward which they feel so bitter and resentful.

It shall be pertinent to quote here the case of a rebellious type of patient who observed, "I am confident that I will cure myself. I'll never worry about it. If they will leave me alone, rest when I want to, I shall be all right. The Superintendent of the Sanatorium reported about this patient that he was very unpopular among other patients, because of his hot temper. He lay for hours in bed with his face turned morosely towards the wall. He was troublesome to the nursing staff, did not carry out their orders, faked a high temperature, and insisted on having special privileges. From the psychodynamic standpoint, we may observe that the typical reaction which the patients belonging to the rebellious type show to their illness, is not determined by the psychological effect of tuberculosis, rather this disease merely highlights the personality characteristics which are always active in one form or another prior to the onset of illness.

III. The Self-driving Type

The initial reaction of these patients to their illness is one of incredulity and improbability associated with a lot of anxiety and emotional upheaval. But in due course they come to adopt a defensive attitude of overt acceptance, or of passive resignation.

Besides suffering from an acute anxiety of social segregation from their kith and kin due to tuberculosis, these patients worry a good deal that illness has entered like an intruder into their lives, devoted as they are to the realization of high ideals and lofty ambitions.

Since the illness necessarily circumscribes the ordinary routine of their daily living and puts a serious ban upon the feverish excitement of their

mental hustle-bustle, the anxiety and restlessness engendered by the retardation and frustration of this continuous psychomotor activity becomes for some of these self-driving type of patients even more painful than suffering due to tuberculosis itself. They find it much more difficult to cope with their unrelieved mental tension and pent up psychophysical energy than to adjust themselves to their illness.

This state of mind is best illustrated in the words of a patient who said "I do not mind having T. B. What I mind is to give up my work more than anything else.... I know that I could not do anything when I came out. I hate staying at home and doing nothing.... I do not mind the complaint. It is what it stands for. It prevents me from doing what I want to do."

On the assumption that in the case of these self-driving type of individuals, an unmitigated drive and compulsive urge to propel themselves into ceaseless activity and physical toil absorbs a good deal of their inhibited aggression and pent up emotions, it would seem that when they fall ill the whole of their psycho-physical energy is canalized in combating the disease itself. It becomes extremely difficult for them to accept a state of passivity and abject helplessness which the disease inevitably reduces them to, as the patient above complained about. Since they have to continually fight down the need to depend upon others for support and the treatment of their complaint, they show a highly unrealistic attitude to their illness. In view of this they attempt to maintain an outward veneer of independence and self-sufficiency, and show a mental state of "SPES PHTHISICA"—exaggerated feeling of hopefulness and confidence of recovery experienced by the tuberculous patients. This mental attitude seems to be in keeping with their basic personality make up. Whereas formerly they have been able to dominate and sway their work situation, now they feel confident they shall succeed in overcoming and breaking the resistance shown by their disease. Thus their unconscious reaction to the disease is that shown to a powerful foe whom they have got to subdue in advance before they are conquered by it themselves.

To sum up, it may be observed that the self-driving individuals are harassed by the same anxiety and depression produced by their illness as that seen in other types of patients, but in conformity with their personality structure they employ a different type of

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character defenses and behavioural stratagems. Being over-concerned and fastidious about cleanliness and perfectionism, as far as their disease is concerned, they feel themselves contaminated by something filthy and undesirable and thus they shun the company of others. Due to their deep-rooted sense of guilt and over-severe conscience they avoid contact with members of their family having a fear of infecting them. Unrealistically oriented, they are unduly tormented by a feeling of over-conscientiousness and overwhelming sense of responsibility that notwithstanding the fact that they suffer from a serious disease, they have failed in their duty in not providing for their wives and children. They continue to entertain the illusion that one day the victory will be theirs in the bitter struggle with the deadly foe of their disease, thus proving to their loved ones that they never acted like deserters even in a situation of such dire emergency as of suffering from an illness like tuberculosis.

Unless some psychological change takes place in their reaction to illness either through self-understanding, or the counselling done by the attendant physicians, the prognosis regarding their ultimate recovery may become very bleak in the event they are allowed excessive mental pre-occupation, or physical over-exertion to compulsively keep themselves busy.

CONCLUDING COMMENTS

In view of the foregoing discussion the reaction of the patients belonging to different personality types would reveal the fact that contrary to customary medical belief that the psycho-pathological disturbances shown by the tuberculosis patients, as a sequel to their illness, are directly caused by the toxicity produced by the disease, the psychological reaction of each patient in this connection is primarily determined by the nature of the pre-morbid personality of the patient.

It is important to note, however, that a number of modern medical writers with extensive experience in study of the personality functioning of the tuberculosis patients have come to adopt the view point that the toxemia of tubercle bacillus alone is not capable of producing far reaching changes in the behaviour patterns of the tuberculosis patients.

BARKER, WRIGHT & GONICK (1946)—these authors provide an exhaustive bibliography on

"THE PSYCHOLOGY OF THE TUBERCULER"—in a survey of 44 authors on this point, noted that 19 of these 44 authors specifically expressed the opinion that there is no unique tuberculous behaviour. A few of these stated that the behaviour of tuberculous individuals does not differ from that of healthy persons; others that tuberculous patients do not differ in their behaviour from other chronically ill persons; some expressed the opinion that there are several types of reaction to tuberculosis, depending upon the previous temperament of the person, upon the socio-economic position of the patient, or upon the course and seriousness of the disease.

After reviewing a large group of patients, BANISTER (1931) reported that he had found no mental disorders which were the direct consequence of tuberculosis. Mental abnormalities which did arise in these patients were regarded by him to be the expression of maladjustments such as occurred in any non-tuberculous individuals.

Similarly, according to DUNBAR (1946)—one of the leading authorities in the field of "psycho-somatic" medicine—"Various attempts have been made so far to show definite mental states or definite psychosis, especially SCHIZOPHRENIA, to be caused by tuberculosis. These attempts have remained so far unconvincing, and for the most part highly uncritical, in that conclusions are drawn from statistical co-existence of tuberculosis and certain mental states, usually without adequate investigation into the psychic and the mental make-up of the total personality of the patient. "She further adds: "It is the consensus of opinion among critical and experienced authors, however, that psycho-pathological manifestations in the course of pulmonary tuberculosis are only psycho-pathic trends present in the personality previous to the disease, and only accentuated or brought to the foreground by it."

In the light of the above, and our own findings, we may conclude that notwithstanding the tremendous importance of various extraneous factors, such as social hardships, physical and mental frustrations which make certain individuals highly susceptible to tuberculous infection, we can best assess the aetiological significance of these factors only within the frame of reference of the total personality functioning of the patients. This thesis is based on the assumption that not all individuals react in a like manner in

any given situation of emergency. The reaction is conditioned by previous life experiences and personality background of the individual. In short, the personality make up of the patients ultimately becomes the deciding factor concerning normal or psycho-pathological adjustments they make to problems created by the onset of illness.

DAY (1946) sums up this viewpoint well: "... we must agree to the generalization that every individual reacts to a disease according to his personality, from which it must follow that the psychoneurotic, when given a touch of tuberculosis, will exploit his disease process to suit his pattern of living—or of dying."

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AGAMMAGLOBULINEMIA—Case Report

BY DR. WALTER D. CHASE, M.D., F.A.C.S.

Bethlehem, Pa., U.S.A.

THOUGH applying to fewer patients, Brunton's observations on the blood of people who seemed never to be free from infections, may be compared to the mental alertness of Ehrlich, the discoverer of Salvarsan; Fleming, the discoverer of Penicillin; and Waksman, the discoverer of Streptomycin. All these men used their minds with intensity; they really *saw* while looking; they did not take things for granted; they continually asked themselves "Why?". How fortunate it would have been if there had been a Brunton much earlier! Well, so it would have been in the case of Von Behring.

Brunton reported in *Pediatrics*, (9: 722, 1952) his observation that there existed "primary" agammaglobulinemia in these cases. Let me quote from *The American Journal of Medicine*, Dec., 1957, the following:

"Three forms of this unique disturbance have been described: (1) a physiologic, or transient form in early infancy; (2) a *congenital* form inherited as a sex-linked recessive trait in *males*; and (3) an *acquired* form occurring in *adults of either sex*. In addition, agammaglobulinemia may accompany a limited number of diseased states in which the protein disturbance is secondary. For convenience, agammaglobulinemia (congenital or acquired) which occurs as a solitary defect in protein metabolism, unassociated with other diseases, may be referred to as 'primary'.

Primary agammaglobulinemia is uncommon. In Monck's study of 6000 serums from persons aged fifteen and over, the absence of gamma globulin was encountered only once."

The authors go on to state that there have been "approximately" sixty cases of this disease reported.

"The cardinal clinical characteristics of primary agammaglobulinemia are: (1) an extraordinary susceptibility to infections; (2) a good response of individual infections to antibiotic therapy, as contrasted to (3) usual failure of antibiotic *prophylaxis*, even though resistant bacteria are not involved. Certain clinical sequences, such as

repeated pneumonias and spru-like syndromes are particularly suggestive of agammaglobulinemia. To these should probably be added, as usual clinical mnemonics, the occurrence of influenzal meningitis, in an adult; herpes zoster; hematologic abnormalities, including neutropenia, lymphopenia and hypersplenism, and failure of the erythrocyte-sedimentation rate to rise appropriately during acute infections.

Characteristic laboratory findings in primary agammaglobulinemia include: absence of gammaglobulin, absence of isohemoagglutinins, failure to form antibodies following antigenic challenge and absence of plasma cells from the bonemarrow." It is also absent from the lymphoid tissue.

The authors then remark that the patient may die, despite the use of antibiotics, if the necessary gammaglobulin is not supplied.

It is commonly noticed that adenoids and other lymphoid tissue are present in very sparse amounts in the juvenile cases, while many cases of *adult* agammaglobulinemia have reticulendithelial hyperplasia. Advanced sinus disease, complicated with bronchitis and bronchiectasis, is a frequent feature in the congenital cases, this being the outstanding feature of my case.

Case report: This male came to me at age of 4½ years, Jan. 30, 1943, with the history of recurring fever bouts with temperature up to 104°, since "grippe" four weeks previously. Pus was washed from his R. maxillary sinus on this occasion. He had some cough. The next visit was for purulent rhinitis, with cough, recurring fever, headache, history of pneumonia two months previously, night sweats. He looked pale. There was "slight enlargement" of cerv. lymph nodes. During 1949, he was treated for chronic sinusitis, the antra having purulent contents. Also, in Dec., 1949, he had acute purulent otitis media. Penicillin cleared up these infections promptly, but recurrences occurred, characteristically. In 1950, an abdominal attack resulted in his being hospitalized for "appendicitis", appendectomy being performed,

though the surgeon found only a "kinked" appendix, with "chronic catarrhal" involvement. At the time, the surgeon stated that he observed "some enlargement" of abdominal lymph nodes. On 30th of January, that year, suppurative otitis media again occurred. Several times that year, maxillary sinus lavage was done. In 1951, the sinusitis continued to require treatments. On August 3, 1951, "windows" were made into both maxillary sinuses (through the inferior meatus). On January 14, 1953, he entered St. Luke's Hospital with meningitis, following "sinusitis" (mother's statement) three weeks previously. Antibiotics and some intravenous sulfadiazine, completely cleared up this infection.

During 1953, repeated sinus treatments were given, the Proetz displacement irrigation of sinuses was given and "Cold Vaccine" was started. Frequent colds with fever, cough with purulent sputum, abundant nasal pus, nasal voice persisted. In January, '54, there was lameness of fingers and soreness in L. popliteal area. In February, that year, he had to be hospitalized with an acute attack of sinusitis, and again in April that year. One ankle was lame in April, '54. In May, '54, acute suppurative otitis media occurred.

In September, 1948, a L. Caldwell-Luc antrum operation, with transantral ethmoidectomy and sphenoidectomy was done.

Postoperatively, the left side of nose then showed almost no discharge for some time.

In October 1954, at the suggestion of an allergist consultant, the patient then began "living away from home" and he was put on housedust extract injections (1:100) and autogenous vaccine. The housedust extract was too strong and the patient reacted to this and the vaccine with exaggerated symptoms.

In January, 1956, house dust extract in the dilution of 1:1,000,000,000, was begun (i.o.c.c. intradermally and the same amount hypodermally, the *hypo.* dose being increased each injection until 1 c.c. was reached; then, the next decimal strength being used successively until the strength of 1:100 was employed).

Not until late 1955 was his agammaglobulinemia discovered. He then was given i.o.c.c. of immune globulin every month. At this time, a trial use of

Nepera Chemical Company's "Bionydrin" intranasally was begun. (This preparation contains Neomycin, Gramicidin, Thonzylamine HCl, Phenylephrine HCl, Thonzonium Bromide, preserved with Thyremosal .002%). This medication definitely reduced the purulent discharge. Also, recently, when polyps appeared in both ethmoid regions, together with much purulent discharge, the resumption of this preparation promptly created remarkable improvement (though I had made one treatment of the polyps with a bead of silver nitrate on a sharp applicator thrust into each polyp-mass). On Feb. 2, 1956, my notes stated "No pus seen"! In May, that year, my notes state that some pus was seen in both sides of nose, a gradual worsening of the sinus state occurring.

In December, '56, he entered the hospital for bronchoscopy by Dr. John Synder, who found bronchiectasis in his left lung. Aerosol was used, a new autogenous vaccine was used, housedust injections were kept up and Staphylococcus toxoid was also used (according to French Hansel³).

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These treatments were continued during the first half of 1957, until in June, when he went to the sunny, dry climate of New Mexico. While there, he continued receiving the monthly injections of Gam-maglobulin, but the sinus therapy (Proetz displacement irrigations, antrum lavage, etc.) was not supplied.

This climate experiment caused slight improvement in his cough and sputum, but on his return he had a mild acute rhinitis which prevented our having the opportunity for comparing the appearance of nose before going to New Mexico and after the benefits of that climate. Later, the sinus signs were about the same as before that climate experience.

It was in June, 1958, that polyps were discovered in left ethmoid region. Much pus was also present. In August, '58, polyps were seen in both ethmoid regions. On June 25th, L. acute suppurative othitis media occurred. Paracentesis and antibiotic medication were instituted. The middle-ear involvement this time was stubborn, a prolapse of the mucosa through the perforation occurring in the forth week. Snaring off this mass brought about early cessation of the otorrhoea.

During the past months, the nose has usually contained abundant pus in all areas, the voice nasal, cough and considerable purulent sputum have continued and the patient has looked pale. Gain of weight has been slight. However, there has been no chill or sharp involvement of sinuses or pulmonary tissue, necessitating hospitalization. He is getting Proetz displacement irrigations ("Polycin" being added to the saline) and the immune globulin injections, no vaccine or house-dust injections being at present used.

His mother, asked how many attacks of pneumonia the patient had had before he came into my

care, stated "about a dozen". He had been hospitalized in another city for these attacks and had always responded well to antibiotics and chemotherapy.

While under my care, I was always greatly impressed by his remarkable response to these medicines, particularly when he had meningitis. And this is strictly in accordance with the character of this disease.

The blood studies on this patient were made during acute inflammatory states and at these times no neutropenia was detected and only once was there a lymphocytosis. Complete absence of gammaglobulins was found in his last two laboratory examinations at St. Luke's Hospital.

We now plan to transplant lymphgland tissue into this patient, Good and Vargo* having reported successful results from this procedure.

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LAB RODENTS BRED

Dental researchers in U.S.A. are breeding a Mongolian rodent, the long-tailed gerbil, whose tooth decay characteristics are similar to that of the human being.

Dr. Dimitri Afonsky, research associate in dental medicine at Rutgers University, told DENTAL TIMES that the gerbil offers superior research possibilities to the ordinary rat whose teeth show decay but are subject to gingival disease in only one strain. The gerbil is much more susceptible to both decay and gingival disease, histological specimens have shown.

Though the animal is clean and easy to work with, it does not breed readily. The original colony here of three gerbils has now grown to 150, but this is still inadequate for large-scale dental research.

The Role of a Doctor in an Industrial Area

BY DR. S. SESHADRI DIXIT,

Paper Town, Bhadravati

SINCE a decade, Industrialisation in India is being paid more attention and particularly towards an Industrial worker, his health and well-being. Till recently, even in Western countries, the Chief aim and object of the employer has to derive as much profit as possible from the Industry regardless of the health of the workers. Absolutely there was no restriction in the working hours, the age of the workman employed and regarding medical facilities. Any injury or illness was attributed to the individuals' responsibility even though it was due to occupational hazards. In certain special circumstances and in rare occasions, if a compensation was given at all—it was too meagre.

In addition to the above draw-backs—here in India our labour is separated from the classes almost as sharply as the Rulers have been separated from the ruled for thousands of years. Secondly, there is distinction between an unskilled labourer and a skilled one, and again between an Overseer and an Administrator.

If the unskilled labourer is to make a full contribution to Industry—he should be persuaded to live a healthy and happy life, proper accommodation, ration, and at least absolute necessary amenities of life should be provided from the Industrial concern. In Western countries, constant riots, block outs and agitation brought out some changes in the life of a labourer. The Government was forced to frame enactments now and then namely, The Factory Act, the Employers' Liability Act, the latter after-wards named as Workmen's Compensation Act. Indian also followed suit. Similarly in Mysore, we have got the Factory Act.

An Industrial Doctor has a big responsibility and has an important role to play in Industrial Health Service — said Dr. U. Krishna Rao, Minister for Industries and Labour on 6-5-1952—when inaugurating the Madras Branch of the Society of the Study of Industrial Medicine in India.

It is a misnomer to say that to obtain satisfactory

work in Industrial medicine, we require highly trained specialists and technicians. There is a definition to quote with regard to a specialist and a general practitioner. 'The former who knows more and more about less and less until finally knows every thing about nothing; the latter who knows less and less about more and more until finally, he knows nothing about everything.' Though in certain circumstances, we require specialists—ordinarily to improve the health of the Industrial worker—an ordinary works Doctor or failing him—the general practitioner working in the area is quite sufficient.

The Medical Officer must first of all have an interest in this type of work and not only should he have training in the arts and mechanics of his profession and special professional knowledge and occupational health but also he should have a thorough knowledge of the laws, rules and directives pertaining to his work. Of course this is influenced by the philosophy of the Management and budgetary allowance. The medical man must have the well-being of the worker at heart just as a family physician. The Doctor should try to establish harmony with the labourer 'as a full human individual' and not merely the eight hour 'work hand'. Sanitation, nutrition, prevention of disease, leisure and recreation will constitute his special field. A Labourers' feelings and fears and his needs and hopes also form part of health problems. The sympathetic human feelings psychologically improves the mental condition, thus helping efficiency and dignity of labour. Secondly, he must judge the disabilities arising from injuries etc. sustained in Industry. His evidence must be "horse high, pig light and bull strong" (Johnstone 1948). For this, he must have some knowledge of the machinery. In toto, the duty of a Doctor consists in making the labourer fit for the job and making the job fit for the labourer. The Factory Act and the Workmens' Compensation Act will serve as a guide to a Medical man. The latter should supervise regarding temperature, adequate lighting and ventilation, sufficient air space to the worker, allowance of proper floor space to avoid overcrowding of machinery, protection of

the moving parts like, belts, wheels etc. provision of first aid, sufficient and wholesome drinking water, good canteens and sanitary latrines etc.

The Workmen's compensation Act provides compensation to certain injuries and occupational diseases. Though the above Acts are responsible for bringing a Medical Man into an Industrial Concern—monitarily, the former is not happy since the tendency of the worker is to use him for obtaining sick leave or to have their minor ailments treated; the Management depends upon him for physical fitness certificates.

Dr. J. C. Patel has said 'In a world which is rapidly changing where there is a transition from an agricultural to an Industrial mode of life, people concerned in any way with the welfare of individuals must pay due attention to the stress and strains involved in this change. We as Doctors and certain other individuals, directly concerned with the people working under industrial conditions must naturally take the lead in making this change as free from harm and damage to human beings as possible. That is the ideal for which Industrial medicine stands and that is the ideal which we will achieve'.

The Industrial Doctors' job is of supreme responsibility and a speciality. He should have a keen knowledge of processes of manufacture, the labourer is engaged in and he must be able to relate the symptoms to the individuals work.

It is a known fact that an Industrial disease is usually well established before advice is sought and often as in silicosis is progressive in nature. There are various reasons for this. His financial resources are small and his family burden is greater. He cannot absent himself unnecessarily and tries to toil hard. He hides small injuries or bodily ailments and faces the job, and naturally the ailment is aggravated and in the end will be responsible for his deep seated illness. At this juncture the quotation of Platto (1705) is worth noting.

"When a handicraftsman is taken ill, he must be cured by vomiting or purging or searing or incision, for if a physician tells him of a long diet, and bolstering up his head, and the like, he personally replies that he has not leisure to lie by it and that it will be of no use to him to lead an idle crazy life and neglect his business. Upon this, he takes leave of the

physician and returns to his usual way of living."

The common ailments that an Industrial Doctor has to face may be grouped under four heading:—

1. *Diseases due to air conditions.*—such as Pneumonomocionous due to (a) Dust—caused by grinding mixing, sieving, loading and unloading.
2. Heat diseases (a) In high temperatures and contacts—causes—cramps—exhaustion and retention.
(b) Compressed air illness.
(c) Vastomotor disturbances.
(d) Minor's. mystagmus.
3. Handling of chemicals—and poisoning by lead, mercury, mineral acids, alkalies and corrosives, tar, cement etc.
4. Inhalation of poisonous fumes etc. such as Ammonia, carbon monoxide, Cyanogen-compounds, Nitrous fumes, chlorine H₂ S, Phosgene, Methyl alcohol, carbon tetrachloride—benzene, analine and allied dye-stuffs.
5. Mechanical causes.
 - (a) Injuries are common in Factories specially of the type of contusions, lacerated or incised ones, Next comes sprains of various parts of the body due to heavy handling, sudden stretchings etc.
 - (b) Burns of various degrees of any part of the body specially hands, fingers, and eyes. These may be heat burns as a result of coming in contact with fire and heated parts or may be due to chemicals, such as acids etc. or may be electric burns.
 - (c) Foreign bodies.

Commonly particles of iron, pieces of wood get imbedded in the mucous membranes of the eyes.

- (d) Industrial Demittities.

These may be due to mechanical causes, as a result of pressure, continued friction or injury or may be due to physical causes, such as extreme heat, intense cold or electricity or may be caused by various inorganic chemicals, or biological agents, such as Bacteria (anthrox in leather workers) fungi (yeast in Bakers) parasites (in grain itch in grocers.)

PREVENTION

The Doctor should examine every applicant for employment in a factory thoroughly and check up the state of health and other disablements. His examination should not be a simple formality.

Periodical check ups of an otherwise healthy labourer regarding eye-sight dental conditions, testing of urine, blood faeces, sputum etc. by X-Ray examinations of chest, alimentary tract and of heart.

Maintaining the correct disease statistics and grouping them up and arrange prevention. If the

Doctor believes that a group of patients suffer from certain diseases like Anthrox, toxic jaundice, toxic anæmia, compressed air illness. Epithiliomatus ulcers and poisoning by lead, arsenic, Phosphorous, Mercury, Manganese, Carbon bisulphide aniline and benzol—it is his duty to notify to the Chief Inspector of Factories and arrange prevention by necessary measures.

The Industrial Doctor should technically supervise regarding the health conditions within the Factory. Safety measures to prevent such occurrences may be devised by requesting the Management to change the labourer from place to places now and then. In this aspect, the reports of the Minors' Nystagmus Committee of the Medical Research Council and the reports of the British Medical Association to the Departmental committee are worth noting. Secondly training the worker to use goggles, gloves, and rubber boots, and rubber coverings, when working in areas of spurling, corrosives and chemicals, gas masks, dust masks in the dusty areas, asbestos covering, when working near furnaces etc.

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Sri K. C. Reddy, the then Chief Minister of Mysore, in inaugurating the IV All India Conference of Industry and Medicines in Bangalore on 10th December 1952 said 'A Healthy worker is an efficient worker, an efficient worker will produce more and make the society enjoy more amenities and good'.

In these days of strains and stresses of modern life, the health of the labourer should be kept at least at par to keep up the efficiency of the factory. Proper feeding, housing, hygiene and attention to the habits are highly essential. These are as important as the hours of work and rates of pay. The Management as yet has not solved the problem of housing accommodation to every labourer. Workers live at a distance from the work spot and cannot afford either the time or money to return home to have their square meal. They carry food prepared in the early hours with haste which is neither balanced nor hygienic. Under the circumstances, if an Industrial Canteen is run by the Management under non-profit scale, that will provide a balanced nutritious food to the worker. Even then, an ordinary labourer cannot afford to the extra money for that balanced nutritious food. The Management should contribute at least half of the cost or the Management should raise the wages of the workers to a 'living wage' according to the local conditions. The Industrial Doctor should educate the Labourer to have the wholesome balanced diet which is necessary for his health and happiness and ultimately for increasing his own earning capacity for his own benefit.

'Do-It-Yourself' Criticized

The "do-it-yourself" dentistry practiced by some members of the profession, who would rather tinker around in their own mouths than submit to the expert care of a fellow practitioner, is criticized by Dr. Arthur Elfenbaum, Professor Emeritus at the University of Illinois and North-western University.

Writing in the July, 1958 issue of **Oral Hygiene**, Dr. Elfenbaum, who is consultant in diagnosis at the West Side Veterans Administration Hospital and the Michael Reese Hospital in Chicago, warns that the most serious neglect of "self-treating" dentists is the failure to investigate small oral lesions.

Prohibition has caused some reduction in spending on luxury but a hard eight hours work requires some mental and physical relaxation. For this, the worker has turned on to gambling or try illicit drink.

Unless and until the Industrial worker is provided with a house and the possibility of a decent home life—the former does not attain that mental stage of voluntary co-operation to work with the Management for the increased production of the factory.

After the Independence of India, the Employees' State Insurance Act, was placed on the Statute book and the Employee's State Insurance Corporation was inaugurated by Sri C. Rajagopalachari, the then Governor General of India. The scheme is financed by the contributions of the State Insurance Fund and grants and donations from the Central and State Governments.

From this scheme, at present the Industrial worker will have facilities regarding 1) Free Medical aid, sickness benefit, maternity benefit, disablement benefit and Dependents' benefit.

This scheme has already been introduced in Delhi, Cawnpore, Madras and Coimbatore. Our Chief Minister Sri Jathi has inaugurated the function of the above Scheme in our State on 26th July 1958 and our Mysore has taken the lead in India to extend the benefit to the members of the Employees' family also.

Without developing "cancer-phobia," says Dr. Elfenbaum, the dentist "should regard his own oral lesions as realistically as he does those of his patient."

As for the dentist who insists he can make a perfect impression for his own dentures, Dr. Elfenbaum points to the many important factors of mouth evaluation and examination which the dentist could not himself perform.

Referring to the neglect of oral conditions in dental students, Dr. Elfenbaum feels that a healthy mouth according to the standards of the school's own clinic should be a requirement for graduation.

RESEARCH IN VIROLOGY

BY DR. J. W. HOWIE, M.D., M.R.C.P., F.R.F.P.S.

Professor of Bacteriology
University and Western Infirmary of Glasgow

A Chair of Virology, the first of its kind in Britain, has been established in the University of Glasgow with a handsome benefaction of £225,000 from the Scottish Hospital Endowments Research Trust (SHERT). This recognition of the importance of microbes in human affairs is the outcome of an academic policy which has developed from three motive forces. The first of these was accepted in 1953 by the Advisory Committee for Medical Research in Scotland, which encouraged the idea that some part at least of the funds at the disposal of SHERT should be used to foster a major venture. The second, much encouraged by the Medical Research Council was the realisation that the scientific study of microbes was a growing point of medical research and that new methods had raised the study of viruses in

particular to what might be termed boiling point. The third was the experience of the University Court that there comes a stage in the affairs of any new, important, and rapidly developing area of knowledge when the best service that can be done to it is to found a University Chair in that subject.

BACTERIAL AND VIRUS DISEASES

It may be of interest to analyse the medical, scientific, and academic motives which have produced this result. As agents of human disease, viruses occupy a position of importance which may quickly be appreciated by naming a few of the important human and animal diseases caused by viruses: influenza, poliomyelitis, measles, smallpox, yellow fever, the

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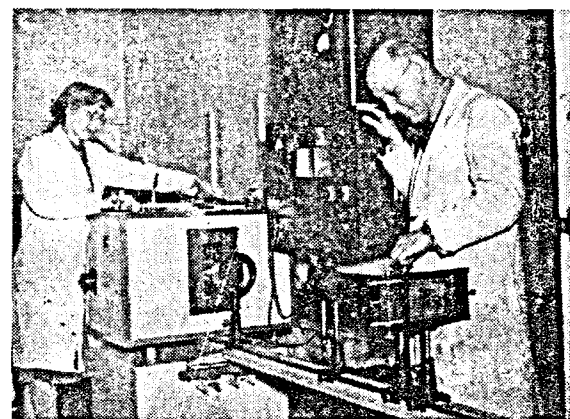
Voluntary Human Guinea-pigs submit to inoculation with the "Common Cold" Virus in order to help British scientists in their research for an anti-dote to it or a prophylactic.

common cold, and foot-and-mouth disease. Much has been learned about the treatment of bacterial infections, such as streptococcal septicæmia and tuberculosis, by chemotherapy - that is, by the use of drugs like penicillin and streptomycin. Much has also been discovered about how bacterial diseases are spread within the community and how they may be prevented by methods of hygiene and active immunisation. To such advances is owed the virtual disappearance from Britain of cholera and diphtheria, to quote only two examples among many. For technical reasons, virus diseases have not as yet been controlled by chemotherapy although it is not impossible that this may still be accomplished. Great importance thus attaches to fundamental studies of the nature and habits of viruses, in order that attempts to discover an effective chemotherapy against them may be rationally directed, and that measures of hygiene and active immunisation may be pressed forward in hopeful and practicable ways. Experience already gained from campaigns against smallpox, yellow fever, and poliomyelitis offers encouragement to the idea that virus diseases may be more readily prevented than cured. But the correct measures of hygiene and the production of safe and effective vaccines for active immunisation demand much more knowledge than we yet possess about the structure of viruses themselves, how they live and die, how they pass from one victim to another. We know that some diseases are the outcome of joint attacks by bacteria and viruses. Some of the chest complications that follow measles and whooping cough - bronchiectasis, for example - are probably caused in this way. The common cold is another disease the

causation of which is obviously complex. The upper respiratory infections generally, with their legacy of chest disabilities, fall within the area of medical research which cannot fruitfully be cultivated without far more fundamental knowledge of viruses than we yet possess.

VIROLOGY AS A SCIENCE

The best way of gaining new information about anything obscure is to present the obscurity to an interested enthusiast, and to encourage him and his assistants to let their imagination flourish. This is profitable however only if there is something to set the imagination working. Viruses have long presented their challenge of obscurity; but until recently their investigation demanded exceptional material resources and remarkable ability to resist the frustration of tedious techniques and intractable agents. For one thing, few viruses could be seen; for another, many could not be grown in the laboratory; and some could be investigated only where experiments could be done on the higher apes or on human volunteers—as in the MRC Common Cold Unit, Salisbury, in southern England. Now suddenly, within a few years, the electron microscope has made it possible to see many hitherto invisible viruses. New facts about their physical structure have been revealed. Recent advances in biochemistry have made it possible to analyse the composition of these minute creatures, and to probe the fascinating borderland in which the chemical differences between living and non-living matter become crucial. Developments in the science of genetics have helped to explain many important facts



Serum being placed in a refrigerated bath (left) as special camera (right) is adjusted in order to work this apparatus which measures electrical properties of proteins in the blood.

surrounding the emergence of new types and strains of viruses. Above all, developments which make it possible to grow viruses in tissue-culture have, in the past four years, added a whole new world to the virologist's universe. Now he can study many viruses almost as a bacteriologist studies bacteria; now he can examine their physiology without so many complications and variables as before; and now he can study many new viruses, some of which may be dormant in the human body without producing any disease at all, and others provoked into harmful activity by influences of which we must quickly gain fuller understanding.

ACADEMIC VIROLOGY

As early as 1952 the University of Glasgow established a separate Lectureship in Virology within the Bacteriology Department, and the lecturer and his assistants have done much useful work in collaboration with the Department of Infectious Diseases and Ruchill Hospital. In the Veterinary School also, virus diseases of animals received considerable attention from about the same time. But both these enterprises have been limited in scale, and have been fully occupied with urgent day-to-day problems. Many such problems remain and will continue to be investigated. But now it will be possible to try to find some of the knowledge without which we cannot fully assess the problems of virology—far less provide solutions for them. The new department is therefore being situated as near as possible to other medical and scientific departments of the University engaged on related fundamental work departments such as chemistry, biochemistry, physiology, genetics, pathology, bacteriology, surgery and medicine. Within the academic and teaching-hospital environment the staff of the new Department of Virology will find the stimulus of related interests and similar outlooks, as well as that which comes from teaching students. A professor with a new department to build, with medical and scientific problems to tackle, among colleagues with whom new and old ideas are constantly being examined and discussed, and with students to satisfy—that is something new for virology in Britain. Virology, as is its right by its own importance and contributions, has been given full academic status. The many people who have sponsored this major venture have no doubt about its significance.

Photos: (Courtesy: NAPT Bulletin)

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INSECTS OF MEDICAL IMPORTANCE (III)*

THE SAND-FLY

BY P. N. GUPTA
Malariologist.

INTRODUCTION

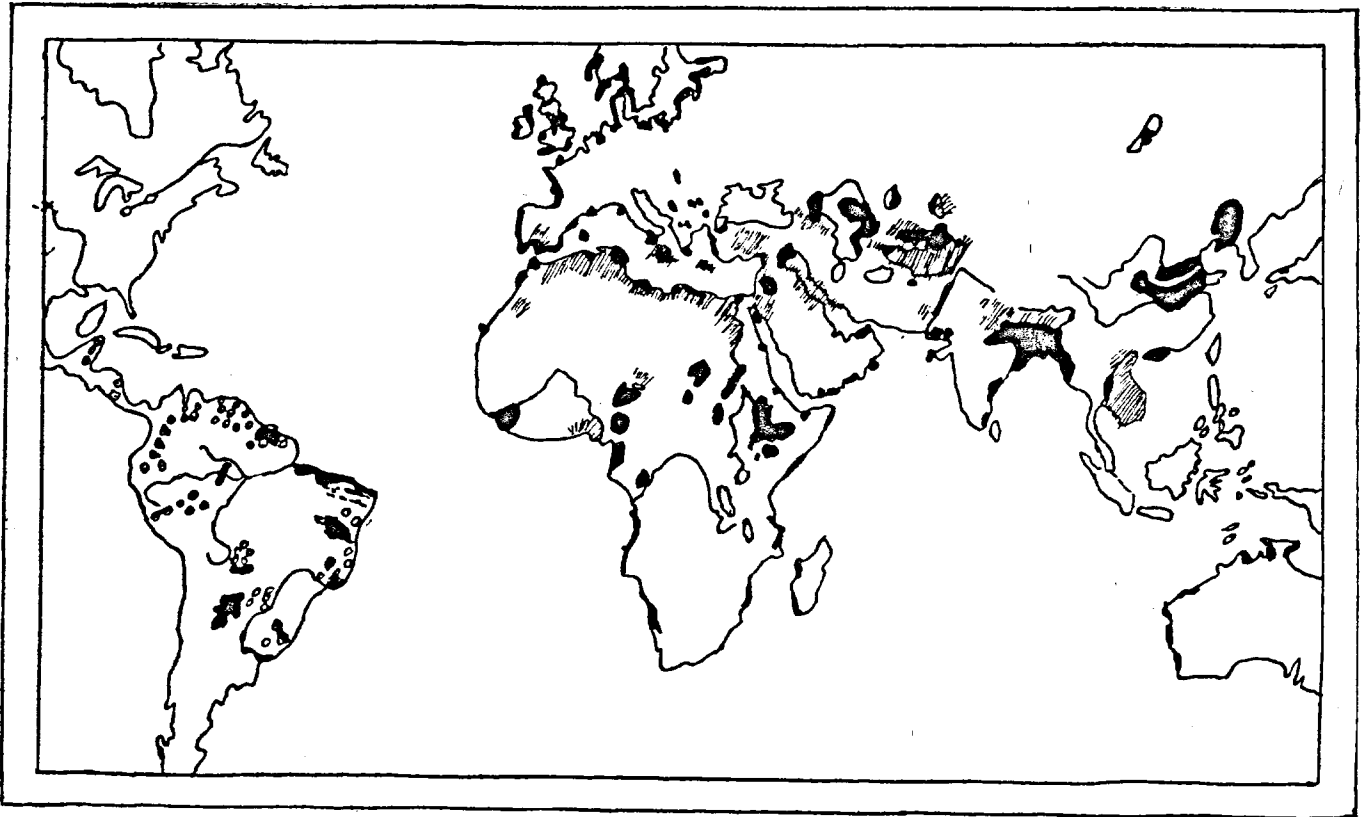
SAND-flies or Papatasi flies are little known and their importance is much less appreciated than they deserve, because the diseases transmitted by these tiny insects do not cause alarming mortality or morbidity, to attract general attention, except in epidemics, but a man suffering from sand-fly fever feels more miserable than the one suffering from MALARIA or DENGUE. These insects are so small that they do not become a nuisance. They are only felt when they have bitten and gone. They are

easy to control. A general description is given in this article to review the existing knowledge about this insect.

GEOGRAPHICAL DISTRIBUTION

The sand-flies transmit a number of diseases, prominent being Kala azar, Oriental sore and Sand-fly fever. A world wide distribution of Leishmaniasis (Kala azar, Oriental sore & Espundia) is shown in the Map. Wherever these diseases occur, sand-flies are found, as otherwise these diseases would not have occurred.

DISTRIBUTION OF LEISHMANIASIS (AFTER MANSON BAHR)



■ = Kala-azar ▨ = Oriental Sore ••• = Espundia

*2nd article in the series was published in this journal in July '58 PP 35-40.

Different species of sand flies (Phlebotomous species) are active in different regions of the world and transmit different diseases, as shown in the chart.

Mediterranean islands, the mainland bordering the Mediterranean sea, Sicily, Southern Italy, Greece & Crete, Egypt, Palestine, Syria, Iraq, Sudan, Abyssinia, Kenya, West Africa, South America, Continental France, North of Yangtse river in China, are all the regions where sand-flies transmit diseases. In India, Eastern India is most affected particularly in the plains and delta of the Ganges, spreading along the Brahmaputra Valley into Assam. The distribution of the different species in different States is described later in this article.

MORPHOLOGY (Fig.)

Sand-flies (Phlebotomous species) in general are minute, 3 mm long, greyish brown insects, thickly covered with fine long hairs all over and as such can be easily recognised. Another characteristic by which these insects can be differentiated from others is that these insects cannot fly any long distance and as such they only hop from one place to another.

The head has (i) two large black conspicuous eyes, (ii) a pair of antennæ which are long, slender and have sixteen joints (iii) the pair of palpi are folded back to protect the proboscis, they have fine segments clothed with hairs & scales (iv) the proboscis is short and contains the piercing organs in females only.

The thorax is not prominently divided and consists of mesothorax mainly which bears the three pairs of relatively long, slender, jointed legs.

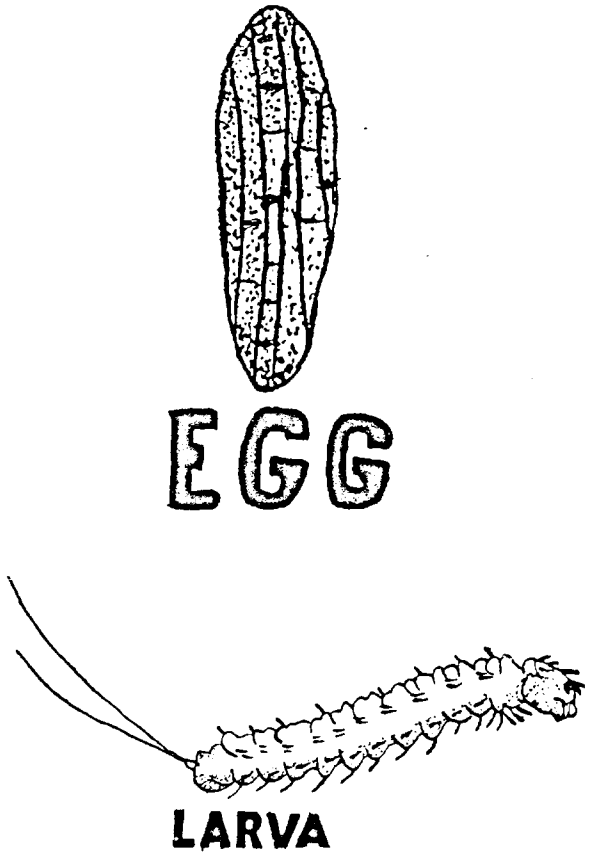
The wings are hairy, pointed and folded roof wise on the back at an angle of 45° from the body, except when newly hatched or shortly before death. The abdomen of the female is rounded at the last segment, but in the case of the male it is upturned posteriorly bearing the claspers as is shown in the figure. The sexes are differentiated by the feature. The male terminalia are complex structures and are useful in the identification of different species.

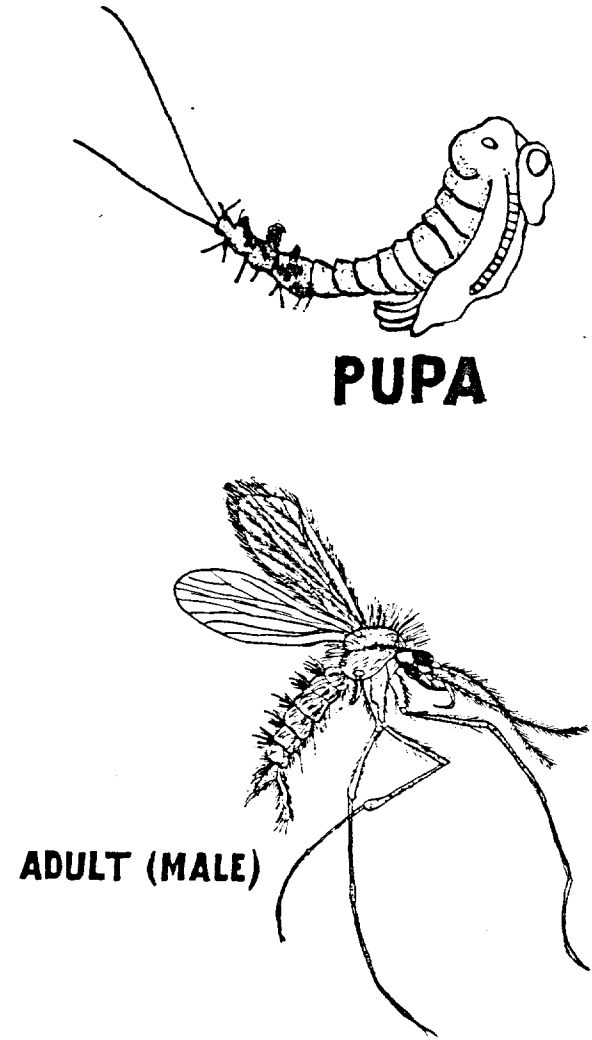
LIFE HISTORY AND BIONOMICS (Fig.)

Sand-flies lay eggs where there is darkness, moisture and organic matter where urine of animals

soaks. Favourite spots are dark damp cellars, dugouts, caves, cracks and fissures in the soil and under damp stone walls. Slightly moist crevices in the banks of nullahs, drains above water level are likely places. Loose earth and debris collected within a few yards of cowsheds, poultry runs & human houses showed a number of larvæ around Calcutta. In the heaps of sweepings from cattle sheds and fowl runs, underneath the feeding troughs of cattle and in spaces between two bricks at the base of a damp and shady compound wall, the larvæ were found. The breeding places differ with the different species as in Peru, breeding is maximal in rubble & loose earth, in Egypt in damp cracks in sand but in India in cracked floors, crevices and soil contaminated with faeces & urine of cattle, fowls. The favourable breeding season is just before and during the monsoons. High relative humidity and a temperature of 80° F are the optimum conditions. Breeding ceases at 60° F. In cold months the eggs do not hatch out and in other seasons, the period for completing the life cycle varies with the atmospheric conditions and the whole period may vary

Life History of Sand-fly





from 20 days to 52 days. The following periods have been worked out for *P. argentipes* in Calcutta area.

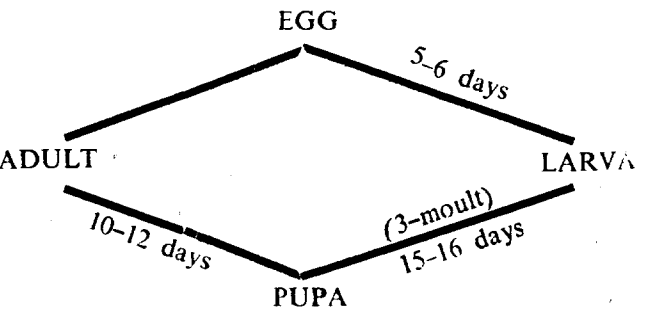
Dec., Jan., Feb.	— Eggs did not hatch out.
Mar., Oct.	— Not known
April	— 22 days
May	— 27 days
June	— 29 days
July	— 23 days
Aug.	— 31 days
Sep.	— 20 & 24 days
November	— 52 days

THE EGGS

The number of eggs laid by a single female varies from 9 to 45. Eggs are 1½ mm long, torpedo shaped. Its surface is moist, shining, pale yellow when fresh and dark in late stages. The surface longitudinal wavy lines appear at this stage. The average time for a larva to hatch out from eggs is 5/6 days. In Calcutta it has been seen that 19.4 percent of the eggs did not hatch out. Highest percentage of the eggs did not hatch out in June.

The Larva is twelve segmented (3 thoracic & 9 abdominal), caterpillar like having long dorsal bristles on the terminal segment. The body is covered with spines arranged in a transverse row. The larva feeds on decaying nitrogenous matter moulds, dejecta of lizards, rabbits' faeces and the bodies of defunct parent flies. Average time for a larva to pupate is 15/16 days and during this period it moults 3—4 times. 7 percent of the larvæ did not develop into pupæ in a Calcutta experiment. Highest percentage of mortality in larvæ was in May. Hibernation takes place during the larval stage. The larvæ may become infected by feeding on the faeces of dead bodies of infected sand-flies, the infection being transmitted to the adults bred from such infected larvæ.

THE PUPA is 3 mm in length, club shaped, moist, shining and of a milk white colour. The head and thorax appear fused and form the head of the club. The abdomen is curved upwards. The integument is clothed with minute spines. Average time for a pupa to become adult is 10/12 days. About 9.5% pupæ fail to emerge into adults. Highest mortality amongst pupæ is in the month of June.



PRINCIPAL VECTOR SANDFLIES (PHLEBOTOMOUS SPECIES)

SPECIES	GEOGRAPHICAL DISTRIBUTION	MORPHOLOGICAL CHARACTERISTICS	BREEDING PLACES	ADULT RESTING PLACES	FEEDING HABITS	DISEASES TRANSMITTED
<i>P. argentipes</i>	India & Ceylon. East and south of a line joining Bombay to Simla. Jammu, Kashmir, Calcutta, Ajmer, Mount Abu, Sambar town & Salt lake, U. P. (Gorakhpur, Benares, Basti, Jaunpur, Faizabad).	Silvery white feet due to white scales on the tarsi. Dark brown.	Under earthen ware feeding troughs in cattle sheds, spaces between two bricks at the base of a damp & shady compound wall.	Cow sheds, Chicken houses.	Cattle, Goats, & men	Kala azar
<i>P. papatasi</i>	India (as far east as Calcutta & as far south as Madras. (Jammu, Kashmir, Calcutta, Ajmer). Southern Europe, North & East Africa & Java.	Large eyes, black & conspicuous. Body with a pale lemon tint.	Cracks in the floor & walls, rat holes.	Human dwellings	Human beings	Oriental sore, Sand-fly fever (L.infantum & canine leishmaniasis in north Africa)
<i>P. minutus</i>	India (Jammu, Calcutta, Ajmer)	Minute size. In female the spermathecae are much less chitinised.	Found even at a height of 6000-7000 ft.		Lizards	
<i>P. montanus</i>	India	Is now ranked as a distinct species, previously <i>P. minutus</i> var. <i>montanus</i>			Lizards	
<i>P. chinensis</i>	China, Jammu	Resembles <i>P. major</i>			Man	Kala azar & canine leishmaniasis
<i>P. sergenti</i>	India, China, North & West of a line joining Bombay to Simla, Rajasthan, (Ajmer Sambar town & salt lake)				Man	Oriental sore (L.infantum & canine leishmaniasis in China).
<i>P. perniciosus</i>	Mediterranean littoral Tunis, Tripoli, Algeria, Morocco, Malta, Portugal, Marseilles, Sicily, Italy, Crete, Spain, Turkey, Bulgaria, Yugoslavia.	Dull red, brown spots in a triangle on the thorax. Eyes black, Thorax & Coxæ pale. Abdomen densely hairy but no tufts.			Cattle, dogs, birds, horses & men.	Kala azar, L.infantum & canine leishmaniasis. Kala azar (Italy)
<i>P. major</i>	Greece, Himalayan foothills, Jammu, China.	Dull greyish to bright yellow variation, abdominal hairs dorsally erect, of uniform golden grey colour. Disc of wings bluish.			do.	Kala azar (China)
<i>P. verrucarum</i> <i>P. noguchii</i> <i>P. peruensis</i> <i>P. langeroni</i>	Peru, slopes of Andes in Bolivia, Ecuador & Colombia. Sudan					Oraya fever & Verruga.
<i>P. whitmani</i> <i>P. intermedius</i> <i>P. persoai</i> <i>P. migonei</i>	Central & South America (Mexico to Buenos Aires)					Kala azar (Sudan) Espundia

THE ADULT

The adult hatches out in the early hours of the morning when the atmospheric humidity is high. The adults do not feed on raisins up to 4/5 hours after birth and do not feed on blood upto 10/12 hours after the birth. The females and males are formed in the ratio of 3:1. The Males are harmless and live on vegetable sap. The females are blood suckers and are smaller. Blood preference in descending order is cattle, dogs, birds, horses & man. Blood feed may be 0.1—0.2 Mgms.

In Eastern India maximum number of adult sand-flies are seen during July-October. In Northern India they persist from March to November with a peak in April and May. They are found in human dwellings, animal houses which are low, dark and damp, have plenty of hiding places in shape of uneven cracks and crevices, huts and sheds that do not have a lot of ventilation and through which air current does not flow, most commonly found in places associated with cattle and poultry. In human dwellings they rest in or near bath rooms near the floor, soakage pits, behind pictures, furniture, fittings and curtains.

The adults are nocturnal in habit. By day they rest in sheltered places. They avoid bright lit rooms but are attracted by dim light. The sand-flies are most active at night, particularly when there is no breeze and atmospheric temperature is high. They bite the men where the epidermis is thin, lower extremity at ankles, wrists even through socks and light clothing. They bite at the back in preference to front of the body. The actual bite is not felt but when the saliva is injected, the pricking sensation is felt. The blood travels to the stomach within ten seconds of the ingestion. It usually takes 2—3 days to digest the blood feed. The female takes a blood meal nearly one day after emergence and on an average it takes two days to lay eggs after a blood meal.

The range of flight is within 50 yards from a breeding place. The sand-flies are very sluggish and are not capable fliers. They only hop from place to place, as such range of their flight higher up is a maximum of three feet. A slight air current makes them move by short rapid flights with sudden changes of direction to left or right like the flea.

Longevity of the adults depends on many factors as environment, mating, successive blood feed. Average

life is 3—4 days but during rainy season it may live even a month. A temperature of 26.7°—27.8° C & saturated atmosphere are best suited. Wenyon (1913) succeeded in keeping a captured sand-fly alive for 40 days by feeding it on water. In Calcutta about 3% survive till 9th day. To be able to transmit disease, a sand-fly must live 7—9 days after the blood feed so that the parasites can develop fully to be infective. After one feed on an infective patient, the sand-flies remain infective for the rest of life. Adults bred from infected larvæ may be infective from the start of their life. Lizards and spiders are among the natural enemies of adult sand-flies.

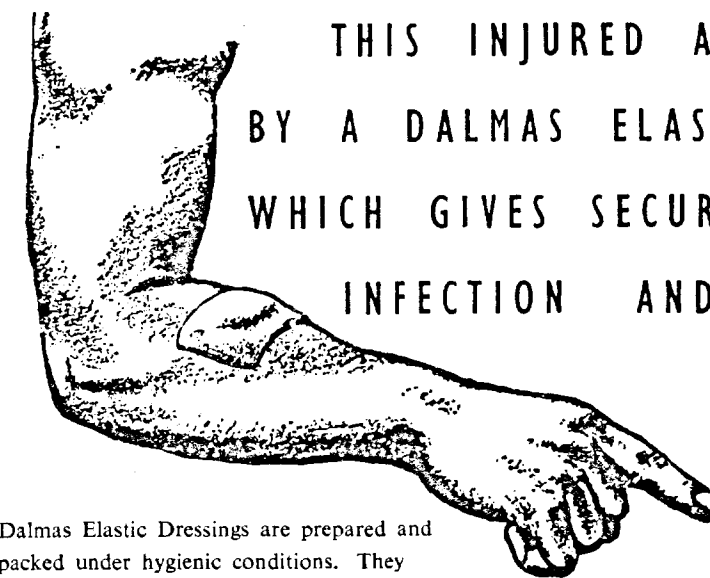
COMMON SPECIES OF SAND-FLIES (Chart)

1. Phlebotomous argentipes is the most common species in India. It is found where the climate is warm and moist. The general distribution in India is to the East and South of a line joining Simla to Bombay. Even at 4000 ft. (Simla Hills) this species is noticed. It has been recorded in Poona, Calcutta, Rajasthan (Mount Abu, Sarnar Town & Lake), Uttar Pradesh (Gorakhpur, Benares, Deoria, Basti, Jaunpur, Faizabad, Azamgarh, Ballia, Ghazipur, Allahabad and Mirzapur). It is the principal sand-fly in Ceylon. The species is recognised by the silvery white feet, except the Poona species where the feet are dark. It is found during and after monsoons.

The species transmits Visceral Leishmaniasis (Kala azar). In 1920—30 Kala azar epidemics of Bengal, incidence was the maximum amongst those living on ground floor which is in conformity with the habits of sand-flies.

2. P. perniciosus is the predominant species in the Mediterranean islands and the mainland bordering the mediterranean sea, Italy, Abyssinia, Kenya and West Africa. It forms 90 percent catch in South Portugal. It has not been reported from India.

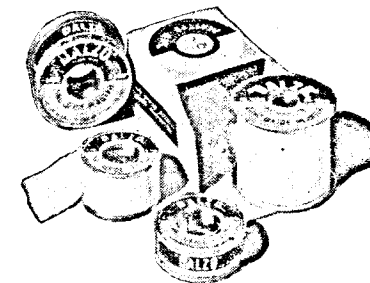
The head may have dark brown spot on the vertex. The eyes are black. The thorax may be pale with dark brown spots arranged in a triangle. The wings are iridescent in a strong light with a distinct metallic lustre. The abdomen is densely hairy, but no tufts as in P. papatasii.



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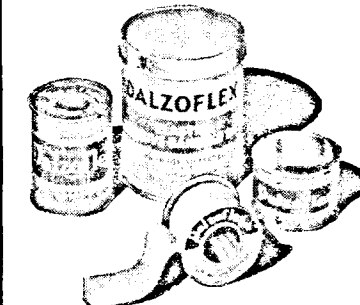
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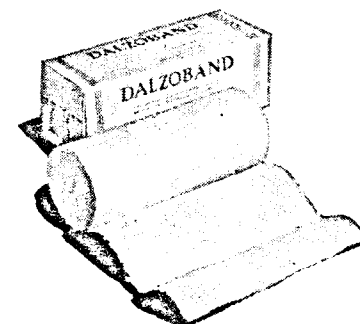
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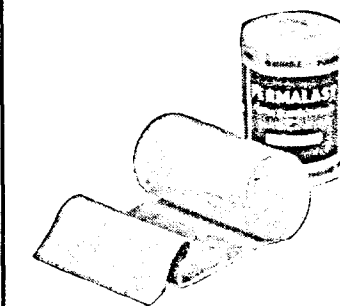
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In Western Mediterranean, Portugal, Italy and North Africa this species is found. This species is responsible for the transmission of kala azar. 96.8 percent of *P. perniciosus* become infected after feeding on infected hamsters. This species has also been found infected with *Leishmania infantum* in nature.

3. *P. major* is a Himalayan species in India occurring at heights of 5000—7000 ft. It is found all along the Himalayan foothills. It has been caught in Jammu province in India. It is the predominant species in Eastern Mediterranean.

In morphology this species resembles *P. chinensis*, described later. This species is responsible for kala azar in Eastern Mediterranean and for *Leishmania infantum* in Greece.

4. *P. chinensis* is a Himalayan foothill species in India, seen in Jammu province, Kashmir, Ladakh. It is the vector species in China.

This species in general morphology resembles *P. argentipes*, *P. papatasi* and *P. major* in that it has numerous erect hairs on the dorsum of abdominal segments but they are of a uniform golden grey colour. The legs are darker than the abdomen. There are long hairs with tufts of longer upright hairs on the dorsal surface of the legs.

P. chinensis is the incriminated vector of kala azar in China. Along with *P. sergenti* var *Mangolensis*, this species is the principal carrier of canine leishmaniasis in China.

5. *P. papatasi* is the widely distributed species in the hot dry plains of India, seen as far as Calcutta in the East and as far South as Madras. It has been seen in Jammu, Kashmir, Poona, Calcutta, Ajmer. It is predominant in Mediterranean littoral, Mid East, Algeria and China. This species is the only proved vector of sand-fly fever. *P. papatasi* is the probable vector for *Leishmania infantum* in North Africa. It is the vector for Oriental sore in French Sudan.

It resembles *P. argentipes*, *P. chinensis* in general morphology, except that the abdomen of the female is spindle shaped instead of rounded at last segment as in *P. argentipes*.

6. *P. sergenti* is confined to the dry hot plains in an area North and West of a line joining Bombay and Simla. It has been caught in Jammu, Kashmir, Ladakh, Ajmer, Sambar Town & Lake (Rajasthan).

It is the vector species for Oriental sore (tropical sore) in Crete, Iraq, India & Persia. *P. sergenti* var *Mangolensis* is the principal vector for canine leishmaniasis in China.

DISEASES TRANSMITTED BY SAND-FLIES (Map)

1. **VISCERAL LEISHMANIASIS** (Kala azar) with various synonyms as Burdwan fever (lower Bengal), Dum Dum fever, Sirkari Disease, Sahib's Disease, Ponos (Greece), Mard of Bicha (Malta) has been known to exist in India (Bengal) since 1850 and dates back to 1869 in Assam. 1891—1900 epidemic in Nowgong (Assam) reduced the population to 31.5 percent. It is most prevalent in Eastern India, plains and delta of Ganges, spreading along Brahmaputra into Assam valley. Bengal is heavily infected. Endemic areas spread along Gangetic plain in Bihar as far west as Lucknow, in North East endemic areas extend into Assam as far as Sibsagar. Extreme south foci are Cape Comorin & Madras. Sporadic cases have been reported from Goa and Bombay.

North of Yangtse river between coast and line joining Peking—Honkew, provinces of Kiangsu, Shantung, Chih li, North to Jehol, Fengtien, S. Manchuria, Mongolia, Hang Chow and South Canton in China are endemic areas.

In the Mediterranean littoral (Tunis, Tripoli, Morocco, Algeria, Sicily, Italy, Crete, Spain, Turkey, Bulgaria, Yugoslavia, Southern France (Marseilles), Portugal, Greece, Malta, and Transjordan, S. Arabia (Yemen), it is endemic in Sudan, Kassala, the Blue Nile district & Abyssinia. It occurs in South Russia and South America.

Leishmania donovani is the causative protozoan parasite transmitted by the bite of different species of Phlebotomous in different countries, *P. argentipes* in India, *P. major* & *P. chinensis* in China, *P. perniciosus* in Mediterranean littoral, *P. langeroni* in Sudan and *P. intermedius* in South America. Dog

is the chief reservoir in Mediterranean form, striped hamster in China, Mongoose & squirrel in Kenya but in India man is the only reservoir of infection.

Chief signs of the disease are irregular fever, asthenia, dysentery, emaciation and enlargement of spleen & the liver. Chronicity is a characteristic. The disease is fatal in from eight months to two years of age. It usually occurs in cold season & does not spare any age or sex.

Prevention of the disease lies in controlling the source of infection i. e. treatment of infected persons, anti-dog measures and in abolishing the vector, anti-sand-fly measures.

2. **SAND-FLY FEVER** (Phlebotomous fever, papatasi fever, Three day fever, Russian headache fever, Dog disease) has a wide geographical distribution in Southern Europe, Africa, Egypt, Sudan, Palestine, Syria, Iraq, Persia, South China, North & South America and in North West of India (Chitral & Himalayas).

The virus is present in the patient a day or two before onset of fever and for a day after. It is found in Phlebotomous species after feeding on infected patients.

P. papatasi is the proved vector species, although there may be other species involved.

The fever is short and sharp. Scarlet flush of the face and neck, very severe frontal headache, pain at the back of the eyes, back & legs as in Influenza, general stiffness of the muscles are the general symptoms.

The only preventive measure is extermination of breeding places of sand-flies and the eradication of their adults.

3. **CUTANEOUS LEISHMANIASIS** (Oriental sore, tropical sore, Delhi boil, Boutonde Bagdad, Salek (Persia), Pandeh sore (Southern Russia). It is essentially a disease of animals which is communicable to man. There are endemic foci in Russia, sporadic cases in North African coast countries and in the Sahara. Infection is wide spread in Asia Minor-Syria (Aleppo), Palestine

(Jericho), Red Sea Province, Egypt (Zagazig & Minia), Eritrea, Iraq (Bagdad), Caucasus, Arabia and Persia. It occurs in Pakistan (Lahore, Multan, Dera Ismail Khan, also in Baluchistan). In India the infection is wide spread in the drier Western parts of the Gangetic plain extending the West coast as far as Bombay and East as far as Delhi with sporadic cases occurring as far as in Benares.

P. papatasi, *P. sergenti*, *P. macedonicum* (Mediterranean), *P. caucasicus* (Russia), *P. intermedius* (Central and South America) are the vector species for the transmission of the parasite *leishmania tropica* by their bite, the mechanism being the same as in kala azar. The distribution of Oriental sores on the body closely corresponds with the area more liable to be bitten by sand-flies i.e. face, ears, hands, feet. The scalp, palms, soles of the feet are never affected.

The main reservoir of infection is the man. A number of animals dogs, jackals, gerbils, cats have been found naturally infected. The bed bugs and certain ticks are doubtful.

The disease is in a mild condition and rarely gives rise to serious symptoms. An attack gives certain immunity.

Prevention lies in control of sand-flies, dogs and by treatment of cases. Mass treatment is not valuable.

4. (a) **LEISHMANIA INFANTUM** (Infantile kala azar) is common in Mediterranean littoral. The causative parasite is *L. infantum* transmitted by the bite of *P. perniciosus* (Algeria, Malta and Marseilles), *P. Major* (Greece) and probably *P. papatasi* (North Africa) and *P. sergenti* and varieties of *P. major* in other areas.

This disease occurs in children and rarely in adults.

There is a close relationship between *L. infantum* and *L. canine*, described below.

- (b) **CANINE LEISHMANIASIS** - Common in Mediterranean region, Spain and in China, has not been seen in India.

L. canine, the parasite is distributed throughout the skin of the dogs and is transmitted from dog to dog by the sand flies. There is a close relationship between infantile kala azar and canine leishmaniasis although in places like Morocco, Tehran (Persia) canine leishmaniasis is common but there is no human leishmaniasis.

Species of sand flies concerned are *P. perniciosus* (Mediterranean), *P. chinensis* and *P. major* var *Mongolensis* (China).

Prevention is by the destruction of dogs and control of sand flies.

5. **BARTONELLOSIS** (Oraya fever and Verruga Peruma or Carrion's disease or Guaitra fever) - This disease which is restricted to South America (Peru, Ecuador, Bolivia, Colombia, Chile and Guatemala) is a specific fever caused by the bacilliform organism *Bartonella bacilliformis*. It is characterised by anaemia, eruption on the skin and mucous membrane consisting of raised, red swellings resembling haemangiomas known as Verruga Peruana. The death rate varies from 10-40 percent of those attacked.

P. verrucarum, *P. noguchii* and *P. peruensis* are the possible vectors of *B. bacilliformis*.

B. bacilliformis has also been reported in India, but the likely carrier is not dog, but tick.

Prophylactic inoculations with formalized suspensions of *B. bacilliformis* have resulted in producing partial immunity.

6. **ESPUNDIA** (Leishmaniasis Americana, Mucocutaneous leishmaniasis, Bupas Braziliana, Uta, Pian Bois, Forest Yaws etc.) is a disease confined to Central and South America in the area extending from Mexico to Buenos Aires.

It is characterised by ulcerating granulomata of the skin and later by lesions of the nasopharynx which often ulcerate. This is an infection of the skin and mucous membrane of the mouth and nose caused by *Leishmania braziliensis* transmitted by the bite of sand

flies *P. whitmani*, *P. persoai* and *P. migonei*, which become infected by feeding on a cutaneous lesion and after a cyclical development.

The only measure of control is by personal protection against bites of sand flies.

CONTROL (PREVENTIVE MEASURES)

1. A planned control is always essential and as such a sketch map of the area showing breeding places should be prepared which should include 100 yards area around the breeding places.
2. All cracks and crevices in the floor, walls, drains, culverts and nullahs should be closed. Wall cracks can be effectively closed by cowdung and earth plastering. Cracks about the edges of doors and windows should be filled up. Facing and pointing of building walls in particular bath rooms is useful.
3. The dirt, rubble from all corners should be removed and buried.
4. The earthen floors of cattle sheds should be stamped down. Easiest method is to dig the earth up to 2" deep, mix the loose earth with some heavy oil like used engine oil, diesel oil etc. and with a sprinkle of water the whole mixture is rammed down as the cattle shed floor.
5. Coating of tar at the junction of the wall and floor up to 3 ft. is advantageous.
6. Any place that provides moisture, darkness and organic matter should be attended to in sand fly infested areas.
7. Good lighting and adequate ventilation providing free flow of air, in building reduces the sand fly population. Fans are useful.
8. Painting and varnishing of doors and windows may reduce breeding.

CONTROL (DESTRUCTION)

1. Fumigation with sulphur or spraying with formaline or cresol are old methods.
2. Trapping of sand flies can be done by smearing electric light shades with vaseline or crude castor oil. Smearing on the bulb is not recommended as dim light will attract sand flies.

3. The long life cycle of the sand-fly, the low replacement rate and the constant adult destruction by the D.D.T. treated surfaces all favour the conclusion that in areas treated with D. D. T. solution, the phlebotomous population has been reduced to the vanishing point.

In Southern United States (Peru), one residual spraying of houses, walls and of caves, stone walls and other sheltering places with a 5 per cent solution in kerosene oil resulted in the control of sand-flies (*P. varrucarum* & *P. peruensis*) for more than 12 months.

In Greece & Levant, the residual application of DDT at 100 Mgms per square foot has resulted in striking reduction in the control of sand-flies and in sand-fly fever incidence. In Crete a sharp fall in the incidence of Oriental sore accompanied the reduction of sand-flies by D. D. T. spraying.

In India, *P. argentipes* & *P. papatasii* were effectively controlled by spraying the mud walls of huts with 2.5% and 5% DDT in kerosene at 6-7 gallons per 1000 square feet. A single treatment at 1500 Mgms per square feet controlled for 7-8 months and 750 Mgms for 4-5 months.

Gamma BHC (Gammexane) as a liquid containing 9% pure gamma isomer diluted 1:20 in kerosene and sprayed at 1 pint per 1000 square feet kept the pests away for a month.

Effect of Pyrethrum, gammexane & DDT spraying is summarised as under :—

INSECTICIDE	EFFECT ON (MORTALITY RATE)			
	ADULT	PUPA	LARVA	EGG
Pyrethrum 2%	Quick knock down	small percentage developed to next stage & no further.		
Gammexane 0.1 %	100% "	100%	94%	100 %
DDT Solution 5%	within 3 minutes 100 %	100% later date than BHC	76%	20%

The surviving stages did not develop into adults with any insecticide.

The spraying should be done on the inside walls of the houses especially upto 4-5 feet from the floor, on inner walls of cattle sheds, with special attention to corners and doors, window frames.

Spraying of outdoor resting places like bridges, culverts and other places as tree trunks, masonry walls, caves etc. gives a high degree of control.

Spraying of bed mosquito nets with DDT solution is also useful as an individual control measure.

CONTROL (PERSONAL PROTECTION)

The personal prophylaxis against the bites of sand-flies is the same as for mosquitoes viz :—

- i) Long sleeved shirts and trousers.
- ii) Application of essential oils as oil of Cassia on bare parts of the body is effective as long as the smell lasts. Out of the sand-fly repellents Dibutyl phthalate and Dimethyl phthalate, pyrethrum vanishing cream, Dimethyl phthalate (DMP) is commonly used. Effect of one application lasts 6-8 hours.
- iii) Sleeping quarters should be on first floor.
- iv) Provision of fans in living rooms repels sand-flies.
- v) A special sand-fly net with 45 meshes to square inch is worth the discomfort due to reduction in air movement. It saves suffering in the long run.

Spraying of the net with DDT is useful.

SUMMARY

Although sand-flies have a restricted infestation in our country, yet the areas where they are found, they cause excessive damage to humanity. The existing knowledge about the sand-flies, the diseases spread by them, ways and means to control the sand-flies have been described in this paper which would be found as a useful refresher for those concerned with sand-flies and public health.

CONCLUSION

Sand-flies are not much of a problem in India. They are still vulnerable to D. D. T. No resistance has developed among them as yet. The National Malaria Eradication Scheme will reduce the adult sand-flies but if side by side the breeding places of sand-flies are also attacked, much preventible sickness and suffering will be reduced.

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Oral Hypo-Glycaemic Agents in the Control of Diabetes

BY MAJOR A. KRISHNAN, M.B., B.S.
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RECENTLY the oral hypo-glycaemic agents have attracted the attention of the medical world and has raised the hopes of the diabetics, who earn for relief of the needle pricks. These drugs have been put to sufficient trial and have stood the experimental and clinical tests and thereby come to a stage when they can be safely used in general practice. Investigations and reports from many sources are so encouraging that they can be put to general use with adequate precautions and observations just as required in case of insulin. Though at present these drugs do not replace insulin, it might be the fore-runner of a related product which will be a boom to all diabetics. With the advent of these drugs the pathology of diabetes has to be revised.

The drugs that are at present in use are Carbutamide (BZ56) and Tolubutamide (D860). It was Carbutamide that was first started to be used for its hypo-glycaemic action in diabetes on a wide scale. It was later superseded by Tolubutamide.

HISTORY

Search for a satisfactory oral anti-diabetic dates back as early as 1927 when 'Synthalin' (decamethylene diguanidine) was developed. Davis observed that this substance induces degenerative changes in the a-cells of the pancreatic islets of normal rabbits. Janson while treating Typhoid, casually observed that I. P. T. D. (p-amino benzene sulphanilamide isopropylthiozodol) produced hypo-glycaemia. Von Holt in 1954 found that I. P. T. D. produces toxic action on a-cells of pancreatic islets, thereby producing hypo-glycaemia. This was followed N-butyl N'-sulphonilurea (B.Z. 55), the hypoglycaemic action of which was reported in 1955 by a group of German workers. Frank and Fuchs, Bertram and others. Further research has added Tolubutamide, which has a reputation of being less toxic than its predecessor Corbutamide.

CHEMISTRY

BZ 56 is a slightly yellowish crystalline substance the chemical name being N-sulphanil-N' butylcarbamide. It is a sulphanilamide compound.

Tolubutamide (D 860) is 1-butyl-3p-tolylsulphonyl-urea, a white crystalline compound. Tolubutamide differs from carbutamide in that it was a para-amino group replaced by a methyl group. It is not a sulphanilamide and it has no chemo-therapeutic action.

Both these drugs are rapidly absorbed from the stomach and the maximum blood concentration is reached in 2 to 3 hours. These drugs were found to have an important effect on the carbohydrate metabolism. From both animal experiments and clinical experience these groups of drugs were found to have remarkable hypoglycaemic effect in some of the diabetics. Though they bring down the blood sugar level in diabetics, they have no action on normal human beings.

There is a positive reduction of glycosuria after administration of these drugs; virtually reducing to no-glycosuria level. There is also reduction in the volume of urine excreted.

The response to the drug has no relation to the weight of the patient. There is no evidence to show that over-weight diabetics are more satisfactorily controlled than the under-weight patients. Some workers have reported increase in weight. Mary, Fredrick et al did not find any change, though they noticed a reduction in weight on discontinuation of the drug. Probably the increased in weight found by some and this latter finding indicate not too strict a dietetic regime.

It has been agreed by all workers that these drugs are not effective in juvenile diabetes. There is more satisfactory response in the middle-aged and the elderly group of diabetics.

Sex has no relation to the responsiveness or otherwise to the drug.

It has been agreed by all workers that these drugs are ineffective in the presence of sepsis or ketosis. Even while under treatment with these drugs, one has to revert to insulin when sepsis supervenes. As also

in cases where operation is necessary, a switch over to insulin is essential.

The effect on controlling the degenerative changes of diabetes have not yet been assessed. Some more years of trial with these drugs is necessary before any information is obtained. There does not seem to be any tolerance to these drugs. The same given for months acts satisfactorily. Even after intermittent treatment with these drugs, they are effective in the usual dose.

SIDE EFFECTS

Various minor side effects have been noted by several workers. Rash has been described, more commonly seen with carbutamide than with tolubutamide, probably, because it is a sulphanilamide. These rashes disappear on reducing the dose or on discontinuing the drug. Often repeating the drug after an interval does not cause rash. Anti-histaminics help to reduce the irritation, if any.

Blood dyscrasias have been described in connection with carbutamide, but has not been noted with patients treated with tolubutamide. Some workers have observed agranulocytic leucopenia and a marked drop in platelet count. Purpura has been noted by some earlier workers. These toxic effects usually manifest within the first few days of administration of the drug.

Boils have been observed during the administration of these drugs. A change from carbutamide to tolubutamide or viceversa make the boils regress. Various other minor side-effects have been described. Loss of appetite, nausea, vomiting and upper abdominal pain are some of them. These are more prominent when initial higher doses are given. Cutting down the dose is all that is necessary. Tolubutamide has a greater tendency to cause upper abdominal pain. Activation of duodenal ulcer has been described. Allergic manifestations may occur as in any other drug. No effect on liver or kidney function have been noted.

Relief of symptoms such as polyuria, thirst, pruritis have been obtained after administration of these drugs. Patients express a feeling of well-being and relief in subjective symptoms as the blood sugar is being brought down.

Those patients who, after a trial with these drugs, do not respond satisfactorily can be reverted back to insulin. Insulin acts in the same way in the same dose.

Earlier workers in Germany thought that only obese people responded to these drugs more satisfactorily. Frederick, Arnold and others did not find any difference in response, though a reduction in weight was noted in obese persons. Some diabetics were found to put on weight. The increase in weight may be due to not too strict a dietetic regime.

The mode of action of these drugs have not been explained exactly. A number of theories have been put forward by various workers ever since the hypoglycæmic action of these drugs have been found. The first suggestion about the mode of action of these drugs was that they inhibit the activity of a-cells of pancreas, Von Holt and others hold the view that the action is similar to I. P. T. D. (p-amino-benzene-sulphane amidopropylthiadazole.) This acts by not only by reducing the glycogen but also by stimulating secretion of insulin by b-cells. Professor Augustus Loubertiers did a no. of experiments on animals. He finds that administration of I. P. T. D. induces substantial hypo-glycæmia in a variety of animals. But in animals after removal of pancreas, the drug has completely prevents the hypo-glycæmic action, although it acts in partially depancreatized animals and also in moderate degree of alloxin diabetic animals. Based on this he presumes that these drugs have dual action; one stimulating the secretion of insulin by b-cells and two depressing the secretion of glycogen by the a-cells. Histological evidences do not show any destruction of these cells.

Some workers have observed varying degree of degranulation of pancreas which is interpreted as evidence of primary liberation of insulin by the cells. Some believe that prolonged use of these drugs leads to hypertrophy of these islets and eventual exhaustion of the islet system. But experimental and clinical findings do not show any evidence of this exhaustion. It is observed that in diabetics treated with these drugs for varying periods require only a small dose of insulin after the drugs are discontinued. It is also found when both the sulphonyl urea compounds and insulin are given, it is found that the dosage of insulin requirement diminishes; and in fact in some cases insulin can safely be discontinued after some time without any relapse.

Mirsky put forward the theory that they act by inhibiting the breakdown of insulin by insulinase. He found the enzyme in the liver and suggests a diminution of insulinase is associated with hypoglycæmia. It may be that they act on the carbohydrate metabolism partly by preventing destruction of insulin and partly by liberating insulin from the pancreas. The inhibiting action of insulinase is not accepted by many because these compounds do not act on very many juvenile diabetes.

Experimental evidences show that some of these drugs tend to increase the glycogen content of the liver. Based on this several workers suggest that the action on the carbohydrate metabolism may be through the hepatic enzyme system. Though experiments suggest that these compounds act by inhibiting glucose-6-phosphatase, therapeutic concentrations do not indicate the same. It is presumed the action is in the phosphorylase system by inhibiting the glycogen formation. Thus the liberation of glucose from the liver is impaired.

There are a few other theories, but none of the theories are conclusive about the action of these drugs in lowering the blood sugar. Further research and further clinical experiments, in the near future, will enable to find out more precise theories. For the present it is accepted that certain amount of endogenous insulin is necessary for these compounds to lower the blood sugar level. It is also found that there is no action on depancreatized animals and in alloxin diabetes.

TECHNIQUE OF TREATMENT

As a guide for the purposes of treatment the patients can be classified as follows; each case must be viewed individually.

1. Diabetics who have had no insulin therapy.
2. Diabetics who are already on insulin therapy, either small, moderate or large doses.

Diabetics who have had no insulin therapy.

It is agreed by all that a relatively high initial doses should be started and gradually scaling down to a minimum. The response should be assessed by urine analysis both in the morning and in the evening. The initial dose should be 4 to 6 tablets a day and the dose can be reduced by one tablet a day. It is always

better to take the tablets in divided doses soon after meals. Urine examination is a very good guide for adjusting the maintenance dose. Most patients need 2 or 3 tablets a day. Some workers have tried a larger initial dose but the response appears to be the same. Single dose instead of divided doses has also been tried but the reduction of blood sugar and urine sugar are the same in both. This suggests that the level of blood concentration is not the determining factor in lowering the blood and urine sugar.

Patients who are already on insulin therapy.

These patients need great care of the practitioners in switching over to oral drugs. In most of these patients this can be achieved at home. Only a small percent of them need hospitalisation for the change over. The change over can be made in one of the following ways depending upon the individual case.

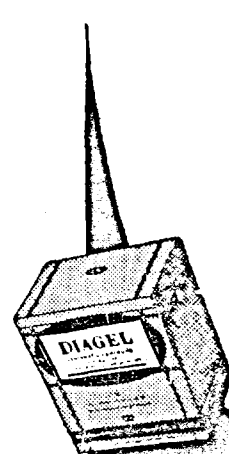
1. Abrupt change to oral therapy.
2. Combined therapy with gradual decreasing dose of insulin.

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Abrupt change over can be made in cases that are mildly diabetic normally needing small doses of insulin, say up to 20 units or less a day. The day following the stoppage of insulin, they can be given 4 or 5 tablets in divided doses and thereafter reducing the dosage by one a day till a maintenance dose of 1 or 2 tablets are reached. Examination of the urine daily, particularly in the evening is a good guide.

Combined therapy with gradual reduction of insulin.

These cases need the particular attention and good judgement of the practitioner. This group comprises those cases that used to take more than 20 units a day. More severe diabetics should be changed over under strict control of blood and urine sugar.

There are some diabetics who do not respond to these drugs. This possibility should be borne in mind while treating this group of patients. Non-response to these drugs may lead to severe consequences like ketosis, pre-comatous condition etc. hence the insulin should be gradually reduced and the oral medication started simultaneously. The following day after the usual dose of insulin 4 to 6 tablets are given and 20 units of insulin are given. Depending upon the severity of the case the insulin can be gradually reduced by 5 units a day and the oral drug also gradually reduced and brought to the maintenance level of 2 to 3 tablets a day. It is of primary importance that urine should be examined twice daily and the blood sugar more often than in the fore-going class of patients. It is this combined therapy with gradual reduction of insulin that offers the greatest measure of safety in moderate to severe diabetics. The chances of ketosis and coma are reduced to the minimum during the transitional period. At the same time one must remember the possibility of hypo-glycæmia. This is rather rare and easily over-come if it occurred. Change over under cover of insulin is the best for long-standing and rather severe cases of diabetes.

In the earlier days of use of these drugs in diabetes, most workers warned that the change-over should be done in hospital and under strict biochemical examination, but now more is known about these drugs that any general practitioner can do it with a little care

and judgement. All patients should have their fasting and glucose tolerance tests done before the treatment started, and the mode of change over determined. During treatment examination of the urine once a day or twice is all that is necessary in most patients. In a few patients who have a severe type or who have high renal threshold more frequent blood examination is necessary. In others a random blood sugar periodically will be enough.

It should be emphasised that all patients do not respond to these drugs. Also only a very small percentage of juvenile diabetics respond. There are no tests to distinguish the diabetics who are likely to respond to these drugs. A trial for a week with the drug will determine the response or otherwise. Diabetics round about the age of 40 or more are admirably suited for this therapy. It should not be tried on those who have a tendency for ketosis or who have sepsis. Such patients should be put on insulin till the sepsis clears and then only these drugs should be tried. All cases of diabetes round about the age of forty and diabetics of short history of duration are worth a trial with these drugs. The trial should last for a week at least and the response assessed. At the end of the trial period an examination of urine and blood, if necessary should be done. If there is a substantial reduction in urine and blood sugar, the case can be considered to be responsive and further treatment continued. Examination of urine twice a day is indispensable during the trial period. If it is considered that the urine sugar is not showing a downward trend or if it is increasing the trial should be given up and insulin resumed.

At the end of trial period, in responsive patients a maintenance dose should be arrived at, and continued. Intermittent administration has been tried but it is not satisfactory. After discontinuing the drug the urine and blood sugar remain near the normoglycæmic level for 3 or 4 days and then rises again. So intermittent administration is not advised.

Patients on these drugs do not show any resistance to insulin. Also diabetics who have discontinued these drugs for sometime can easily be restarted on them again.

NON-FOGGING MIRROR

A Device to prevent fogging of dental mirrors has been granted a patent by the U. S. Patent Office. Invented by Allan W. O'Hara, of Kingston, Ontario, the instrument carries air under pressure and distributes it over the surface of the dental mirror. The air-tube may be incorporated in the handle, or clipped to the conventional mirror.

AGING IN HARNESS*

What it Means to Management, Stockholders and the Individual Worker

BY DR. ROBERT COLLIER PAGE, M.D., F.A.C.P.,

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RETIREMENT has been too long thought of purely in terms of severance. It is too often looked upon as something essentially negative. After a certain amount of financial planning and perhaps a few sessions devoted to advice and guidance, the retireable individual is given a gala send-off, complete with gold watch, and then, as far as the company is concerned, he ceases to exist.

This view of retirement cannot lead to constructive retirement planning. It is often not even realized that retirement planning can and should be constructive, not only in the interest of the retired individual but in the interest of his company.

The executive in charge of over all retirement plans and policies will say:

"Of course we owe our people a decent retirement. We want to see to it that they're all set up, with a home and enough to live on after they leave us. That's not only good human relations; it's good community relations. But that's as far as retirement planning can go. You can keep on improving pension plans and various retirement insurance deals, but what can you do that's really constructive, outside of building up the people who are to replace the ones going into retirement?"

To answer this it is necessary to analyze what retirement really means (not what it seems to mean) to an employed individual in terms not only of his wants and needs but of his actual productivity as well.

Everyone realizes that the employed individual himself can be constructive or otherwise in *his own* planning for retirement. He can arrange his finances

wisely or foolishly; he can conserve his health or burn himself out ahead of schedule; he can develop a philosophy of life that will keep him in harmony with the facets of aging, or he can fight life. But in the end, what he does about such matters is up to him. His company can counsel him and that is all.

How then can retirement planning be constructive from the point of view of the company as well as that of the individual?

First, the severance aspect of retirement should be trimmed down to size. It is the least important part of the retirement story. To make it the be-all and end-all of retirement planning is the same as to spend days writing an elaborate *cantata* just as a build-up to a grand Amen at the end. Constructive retirement planning begins many years before the actual act of severance, and ends many years after it. The severance itself is (or should be) merely an incident along the way.

Just to bring the significant aspects of retirement planning into proper focus, it might be a good idea to forget severance altogether, and think in terms of *AGING IN HARNESS*. In other words, retirement procedures should be *operating* procedures, having to do with men who are producing, but whose productivity is undergoing changes in keeping with the aging process. Retirement planning should set policies for dealing with each individual from the *onset of aging* (at a time when he has not yet reached his peak of productivity) through the twilight years when duties must be modified periodically in keeping with his normal changing ability to perform,

Just when is this "onset of aging?"

*Presented at the Second Annual Seminar of (July 1958) The Retirement Council Inc., Princeton, New Jersey.

This, of course, varies with the individual. The irreversible physiological changes that mark the beginning of the aging process may appear in some individuals in their late thirties, and may in other individuals be postponed until the middle forties. For all practical purposes, it is usually most expedient to set an arbitrary age of 40 or 45 as the date of the "onset of aging," and institute a program of retirement planning for each employed person as he reaches that age.

Any one with the old-fashioned view of retirement may be shocked at the idea of applying retirement procedures to individuals under 50.

"Sure," he will say. "We bring them into the pension plan as soon as they join the company so that they can build up an equity for themselves. But otherwise we don't worry about their retiring until they're past 60 and ready to slow down a bit. Hell, a man in his forties often hasn't really started to produce yet. Nearly all of our best executives are in their 50's or 60's, and most of our best salesmen are past 40. The same is true of the skilled men in our machine shops and our clerical people. Why should we start think about retiring them when they haven't even hit their stride yet?"

This is how the idea of severance comes to dominate retirement planning.

It should be borne in mind that any individual who has passed 45 is a potential candidate for a health setback that can put him out of gainful occupation overnight. This of course will not happen (at any rate not with surprising suddenness) if the individual is a participant in a constructive retirement program, involving periodic assessment of aptitudes and adjustment as well as physiological and psychological health.

In the absence of such a program, however, it must be assumed that every single employed person is in danger of becoming totally and permanently disabled at any moment. The most promising junior employee in the company may call up the day he is to step into his new job as sales manager and announce that his doctor has told him he can never work again. The irreplaceable technician may have a crippling stroke in his laboratory at a time when the shortage of technically trained men was never so acute. The expensively trained, newly appointed shop foreman may have a cerebral hemorrhage before any of the

green men under him have learned to do their own jobs adequately, let alone step into his shoes.

These are the big things that can happen. Then there are the little insidious things, that can creep in with the aging process in the absence of a constructive program. The loyal and efficient file clerk who has been with the company for twenty years may become snappish and slovenly in her work. The indispensable secretary to a key executive may develop an astonishing absentee record, with a wide range of excuses. The dynamic department head may show a creeping tendency to make ill-advised snap decisions and wear a chip on the shoulder when called on the carpet. The eager beaver vice president who has always put the company ahead of wife, children, and friends may suddenly begin to appear in various downtown saloons when he is supposed to be off on certain not-too-well-defined "public relations missions" (for example: representing the company at the annual banquet of the Keep Our City Beautiful Club.)

Assuming that all of these people were once highly competent, and assuming that there has been no change in the nature of their jobs, the changes must be taking place within the individuals themselves. If upon analysis, it is determined that these changes are progressive, and have to do with the aging process, then it can be seen that these people are moving toward retirement at varying rates of speed, and should therefore be dealt with as potential retirable persons—not as of age 65—but as of any time, perhaps as of tomorrow.

The aging process brings about in all of us, physiological and psychological changes which can, if ignored or uncompensated for, put us out of action with shocking rapidity. Hence, it follows that everyone past 45 (or better yet, past 40) should be looked upon as someone who might have to be replaced without warning at any minute. From this, it follows further, that everyone past 40 (being on his way to his peak of performance) should be maintained as scrupulously as the most valuable piece of machinery, and assessed periodically, with an eye to postponing his retirement as long as practicably possible. Many businesses set up constructive depreciation programs with respect to machinery, under which the emphasis is on maintenance of the equipment and *retarding* depreciation, not on mere cold-blooded preparation for depreciation itself. This thinking should underlie retirement planning.

At this point, the old-fashioned retirement planner will say.

"That's all very true. People do have sudden illnesses, and they can cause a tremendous amount of extra expense and trouble. But that still needn't come under the heading of retirement. It comes under sickness and accident. Most people who are employed are covered by insurance. Some of them have their own policies in addition to company group insurance."

There are a number to rebuttals to this argument. First, it should be observed that the argument does not distinguish between younger and older employees. In the majority of cases, when a young person takes advantage of medical benefits, it is because of some infectious disease which is completely curable and which puts him out of action only temporarily. There are, of course, exceptions to this, but they are rare.

On the other hand, when a person in his 40's or 50's has to take advantage of health insurance, it is more likely than not that his illness has to do with aging, and that it is not wholly curable. Every illness is likely to bring him an irretraceable step closer to retirement.

From the point of view of everyone concerned—the employer, the stockholders and the employee himself—the ideal solution is to prevent such illnesses and arrest the aging process insofar as this is humanly possible. If the illness is unpreventable and the aging process uncontrollable; in other words, if premature retirement is inevitable, it is at least desirable for all concerned to know in advance *what* physiological or psychological changes are going to take place, and *when* these changes are likely to occur.

It is obviously that no kind of mere financial coverage can accomplish either of these ends. Such coverage serves a useful purpose in that it removes some of the financial complications of illness and tends to eliminate the old practice of self-deception about illness. ("I can't afford to be ill; therefore I am *not* ill.") All this, however, is secondary, and does not get to the heart of the matter. What is important in the case of those who are aging in harness is not to treat them hopefully (but often rather futilely) *after* illness strikes, but to detect illness in its

incipiency while it still may be eliminated or kept at bay.

In other words, health planning and retirement planning are *one and the same thing* when one is dealing with the individual who has crossed the border into his middle years. Health and retirement cannot be put into two separate pigeonholes—one crammed with insurance benefit plans, the other with pension arrangements. Insurance plans and pension arrangements are important, but they should be a matter of routine; they should be taken as supplementary to the primary goal of planning, which is to keep every individual happy at his job and fully productive within his natural limitations while he is undergoing the aging process. The questions to be asked about any individual past 40 are not "how is he provided for in case of sickness?" nor "when will he retire, and on how big a pension?" but "what are his peak capabilities, how can he be kept at his peak for the longest possible period of time, and how can he be most gradually and painlessly decelerated after he has passed his peak?"

Not only is this attitude a sound one from the point of view of the stockholders, but it is coming to be more and more a part of the thinking of organized labour, which has weighed most health insurance plans and purely fiscal retirement plans in the balance and found them wanting insofar as the aging worker is concerned. The United Auto Workers of America have sponsored a widespread community health plan in Detroit which makes sense to me, from the standpoint of management as well as labour, in that it goes directly to the heart of the matter.

This plan, which is similar to the Health Insurance Plan in New York and the Kaiser Plan on the west coast, offers its participants what they really need: *quality medical care*. Theoretically, this is what all health insurance programs offer, but in practice it doesn't work that way.

The early health insurance programs were designed to cover (or partially cover) hospital costs, which were, for most people, the most expensive part of medical care. It was hoped that this coverage would make medical care available to anyone who could afford to pay the then negligible premiums. Group plans covering all the employees of participating industrial concerns extended this coverage to the majority of American employed people, and it looked

as though we were on the threshold of a new era of health for the rank and file.

The result of this was that hospitals soon found themselves crowded with people who had never before been able to afford hospital care. These institutions had to expand or burst, and in the process of expanding they had to keep up with the rapid advances of medical technology. Moreover, they had to compete for manpower at a time when this commodity was in short supply. As a result, hospital costs zoomed upward faster than insurance benefits could keep up. It became necessary for the underwriters either to raise premium rates or reduce benefits. In many cases they did both.

At the same time that the participants in these plans were becoming sharply aware of the fact that hospitalization was becoming increasingly expensive in spite of their insurance, they were also finding out that hospitalization was only a small part of the medical care picture.

Older people in particular were coming to the realization that the kind of medical care that was most likely to count was the kind designed to keep them out of the hospital. An aging circulatory system, for example, may not call for hospitalization until it is too late for any kind of effective medical care; what is more likely to be needed in this case is diagnosis, early detection, and prevention of complications while the individual is still on his feet—vertical and on the job.

Even among younger people it becomes apparent that coverage of hospital costs alone was not the answer to the medical care problem. The majority of these people could go for years without requiring hospitalization. Their main problem was doctors' bills for the sort of problems that could be treated at home or in the doctors' office. Sometimes a doctor, realizing that a patient might be financially embarrassed, would send him to the nearest hospital for simple diagnostic services that could be done just as easily in the office. This would enable the patient to take advantage of his hospital benefits, but it also tended to complicate the already serious overcrowded condition of the hospital.

Inevitably there grew up a demand for a type of health insurance that would pay doctors' bills as well as hospital expenses. Such coverage was bound to

be tricky; there were innumerable possibilities for abuse; hence the coverage had to be rather severely limited.

For example: It was extremely difficult, if not impossible, to prevent unscrupulous doctors from offering a minimum of medical service for the maximum fee possible under the terms of the coverage. There was nothing to prevent the insured from seeking incompetent help in order to get the most for his allowances, in terms of quantity—not quality—medical care.

Moreover, since plans of this sort provided only funds for medical services, with no control over the kind of medical services obtained, it was virtually impossible to provide coverage for preventive or diagnostic measures. It was almost impossible to prove whether a payment for diagnostic or preventive services was valid, legitimate and reimbursable. Hence, coverage was limited to after-the-fact treatment, which is often too late, particularly in the case of the older insured person.

Premium payments for major medical expense, involving what might be called catastrophes, such as the need for heart surgery, installation of major prosthetic appliances, excessive periods of hospital rehabilitation and the like, were necessarily too high for the average pocket book. For this reason, the majority of people were willing to take a chance on the big disasters, while they protected themselves against the small ones. As has been pointed out, many of the small ones were almost too small to demand any medical attention whatever, but since they were covered by insurance they were assiduously seen to. The man with a minor sprain of the umb availed himself of elaborate medical care, including a night at the hospital for x-ray examination, as long as his insurance was paying the bills. Unwittingly he was doing his bit to compound the confusion in the general medical care picture; at the same time he was helping boost health insurance rates and reduce available medical benefits.

Then, one day, perhaps, this same individual had a serious health set-back. He was, let us say, 45, and suffering from a previously undetected progressive condition which had to do with the fact that he was aging. Had this condition been detected in its incipency it might have been corrected, or placed under sure control. Now it was too late for this. It

was necessary for the patient at this stage to undergo a long-drawn-out and costly treatment which would keep him away from gainful occupation for many months. Moreover, even after discharge from the hospital he would have to face life as a chronic invalid, and make some radical adjustments in his work schedule.

At this stage, he realized that in spite of his coverage (even if he had been willing and able to supplement his regular sickness and accident insurance with major medical insurance) he had not really assured himself of any kind of effective medical care.

As a result, the demand today is only secondarily for the money with which to pay doctor's and hospitals. The big demand is for the *medical care itself*.

Constructive medical care means *maintenance* along the way; not just *repair after the fact*. A good mechanist *keeps* his equipment in shape from day to day; he doesn't wait for a machine to break down before oiling it. The same principles hold true with regard to the maintenance of human beings.

The U. A. W.—sponsored health plan, like the H. I. P. plan in New York, and the Kaiser plan in the west is based on this idea of human maintenance. These plans differ considerably in detail, but in essence they are similar. Benefits include not only payments of medical expenses but actual medical services, rigidly supervised, with emphasis on diagnosis and early detection or prevention of illness instead of after-the-fact treatment.

The same constructive kind of thinking can be applied by any business, large or small, to the problem of manpower that is aging in harness. Instead of focussing attention on how to pay doctors' bills before the final day of severance or how to build up a pension fund for *after* severance, management should concentrate on the job of bringing out the best in its human beings, of understanding them, of keeping them fit for the jobs best suited to them, and of preparing them for the normal changes that will come with aging.

This is good dollars-and-cents business as well as good human relations. Any one who can read a balance sheet or a profit and loss statement should be able to reason this out. Take for example the specific case of Jæ X, composing room foreman in a

(Continued on page 76)

printing shop. Jæ's employer knew the value of constructive health maintenance; seasoned experts like Jæ were not easily replaced. In the front office there was a complete file on Jæ, covering his aptitude, his strong and weak points, his known likes and dislikes, his mental attitudes, and his health. After Jæ's 40th birthday, the boss saw to it that this file was taken out and brought up to date at fairly regular intervals. This involved medical evaluation by Jæ's own doctor from time to time, at a pre-arranged cost which was not high. Since Jæ's doctor knew him and saw him at sensible intervals, he did not need to "give him the works" in the course of each visit. The doctor knew what facets of Jæ's health needed careful watching, and what facets could stand a "once over lightly" or could safely be taken for granted.

In the course of one of these routine visits the doctor noticed the early signs of incipient diabetes. Jæ was alerted, and modified his life accordingly. In a subsequent visit, it was noticed that suppressed resentment over a misunderstood job assignment was threatening to undermine Jæ's value as an employee. Since this was discovered in its early stages, the problem was easily ironed out.

Jæ is now 62 and is still an efficient employee. He knows the limitations imposed by his age, and he is gradually relinquishing his authority to a younger man who will be fully able to take over when Jæ comes up for retirement. Jæ's mental attitude toward retirement is good. He knows what he can and cannot do, and he knows what he wants out of life. He acquired this knowledge as a result of constructive maintenance while he was aging in harness. His value to his employer and to the stockholders of his company has far exceeded the modest sums expended in *keeping* him vertical and on the job. Not only has he been able to turn in his best potential performance on the job, but he has been absent only four days out of eight years.

If Jæ's employer has been content to handle Jæ's potential health problems merely by setting up some sort of group medical costs insurance plan, Jæ would in all probability have acquired a full-blown case of diabetes. This would have come as a nasty surprise, perhaps with serious complications, and Jæ would have found himself, despite his coverage, deeply in debt to his doctor and hospital. Moreover he would

THE SURGERY OF THE HEART

BY DR. GEOFFREY FLAVELL, F.R.C.S., M.R.C.P.

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SINCE the end of the Second World War, one of medicine's greatest single advances has taken place—the surgical conquest of the heart. This organ, hitherto surrounded by an almost superstitious barrier of fear, has proved to be a sturdy muscle-pump as tolerant of surgical interference as any other structure; and the obstructions and leakages which occur within it can, and must, be relieved as urgently and as effectively as strictures or fistulae in the urinary tract, the bowel, or the bronchial tree. Furthermore, in the heart as elsewhere, it is better to correct such defects before they cause secondary changes which soon become irreversible.

Many corrective operations on the heart and its great vessels are performed without interfering at all with the flow of blood through it. Others call for the brief arrest of this flow, for periods up to six or seven minutes. As the brain suffers permanent damage when deprived of oxygen for more than three minutes, it is first necessary to diminish oxygen consumption by lowering the body temperature to 30°C so that cell activity is greatly decreased. This process is called hypothermia, and gives sufficient time for some operations to be performed under direct vision within the atria, but not enough for more complicated and lengthy procedures within the ventricles. For these it is necessary to bypass the heart, oxygenated blood being supplied to the brain and the rest of the body either by some form of mechanical heart-lung pump, or by



Fig. 1 (a)

Fig. 1 (a) The two leaflets of the mitral valve leave a wide orifice between them through which the blood flows from left atrium to ventricle.

(b) In rheumatic disease these two cusps become adherent so that the mitral orifice is greatly diminished.

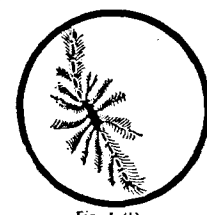


Fig. 1 (b)

means of cross-circulation through the body (and consequently the heart) of another individual.

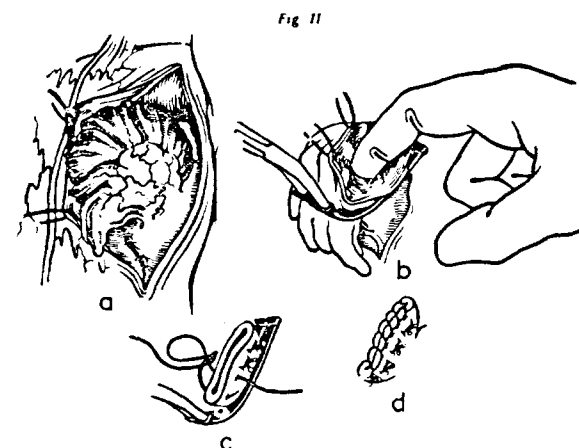
Unxygenated, venous blood returns from the tissues to the heart by way of the superior and inferior vanae cavæ, entering first the right atrium. Thence it passes through the tricuspid valve into the right ventricle which pumps it out through the pulmonary artery to take up oxygen in the lungs. From them it is returned fully oxygenated to the left atrium, and passes via the mitral valve into the left ventricle which in turn contracts to drive it out into the peripheral circulation by way of the aorta. Blood is prevented from returning to the heart either from the pulmonary artery or aorta during the phase of relaxation by valves which separate these two great vessels from their respective ventricles.

The heart thus has four valves, each designed to facilitate the onward passage of blood and to prevent its reflux. Either as a congenital abnormality, or

(Continued from page 75)

have lost many days on the job, creating innumerable snarls in the shop schedule. If he had survived all this, there is no telling what the later *resentment situation* might have done to him. Because it was his nature to bottle such things up, the situation would not have come to light in its early stages. By degrees Jæ would have become an inefficient, senile, thoroughly sick person. Just how much he would have cost his company cannot be accurately determined, but common sense says that it would have been much more than he actually did cost his company under a constructive health maintenance program.

Every company has more than its share of Jæes who are either burning out ahead of schedule or are carrying within them the unseen beginnings of irreversible illness. For the sake of the stockholders, for the sake of management, for the sake of the employed individuals themselves, constructive programs need to be gotten underway which will put the accent on *Man talent Development*, on *Human Maintenance*—not on after-the-fact patch jobs. This philosophy belongs at the core of all personnel planning, all the way from recruitment through retirement.



The illustrations to this article are published by kind permission of the Oxford University Press and are taken from "Introduction to Chest Surgery" by Geoffrey Flavell.

(far more often) due to acquired disease such as rheumatic conditions any one (or more) of these valves may become stenosed so that the ventricle behind the blockage labours in vain to force blood through its insufficient orifice; or they may be rendered incompetent, so that blood regurgitates with each heart-beat against the farward stream, causing progressive distension of the related chambers, and ultimate heart failure.

In practice much greater success at present attends the surgical relief of obstructed than of leaking valves, and effective cure of the latter awaits further development of a satisfactory artificial heart. On the other hand, the surgery of mitral stenosis is a resounding triumph, and of all cardiac operations has brought most benefit to most people.

In addition to defects of the valves, caused mostly by disease, deficiencies (invariably congenital in origin) sometimes exists in the walls separating the heart chambers, so that oxygenated blood from the left side of the heart (in which the pressure is normally higher) flows freely into the right side causing its distension. Hypertrophy of the right ventricle ensues, and if the pressure within it rises sufficiently, flow through the defect is reversed and the consequent admixture of unxygenated blood causes cyanosis. In any case such fistulae are incompatible with long life, and surgical closure is therefore desirable. Atrial septal defects are dealt with under hypothermia; but deficiencies in the wall between the ventricles cannot be closed in the short

time available, and for their treatment an artificial heart-lung or crossed donor circulation is necessary.

A comparable leakage occurs when the ductus arteriosus, a vessel just outside the heart itself, bypassing the lungs by joining the pulmonary artery to the aorta during foetal life and normally closing at birth, remains patent. It is generally closed surgically by simple ligation. Another congenital abnormality which though itself extra cardiac, exerts its effects upon the heart and is curable by surgery, is coarctation of the aorta. This is an area of extreme narrowing of that great vessel close to the point at which the ductus joins it. It is treated by local excision, the cut ends of the aorta being then rejoined.

MITRAL STENOSIS

Although some of the more recent operations upon congenital heart deformities in children attract much publicity it is necessary to keep a sense of proportion: 25 per cent of all cardiac invalidism is associated with rheumatic heart disease, only 2½ per cent with congenital defects; and in more than half of the former the predominating lesion is mitral stenosis. This represents more than a quarter of a million people in Britain alone, of whom a great many can benefit by surgery.

Mitral stenosis, which is four times commoner in women than in men is caused by the two leaflets



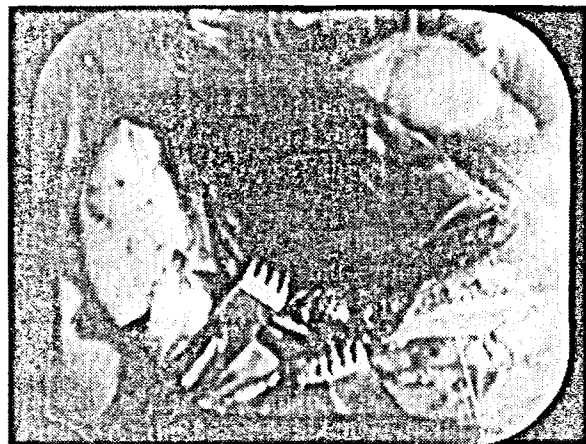
A miniature Pye industrial television camera looks down at the operating table at the Hospital for Sick Children, Great Ormond Street, while famous surgeons from all over the world watch on screens in a lecture room five floors below. During the afternoon five operations, including a hare-lip operation, a hernia operation, a heart operation and an abdominal operation, were carried out.

of the mitral valve becoming stuck together so that only a small orifice is left through which blood can pass from the left atrium to the left ventricle. As a result blood is dammed back in the atrium, in the lung, and in the right ventricle which labours in vain to force it on. The right ventricle enlarges, and the lungs become congested with blood which the patient sometimes spits up. In contrast insufficient blood gets through to the left ventricle (which therefore remains small) and to the peripheral circulation, so that patients with mitral stenosis tend to have cold hands and feet and to have a pinched look, with the reddened or bluish nose and cheeks one sees in everyone on very cold days. The chief disability of such patients is breathlessness which increases with effort and with time. They may be quite unable to do house work or climb more than a few stairs at a time. Pregnancy is particularly dangerous, and often had to be terminated. Today it is instead an urgent indication for operation. Atrial fibrillation is common, and eventual heart failure likely. Clots from the semi-stagnating blood in the left atrium may become detached, reach the brain and cause serious paralysis.

As the whole mechanism of the mitral valve is impaired by the disease, some reflux through it during the heart's contractions is likely. In addition, rheumatic inflammation may have caused damage to the aortic valve. It is of great importance to decide whether a patient's symptoms are caused chiefly by obstruction (which can be relieved by surgery) or by these other lesions (which may be made worse by it).

Changes in the heart sounds help to distinguish between the two; but the final decision depends on the relative size of the ventricles; if the right is greater, obstruction is predominant, if the left, leakage; and operation is then contraindicated. Surgery is seldom advised under the age of 20, lest rheumatic activity still be present; or over the age of 50, for by that time the heart muscle itself is likely to be damaged and unable to respond to new demands. The onset of symptoms is commonest in the early thirties, the average period of survival from their commencement 18 years, and the average age at death 47.

The surgeon's object is to separate completely the adherent valve cusps so that normal movement and function is restored and obstruction wholly relieved. As interruption of the blood flow is only momentary



The photograph shows a picture taken off the screen of a monitor during the operation on the heart.

an ordinary general anesthetic is all that is required. The heart is approached by an incision between the ribs of the left chest, the lung retracted, and the pericardial sac opened. The preoperative findings are confirmed by direct examination of the heart.

A light clamp is placed across the base of the atrial appendage—a small pouch easily isolated—whose wall is then cut with a knife sufficiently to admit the right index finger. The clamp is removed to allow the entry of the finger into the atrium itself, and as the finger fills the incision in the heart wall no blood is lost at all.

The mitral valve is carefully felt, the size of the orifice and the shape and mobility of the cusps being determined. If the latter are greatly thickened and retracted so that the whole valve resembles a fibrous cone it is very unlikely that a good result will be obtained even after complete separation of the leaflets, for they clearly will never be able to function as a normal valve again. This is the consequence of long-standing disease, and is an argument for surgery early rather than late. In about a third of the cases actual calcification of the cusps is already present.

If possible, splitting of the adherent valve is carried out with the finger; but often this is wholly impossible, or incomplete. A special knife attached to a finger ring is therefore employed and the leaflets completely cut apart so that the full width of the mitral orifice is again available for the blood to flow through. As the finger is finally withdrawn from the heart, the clamp is again applied to the base of the

appendage. The latter is then amputated, its stump securely sewn up, and the clamp finally removed.

Most patients are able to get out of bed in about two weeks' time, and usually at once feel able to breathe more freely and notice their hands and feet to be warmer. The full benefit of surgery are not apparent for some three or four months, but in 60 per cent of patients are dramatic: they are often able to swim, play tennis or even climb quite formidable hills. The operative mortality in skilled

hands is less than 4 per cent.

The really astonishing thing about this operation is that whereas we tend to associate it with the names of such present-day surgeons as Brock in Britain or Bailey in USA, it was in fact first performed in 1925—and with perfect success—by Sir Henry Souttar in the very theatre where I now work. No cardiologist would ever trust him to do it again!

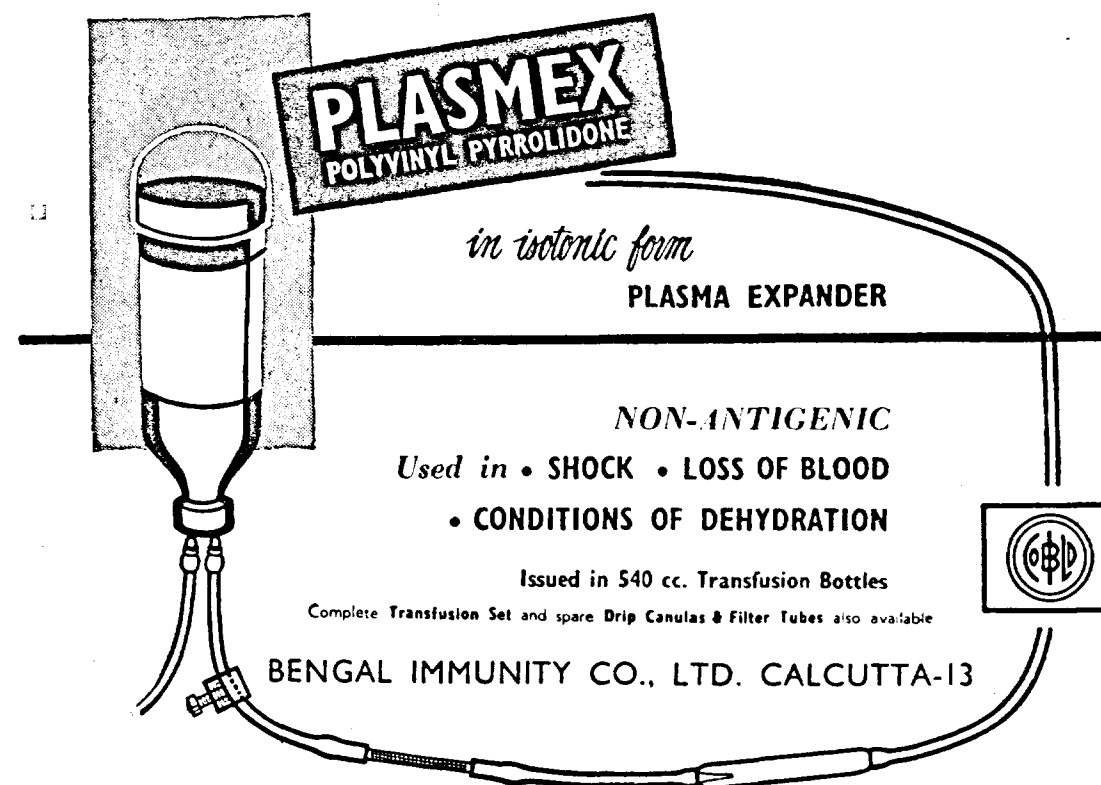
(Photos: Courtesy: N.A.P.T. Bulletin)

VITAL STATISTICS on the dental laboratories of the U.S.A. will begin rolling in late this month as questionnaires are filled out by some 6700 establishments.

Information is being sought on laboratory personnel and facilities, economy of operation, as well as other matters of interest to the dental profession.

Conducting the survey are the A.D.A.'s Council on Dental Trade and Laboratory Relations and the Bureau of Economic Research and Statistics.

TELEVISION ADVERTISING of secondary dental products such as toothpastes, brushes, etc., jumped sharply upward at the beginning of 1958, while newspaper advertising of these products declined. According to ADVERTISING AGE, a 112 per cent increase in expenditures for TV spot commercials was made in the first quarter of this year, compared to the similar 1957 period. Newspaper ads for dentifrices dropped from \$ 7 million in 1956 to \$ 4 million last year.



ANTI-TUBERCULAR ACTIVITY OF SESAMIN AND RELATED COMPOUNDS

BY DR. A. S. RAMASWAMY

Pharmacology Laboratory, Indian Institute of Science, Bangalore.

SESAME oil also known as gingelli oil is obtained from the seeds of a herbaceous plant *Sesamum Indicum* Linn [N. O. Pedaliaceae] of which several species are known. There are two species of sesame as (1) *Sesamum Indicum* which produces white or yellow seeds, and (2) *Sesamum Orientale* which produces dark (red or brown) seeds. According to A de Caudelle (cited from Jamison, 1943) sesame seed was brought from the Sudan Islands to India several thousand years ago and has migrated thence through the Euphrates basin to Europe.

The sesame seed is rich in oil (50%) and proteins (20-25%). The oil is processed for use as a cooking oil and is used in almost all parts of our country in various forms both for dietetic and other purposes. It is also used in making margarine, in the manufacture of soap, in perfumery and also in pharmacy.

Sesame oil has been recognised by the indigenous system of medicine to be one of the very essential foods for the upkeep of the body. In order to keep the body free from 'Kapha' diseases (diseases like tuberculosis where much loss of phlegm occurs) this oil and its preparations are much in use. It is recommended in Ayurvedic system of medicine for several ailments such as dry cough, asthma and diseases of the lungs.

The data on the chemistry of *Sesamum Indicum* is scanty in the literature and relevant information available has been presented here along with some anti-tubercular activity shown by a minor component of sesame oil and its isomer asarinin in this laboratory.

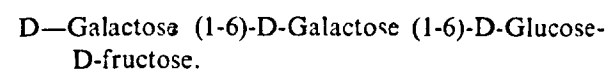
Chemistry of *Sesamum Indicum* seeds :—

The analysis of the chemical composition of *Sesamum Indicum* seeds has been made and has been shown to contain unusual but very interesting chemical components. The glyceride composition of the sesame

oil has been studied by Hilditch and Riley (1945) and has been shown to contain the following fatty acids.

Component Fatty acids	(% wt.)
Saturated : Myristic acid	0.1
Palmitic acid	9.1
Stearic acid	4.3
Arachidic acid	0.8
Unsaturated : Hexadecenoic acid	0.5
Oleic acid	45.4
Linoleic acid	40.4
Unsaponifiable fraction	0.5—1

The carbohydrates of sesame seeds has been studied recently and shown to contain a tetrasaccharide—stachyose and an unknown trisaccharide. Probably α -galactosido-B-fructosidoglucose (Planteose) by Hasegawa et al (1951). The significance of the presence of these unusual polysaccharides is not known. The structure of stachyose is



5:6

The sterols of sesame oil has been shown to be Δ stigmasterol (Allan and Moore, 1927).

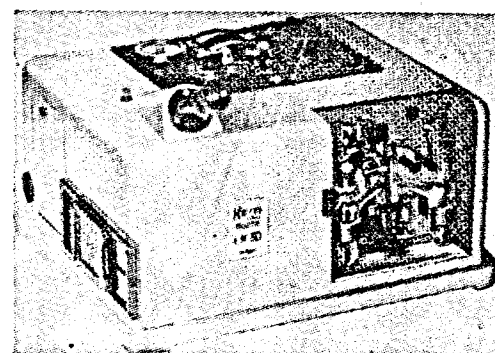


Fig. 1 (a)
Kern's Micro-electrophoresis apparatus.

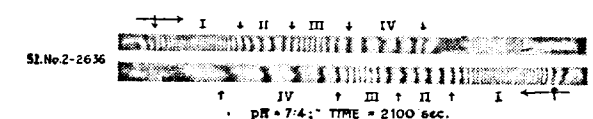


Fig. 1 (b)

Electrophoretic patterns of protein components (Sesame globulins.)

a. ascending. d. descending. -I
ionic strength. O. I. voltage gradient 4v cm

PROTEINS AND AMINO ACIDS

Jones and Gersdorff (1927) have studied the sesame proteins from the sesame seed meal and have isolated 2 globulins and other unidentified fractions. Ravindranath and Giri (1957) have made a detailed study recently using Kern's micro-electrophoretic instrument yielding an interferometric band pattern (Lotmer 1951). The apparatus is shown in fig. 1 (a) They have obtained four fractions designated as α , β , λ and δ components and the results obtained are given below compared with proteins from cotton seed meal and peanut meal (Karon et al, 1950) in Table I.

TABLE I

Electrophoretic analysis of proteins from seed proteins (ionic strength 0.1; pH 9.17; temp. 1°C)

$-u \times 10^3 \text{ cm}^2 \text{ v}^{-1} \text{ Sec}^{-1}$ (Relative areas % in brackets)

No.	Oil seed	Globulin fraction			
		α	β	λ	δ
1	Cotton seed-meal	5.6 (25)	4.1 (54)	1.8 (10)	1.1 (11)
2	Sesame meal	8.8 (14.5)	6.4 (51.5)	3.9 (10.0)	2.4 (24)
3	Peanut meal	6.8 (86)	5.3 (4.0)	4.2 (5.0)	3.1 (5.0)

It will be seen from the data presented that the sesame seed protein resembles more closely to the cotton seed proteins.

The amino acid composition of the sesame seed meal has been made by Ravindranath and Hanumantha Rao and Giri (1957, Part III) on the four globulins separated, using paper chromatographic methods and

the results of the investigations are give in the Table 2.

TABLE II

Percentage amino acid composition of sesame protein fractions
(Calculated to 16% nitrogen basis)

Sl. No.	Amino acids	(globulins) Sesame fraction		
		I (α) (1)	II (β) (2)	III+IV (3) (λ and δ)
1.	Cystine	3.50 $\pm$ 0.10	2.53 $\pm$ 0.10	3.13 $\pm$ 0.20
2.	Lysine	2.90 $\pm$ 0.24	2.55 $\pm$ 0.14	2.80 $\pm$ 0.26
3.	Histidine	3.60 $\pm$ 0.20	3.20 $\pm$ 0.20	2.50 $\pm$ 0.10
4.	Arginine	8.40 $\pm$ 0.26	7.46 $\pm$ 0.20	9.26 $\pm$ 0.40
5.	Aspartic acid	4.34 $\pm$ 0.22	6.56 $\pm$ 0.30	5.10 $\pm$ 0.10
6.	Serine	3.17 $\pm$ 0.10	2.62 $\pm$ 0.17	3.16 $\pm$ 0.17
7.	Glycine	3.45 $\pm$ 0.10	2.55 $\pm$ 0.17	2.42 $\pm$ 0.10
8.	Glutamic acid	7.83 $\pm$ 0.10	8.36 $\pm$ 0.14	9.37 $\pm$ 0.14
9.	Threonine	6.13 $\pm$ 0.20	3.66 $\pm$ 0.14	4.30 $\pm$ 0.20
10.	Alanine	3.50 $\pm$ 0.10	3.45 $\pm$ 0.14	3.60 $\pm$ 0.20
11.	Tyrosine	4.10 $\pm$ 0.10	4.00 $\pm$ 0.10	4.00 $\pm$ 0.20
12.	Methionine	2.65 $\pm$ 0.24	1.83 $\pm$ 0.17	2.17 $\pm$ 0.10
13.	Valine	4.65 $\pm$ 0.22	3.20 $\pm$ 0.24	3.20 $\pm$ 0.14
14.	Phenyl alanine	2.65 $\pm$ 0.17	5.25 $\pm$ 0.24	4.84 $\pm$ 0.10
15.	Iso-leucine	3.92 $\pm$ 0.34	4.13 $\pm$ 0.10	5.00 $\pm$ 0.24
16.	Leucine	9.00 $\pm$ 0.14	10.09 $\pm$ 0.10	10.59 $\pm$ 0.10
17.	Proline	1.05 $\pm$ 0.17	1.40 $\pm$ 0.10	1.43 $\pm$ 0.26
18.	Tryptophan	1.72 $\pm$ 0.10	2.06 $\pm$ 0.07	2.40 $\pm$ 0.02
19.	Amide Nitrogen	1.74	1.92	3.40
20.	Chemical rating	44.0	35.0	42.0

A typical chromatogram showing the resolutions of amino acids is given in Fig. 2 It will be seen from the table that the sesame proteins are rich in sulphur containing amino acids, viz., cysteine and methionine.

The sesame oil contains two other minor components which are not present in any other vegetable oil. These are sesamin and sesamol belonging to a group of compounds called lignans. These are generally found in the heartwoods and the overflow resins of Coniferae plants. These components have

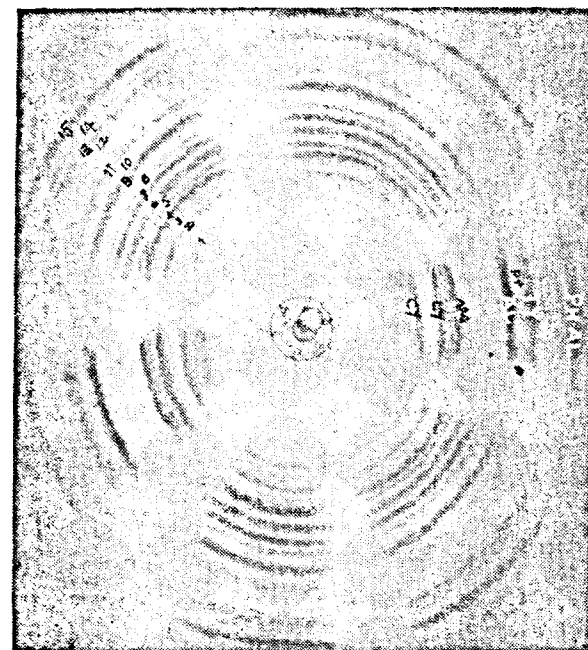


Fig. 2. Chromatogram of hydrolysate of sesamin globulins from sesamin seed meal.

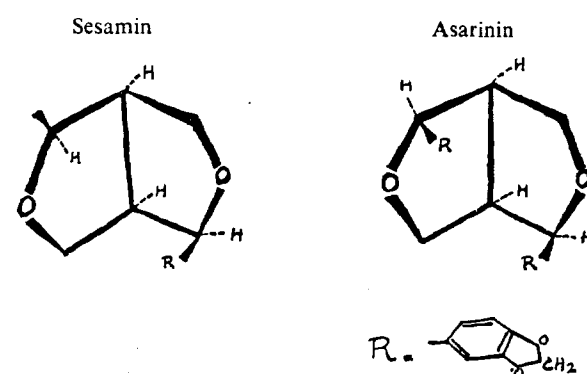
Solvent system: Butanol, Acetic acid, Water (40:10:50)

S 1, S 2 a and b globulins. S = unknown amino acids.

1. cystine 2. lysine 3. histidine 4. arginine 5. aspartic acid 6. glycine 7. glutamic acid 8. threonine 9. alanine 10. proline 11. tyrosine 12. methionine 13. valine 14. phenyl-alanine 15. leucine & isoleucine.

attained importance because of their use as antioxidants and as pyrethrum synergists (Gersdorff, Mitlin and Beroza 1954, Budowsky and Markely 1951). It is interesting to note that d(+) sesamin has been identified to be present in *ocotea usamberensis*-Ibeancamphor tree—S. Africa. (Rutaceae) formerly identified as pseudocubebin (Carnmalm 1956). B. Carnmalm (1955) has also shown that Fagarol from *Fagara xantho xyloides* (Rutaceae) also to be d(+) sesamin. 1-sesamin has been obtained from the roots of *Asarum sieboldi* where it occurs along with 1-Asarinin (Kaku, and Ri, 1937). The diastereoisomer 1-Asarinin has been obtained from the roots of *Asarum sieboldi* (Kaku and Kondo 1931) and from the bark of *xanthoxylum Carolianum* (Rutaceae) (Crombie 1952, Dieterle and Haubold 1931). Recently d-asarinin has been isolated from the leaves of *Acronychia mulleri* (Davenport and Sutherland 1954). The chemical structure of

these compounds have been established quite recently (Beroza and Schechter 1956, Freudenberg and Fischer 1956, Brauchhausen, and Lingner, 1957). The extensive literature on these compounds has been reviewed recently by Hearon and Macgregor (1955). The structure of these compounds are given below:



Crystals of d-sesamin isolated from natural material is given in Fig. 3. Both are chemically 2,6-Bis (3, 4

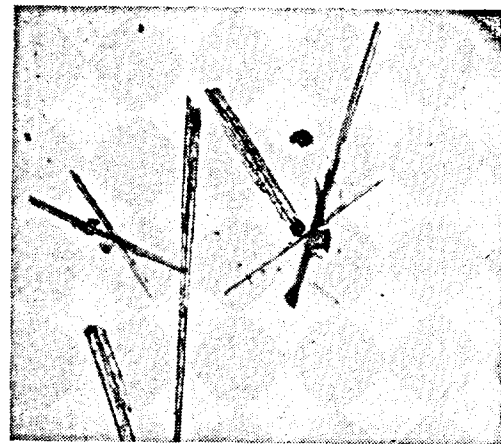


Fig. 3. Photomicrograph of sesamin crystals. x 120.

methylenedioxy phenyl) 3, 7-dioxabicyclo [3, 3, 0] octane, of molecular formula $C_{20}H_{18}O_6$. The anti-tubercular activity of sesamin isolated from sesame seeds (*Sesame indicum*, Linn. N. O. Pedaliaceae) was reported from this laboratory by Gangadharam et al (1952). Subsequently Ramaswamy and Sirsi (1957) studied the diastereoisomers of sesamin using liquid Youman's medium in their study to obtain critical condition for biological activity. The results obtained at the end of 2nd week are given in the Table 3.

TABLE III

Antimycobacterial activity (H_3R_+ strain of *Mycobacterial Tuberculosis*) of sesamin isomers (2nd week)

No.	Compounds	Dilutions					Control*
		10^{-3}	10^{-4}	10^{-5}	10^{-6}	10^{-7}	
1.	Acetone Control	2+	2+	2+	2+	2+	2+
2.	D-Sesamin	—	—	S	+	+	2+
3.	L-Sesamin	—	S	+	2+	2+	2+
4.	D-asarinin	S	+	2+	2+	2+	2+
5.	L-Asarinin	—	—	—	S+	S+	2+

— No growth S = slight growth

+ moderate growth 2+ = good growth

* Youmans media only

PHARMACOLOGICAL CHARACTERISATION OF SESAMIN

A. *Acute toxicity.* It has been determined in rats (average wt. 25 gms.) by oral, intraperitoneal and intramuscular administration. The dosage was between 200—600 mg. per kilogram body weight of rats. In the dosage studied none of the animals in any group showed any symptoms of toxic nature. Haematological changes during chronic toxicity experiments also did not show any pronounced departure from the normal blood picture. These facts indicate that in the doses studied that either the sesamin is non-toxic or it gets easily metabolised and excreted in which case it cannot produce serious damage to the organs of the body.

BLOOD PRESSURE AND RESPIRATION

B. The insoluble nature of sesamin in water and lower concentrations of alcohol presented a serious difficulty in these studies. The method of Chopra et al (1936) for studying the pharmacology of camphor (an insoluble substance) has been followed here. Sesamin is taken in olive oil solution in the experiments with dogs for the studies on blood pressure and respiration and in acetone or alcoholic solutions for the studies on isolated organs. The effect of sesamin on Blood pressure and respiration is given in Fig. 4. It will be seen that there is a marked fall of blood pressure for a short period and the fall is restored quickly in doses of 5 mg., 10 mg., per k. gm. of body weight but persists for a long time at a dose of

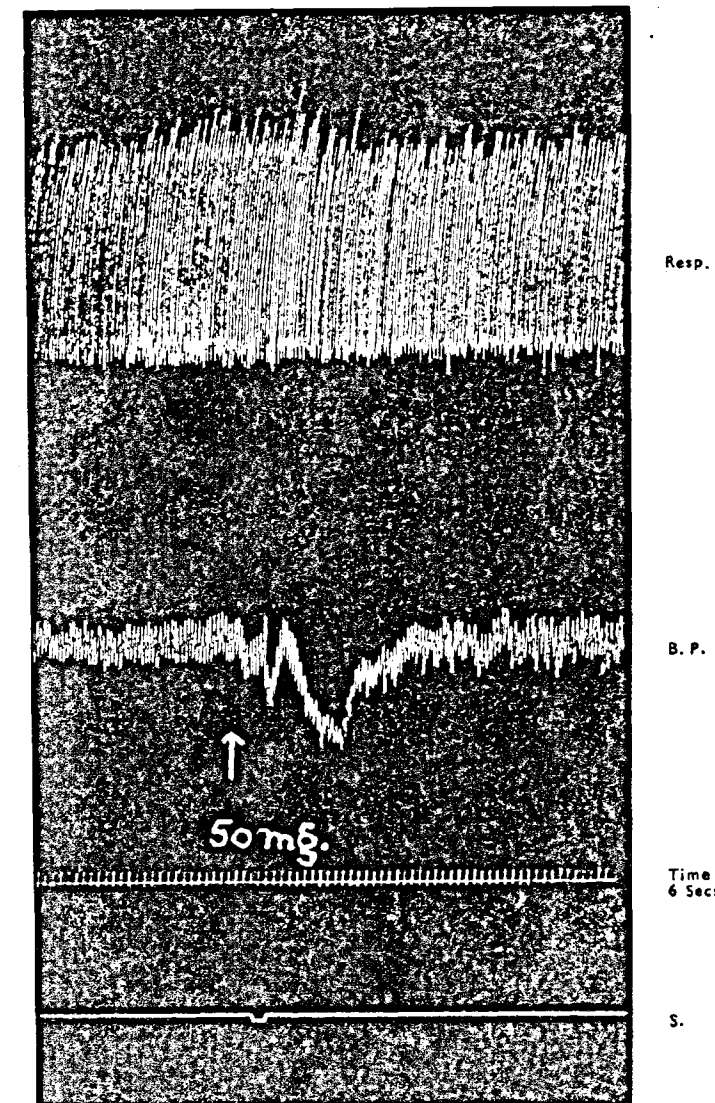


Fig. 4. Effect of sesamin on blood pressure and respiration.

Female dog. 3 Kg. B.W. Second sodium anaesthesia dose 20 mg./Kg.

50 mg. per kg. Bw. of dog. The respiratory tracings show at 10 mg. dosage level a slight increase in the depth of the respiration. At higher doses there is hurried shallow breathing and a short period of apnoea is sometimes observed. The effect is the same even after atropinisation indicating that the action is not through the vagus nerve.

THE EFFECT OF SESAMIN ON ISOLATED HEART OF RABBIT

C. There was no marked action on the heart

muscle at 20 mg. dosage levels. At 50 mg. dosage level a decrease in the amplitude of the beat of the heart was noted with tachycardia, and after 2.5 minutes irregularity of the beats sets in from which heart never recovers. These experiments indicate the effects noticed on blood pressure and blood pressure may be due to the direct action of sesamin on the musculature of the heart (Fig. 5)

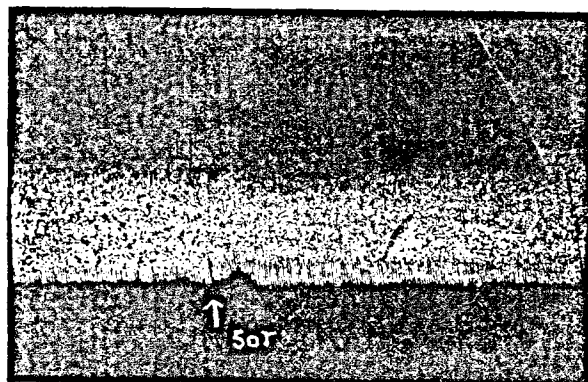


Fig. 5. Effect of sesamin on isolated rabbit heart. male 200 Gms. B. W. Dose 50 mg.

THE EFFECT OF SESAMIN ON RAT UTERUS

D. The effect of sesamin on the rat uterine muscle at 10, 20 and 30Y concentration causes contractions while lower concentrations do not have any effect (Fig. 6).

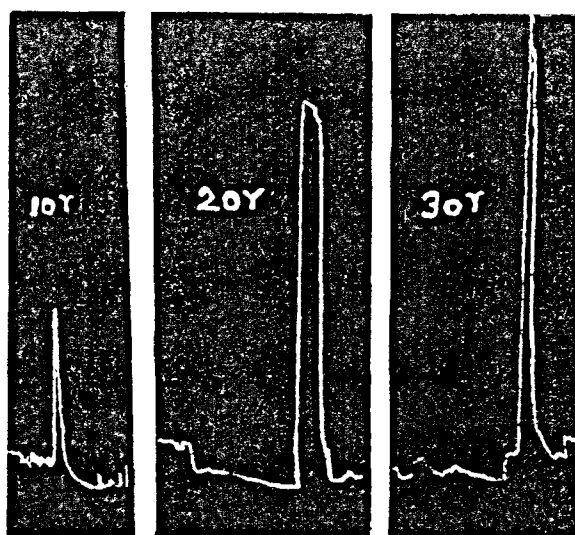


Fig. 6. Effect of sesamin on isolated rat uterus. female 30 Gms. Dose 10, 20, 30 mg.

THE EFFECT OF SESAMINS ON THE GUINEA-PIG INTESTINE

E. Slight contraction of a transient nature has been obtained at 10, 50 and 100Y doses.

It will be seen from the above data that sesamin exhibits no physiological effect on blood pressure and respiration and cardiac musculature in lower concentrations. In higher doses it lowers the blood pressure and causes respiratory apnoea. Since the same results are obtained in atropinised animals also, the effect observed are probably due to direct action on the cardiac muscle and also on the smooth muscles of the bronchioles and other organs.

SUMMARY

1. Study on sesame oil and protein fractions from sesame meal has been presented. The electrophoretic analysis of sesame globulins show four fractions. The amino acid analysis of globulin fractions show that fractions I and (III and IV) give a higher chemical rating as regards their nutritive values.
2. The carbohydrates of sesame seeds have been shown to contain stachyose and an unknown tri-saccharide probably planteose.
3. The lignans contained in sesame oil have been shown to possess anti-tubercular activity *in vitro* (against H_3 , R_v) and the diastereoisomers sesamins and asarinin exhibit differences in biological activity probably due to stereo-isomeric complexity and optical activity.
4. Toxicity studies and pharmaco-dynamical studies though incomplete show that the isomers are relatively not toxic to the host system than to the bacterial system.

ACKNOWLEDGEMENTS

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ILLNESS IN OLD-AGE

BY DR. CH. KRISHNAMURTY

Retd. Asst. Surgeon
7/604 Maharanipet, Visakhapatnam-2

THE onset of illness in old-age is due to physical or psychological causes or both. It is usually of a degenerative type with a tendency to progress and slow repair, and is insidious in its onset. Apathy and general disinterest may occur in old-age amongst those who have led an active and responsible life, if no adequate preparation has been made, especially in those, who have developed no hobbies. A sudden change from an active life to one of practical idleness, has marked effect soon after retirement in old-age. This is particularly so in those, who are emotional. If one does not occupy himself in some suitable form or other, his complaints multiply and he rapidly becomes older. Work is the best tonic and an idler's brain is a devil's workshop. Rehabilitation of the physically fit old people, as in other countries, is an advantage to the country and the individual.

Hypertension, arteriosclerosis, intermittent claudication, myocarditis, Diabetes mellitus, Rheumatoid and Osteo arthritis, Enlarged prostate, Vitamin deficiencies and gastro-intestinal troubles and fairly common as age advances. Shortness of breath is noticed at first on walking up a gradient or going up the stairs or talking continuously for some time. There may be giddiness, a tendency to fall, faintness, occasional blackouts, difficulty in getting about, tingling and numbness, indigestion with fullness after meals, constipation, frequency of micturition or getting up at night twice or thrice and passing large quantities of urine, inability to sleep well, tired feeling, loss of energy, lack of concentration and failure of memory. Every complaint though appearing trivial, is a precursor in most cases of a future catastrophe and if prevented or prolonged, would go a long way to make life in old age comfortable.

The reactions of old people to failing health are influenced by emotions and fears, not common in young life. There is a feeling of insecurity with advancing years and loss of independence. This is increasing during the last 20 years due to antibiotics, which have raised the expectation of life but producing degenerative changes. Again during this period there

has been a marked change in the youth of the country. The youth has become independent in most cases, lost his regard for elders and is often rebellious. The simple rules of health are defied. He has no respect for God or religion and is hypercritical and argumentative in his dealings with elders. The behaviour of the young towards the old causes worry, depression, and discontent in the aged and is a major factor in the illness of the aged. One worried is said to be ten times more prone to infection. In some cases, there is a fear of being a burden in old age and be dependent, a life to which he cannot adjust. It is therefore essential that the younger generation should understand the aged and conduct themselves in a tactful and sympathetic manner, giving the maximum latitude for those, who brought them up. This goes a long way to make the aged lead a more tolerable life. As age advances, a degree of deafness or impaired eye-sight is common and this may cause a fear of isolation from others. Memory in many, begins to fail in old age and particularly so, for recent events. It would be surprising to remember events of childhood or adolescence, more readily and the more recent ones are forgotten temporarily or permanently or suddenly remembered like a flash after racking the brains for a long time.

Menopause in the female, and climacterium in the male due to imbalance of glandular secretions account for some of the illness in the aged, as irritability, flushings, hypertension, lack of concentration, etc. Thus nearly all proprietary geriatric preparations contain oestrogen and testosterone-propionate in addition to all vitamins, minerals and lypotropic agents.

Every person even apparently normal, develops some degree of narrowing of his coronary arteries in old-age producing insufficiency with no serious symptoms, except perhaps slight breathlessness on more than ordinary exertion. The significance of apparently trivial symptoms complained should be interpreted rationally to avoid future catastrophes. Thus headache, giddiness, faintness, disturbances of vision and tinnitus may be due to *Hypertention* and he

should have Rest, mental and physical, assurance and sedatives to start with and hypotensive drugs could be used only when the above measures fail. A major accident like thrombosis, embolism or hæmorrhage can be avoided, if the above symptoms are properly evaluated. "Fuss, fluster, fidget, flurry and fury should be avoided. Even the ordinary pursuits of life should be carried on with even tenor and a hypertensive should learn to wall like a lady." I have known a lady with hypertension, who once had an attack of Cerebral thrombosis and recovered fairly soon but on a second occasion, she had a fit of anger over a domestic affair and had a second attack and now of hæmorrhage from which she passed away. Often hypertension is associated with *Chronic interstitial Nephritis* with passing of large quantities of urine at night as the earliest symptom. He may complain of temporary forgetfulness and momentary giddiness and on examination there may be an accentuated aortic second sound and thickened cord like feel of the radial arteries. This may or may not be associated with hypertension. This points to *arteriosclerosis*. He may complain of pain or numbness on walking some distance, which in the early stages is got-over with rest and massage. It is possibly *intermittent claudication* from narrowing of arteries in the extremities and poor blood supply to the muscles and if neglected may lead to gangrene. An effort syndrome, a pulse rate of over 90 even at rest, a diffuse cardiac impulse, muffled heart sounds, and hyperesthesia of the precordial region may mean *myocarditis* and the history may point to an old Rheumatic trouble or an infectious fever or some source of septic infection like Pyorrhæa, Septic Tonsil, Gonorrhæa, Syphilis, Amœbiasis or a urinary infection. An apparent indigestion or symptoms simulating a peptic ulcer or so called biliousness may be the beginning of a *Coronary insufficiency*. *Diabetes mellitus* may start insidiously. The patient may complain of nothing more than progressive weakness and there may be no Polydipsia, polyurea or polyphagia in the beginning but on examination, there may be Glycosuria and Hyperglycæmia. A low specific gravity does not necessarily mean absence of sugar in urine. Insulin and antibiotics have in part saved the life of a diabetic from his old enemies of infection and Ketosis only to expose him to chronic complications of diabetes, which increase with the length of his illness and his age.

Rheumatism and Osteoarthritis are common in old age, the later is more common. Previous attacks of

rheumatic fever, neglected or imperfectly treated, or other acute infectious fevers, septic infections, Gonorrhæa, gout, Syphilis, tubercle have all to be considered for proper treatment. *Osteo arthritis* is a degenerative change, which most old people do not escape. The cartilage in the joints begins to be supplied with blood vessels from the underlying bone, as a result of which the cartilage slowly becomes ossified and begins to crumble under the weight of the body having lost its elasticity. This process does not appear to be active always, for, there will be periods of intermission when the patient is fairly free from acute or subacute attacks. It is perhaps due to absorption changes in the joints.

Enlarged prostate is a common condition setting on the old insidiously. There may be a fullness or heaviness in the rectum, a frequency of micturition or sudden retention of urine after a heavy late dinner or exposure to cold or he may complain of delay in the starting of the act of Micturition or passing residual urine twice or thrice after the first act. *Vitamins, mineral and other deficiencies and gastro intestinal troubles*. The commonest Vitamin deficiency in the aged is a B-Complex and B12 deficiency, on account of which he may complain of langour, lassitude, lethargy, lack of energy, lack of appetite, constipation, indigestion, Tympanitis with reflex affects on the nervous system, such as irritability, inability to adjust himself to his surroundings and often considered tyrannical by his own household or others. They are due to lack of Vitamin B produced from his normal diet, which is not sufficient, being converted into Pyruvic acid mostly. A course of Vit. B complex and B12 sets him alright for a time and with similar courses the aged can be kept comfortable from time to time. In some there is also some degree of anæmia, from an iron deficiency or of a megaloblastic type or a low serum Calcium level or lypotropic factor which have to be supplied according to indications.

Regular habits, moderate exercise, nourishing easily digestible food and a suitable occupation are necessary in old-age. Occasional relaxations from domestic worries, as visits to pictures or Health resorts, pilgrimages or visits to Kith and kin are all conducive to happiness in old age. Diet in old age should have a change as foods containing a high protein or fat content are not digestible as before, for want of active work and exercise. If indulged in, in spite of it, cholesterol deposits in arteries, atherosclerosis and

(Continued on page 88)

Heart-Lung Machine At Guy's Hospital, London

FROM A MEDICAL CORRESPONDENT

NEWS POINTERS

Patients have been operated on and survived after the heart has been stopped for 20 minutes.

Iron curtain doctors have flown over to view the machine.

The machine is comparatively cheap and extremely simple to operate.

The machine incorporates a heating system developed in this country by G. E. C.

At the moment only patients whose life would definitely be finished in measurable time but for an operation are being operated on, but progress is very rapid.

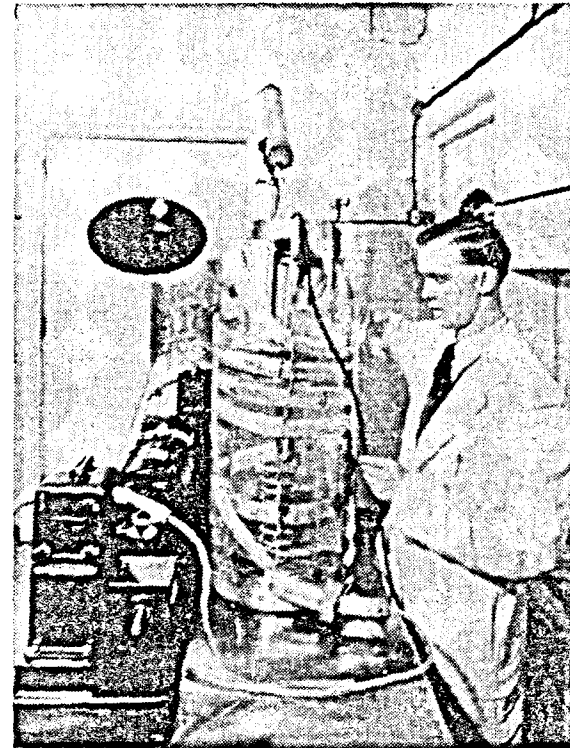
Britain is now considered surgically ahead of U.S.A. in cardiac surgery.

* * *

Successful operations on the heart using the Lillehei pattern bubble oxygenator have been performed at Guy's Hospital. These entail the machine taking over from the heart for periods up to 20 minutes.

The apparatus built by Guy's Hospital Thoracic Research Unit follows closely that developed by Lillehei in the United States. It has the advantage of simplicity, facilities for manual operation in the event of an electrical failure, and can be built for about £500. The pump unit has been supplied for American manufacturers, but the heating apparatus, necessary to keep the blood at constant body temperature, has been developed by The General Electric Co. Ltd.

During an operation, the patient's circulatory system is first stabilised through the oxygenator, then



This heart lung machine (Lillehei pattern bubble oxygenator) actually being set up for an operation at Guy's Hospital, London, carries heart surgery a stage farther than the use of hypothermia. Using hypothermia, the body temperature is lowered to 28°C. so that brain cells can survive for a short period without any blood when the supply from the heart is stopped. Using this machine, however, which actually takes over the function of the heart, the blood supply to the brain and body continues normally and is kept at normal temperature by a specially developed G.E.C. heater even though the heart is stopped. Consequently, the heart can be stopped for much longer periods, as much as double the previous time, enabling surgeons to carry out much more technically difficult operations on the heart.

the heart is arrested. Once the heart ceases to function the oxygenator takes over completely. The

(Continued from page 87)

thrombosis set in, which may lead to fatal terminations like Coronary attacks or Cerebral hæmorrhage. More fresh fruits and vegetables and a fair quantity of milk with the least amount of sweets, fried foods,

pastries etc. would be more suitable.

I have made an attempt to collect some of my thoughts and observations which are perhaps perfunctory.

variable geared pump machine 'milks' the blood, by means of metal fingers, from the superior vena cava (or venous end of the heart) into translucent tubing which is receiving oxygen. Blood from the coronary sinus is also pumped separately into the main circuit. The tubing is fed to a defoamer so that bubbles in the blood can be eliminated. On leaving the defoamer the blood is passed along a twelve foot length of the translucent tubing which is wrapped round a frame of spacers at predetermined intervals.

The spacer frame with the translucent tubing wrapped round it is situated in a transparent Perspex tank containing 9 gallons of water. This is kept at a constant temperature of 37°C (98.6°F) by means of a special element controlled by a hot wire vacuum switch. At the outset of an operation the tubing in this tank is 'charged' with 1000 c. c. of donor blood to give sufficient supply until the patient's circulatory system has been stabilised through the oxygenator. The oxygenated blood in the translucent tubing having passed through the tank and warmed to body temperature is then 'milked' into the left subclavian artery by another variable geared pump machine using the same motor drive as the first pump. The gears of the pump machine are carefully varied and set to provide a balance between the arterial and venous ends. Should the motor break down the gears and pump can be operated by means of a hand wheel.

The heater element used in the tank is placed absolutely co-centrally in a nickel-plated copper sheath by means of a G. E. C. patented process. The element, which has a loading of 750 watts, has a length of one hundred inches and is so wound in a spiral as to give perfectly even heating without any apparent temperature differential in any part of the tank. The heater is placed on circuit in the tank some appreciable time before an operation takes place so that any overshoot of temperature due to residual heat in the element, governed by the metal and its heat storage capacity, is lost and the thermostat is able to keep the temperature absolute.

This heart-lung machine (Lillehei pattern bubble oxygenator) actually being set up for an operation at Guy's Hospital, London, carries heart surgery a stage further than the use of hypothermia. Using hypothermia, the body temperature is lowered to 28°C so that brain cells can survive for a short period without any blood when the supply from the heart is stopped. Using this machine however, which actually

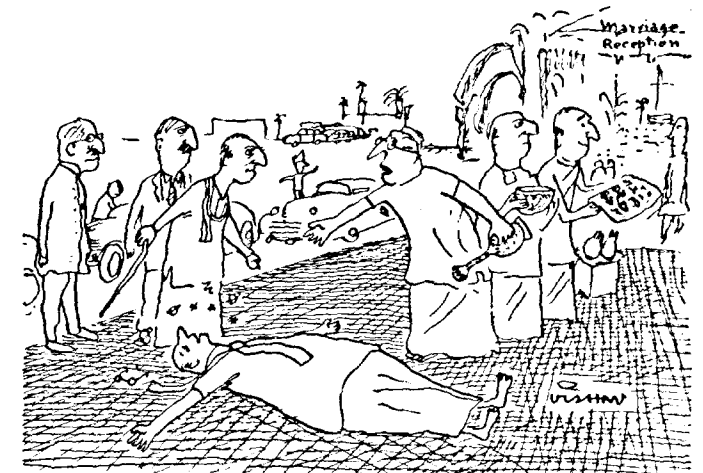
takes over the function of the heart, the blood supply to the brain and body continues normally and is kept at normal temperature by a specially developed G. E. C. heater even though the heart is stopped. Consequently, the heart can be stopped for much longer periods, as much as double the previous time, enabling surgeons to carry out much more technically difficult operations on the heart.

CONCERN is being expressed by British dentists over the fact that during the past year the already high consumption of chocolate and sweets in Britain increased to eight and one-half ounces a week per capita.

* * * * *

CONTRIBUTIONS TO THE USE OF ISOTOPE I¹³¹ FOR THE LOCALIZATION OF INFLAMED AREAS (FOCI, TUMOURS)

The authors state that experimental cerebral tumour in dogs can be localized externally by the aid of isotope I¹³¹. The procedure is based on the well known marked affinity of iodine to inflamed tissue. The results of measurement were confirmed by autopsy of the brain and autoradiographic investigation. The accumulation of iodine by the thyroid gland was prevented by the administration of potassium perchlorate. This method appears to promote the increased storage of iodine isotope by the extrathyroid tissues of the organism.



"I forgot that he was allergic to rose-water.."

Chemistry's Contribution to Medicine

From A Special Medical Correspondent

CHEMISTRY'S growing understanding of molecules and atoms is giving man greater insight into the compositions and workings of living organisms, including himself. Thus it is providing him with new ammunition with which to battle his ancient enemies of disease, pestilence, hunger and many of the ravages of nature, and is opening doors to increased understanding of the chemistry of the universe.

American chemistry has made and is making outstanding advances in uncovering this chemical knowledge and in putting it to use. Brilliant minds of chemists from all over the world have made important contributions, both in coming to America to continue their work or in sharing their knowledge and findings from their homelands. Research is long, slow and expensive. Vital to America's accomplishments are the freedom and opportunities for research afforded to its chemists, and for many the satisfaction of seeing their findings put to use.

At the Museum of Science and Industry in Chicago, there is inscribed on the main rotunda: "Science discerns the laws of nature, industry applies them to the needs of man." American industry's expert technology and mass production methods bring the new knowledge out of the research laboratories, translating the mysterious formulas and chemical terms into products that can be used for the good of mankind.

CONTRIBUTION TO MEDICINE

The development of chemicals to prevent, cure or control bodily afflictions has performed seeming miracles. Countless lives have been saved; new hope has come to millions of persons. It has given new techniques to medical care and surgery; it has drawn the medical profession and chemistry into close union in the struggle to understand and conquer illness—to help give man a longer life and a healthier, happier one.

A major breakthrough came in the 1930's with the discovery of the first "wonder drug," sulfanilamide. Its story goes back to 1856 when a young English student, William H. Perkin, accidentally discovered a synthetic dye while trying to make quinine from coal tar. His finding set chemists everywhere to working with coal tar. German chemists became famous for synthetic dyes with unusual fastness in silk and wool. One of these dyes, Prontosil, also had the capacity to destroy harmful bacteria. This caused some chemists to wonder if this dye might not also destroy parasites in the human body. They found it was a part of the Prontosil molecule, sulfanilamide, that killed the bacteria. From published findings, research on sulfanilamide was begun in America at Johns Hopkins University. Amazing results were achieved in treating severe streptococci infections, pneumonia, childbed fever, and other ailments that formerly, if not fatal, resulted in long-drawn-out debilitating illnesses. There was no doubt that a "miracle" drug had been found, and the sulfa drugs were developed.

These drugs have since been improved and designed to cover a broad range of diseases. Some 5,000 derivatives of sulfanilamide have been synthesized and screened to find better, more effective drugs. One attempt to counter toxic side effects often produced by large dosages of sulfa compounds is a 1957 development that permits the effective dosage to be cut by as much as 75 per cent.

The antibiotics came next. These chemical substances produced by microbes have the power to inhibit the growth of or to destroy other microbes. Penicillin was the first of these powerful new miracle medicines, discovered in molds by Sir Alexander Fleming of England. A previous antibiotic, gramicidin, had been discovered by Dr. Rene J. Dubos of the Rockefeller Institute for Medical research, but it proved too toxic for human use. Penicillin was developed extensively in America, and its once prohibitive cost was brought down drastically through mass production methods. It has saved and is saving countless lives. Although some persons exhibit

allergic reactions to it, its triumph over pneumonia, meningitis, osteomyelitis, syphilis and a host of other bacterial infections has made it the most widely used of all the antibiotics.

Because the penicillin molecule disintegrates rapidly it has been difficult to synthesize. American chemists recently have produced ten varieties of synthetic penicillin, which are believed to offer hope in fighting certain disease organisms presently resistant to natural penicillin.

The fabulous family of "mycins" followed after penicillin. In the early 1940's, Dr. Selman Waksman, of Rutgers University, discovered streptomycin from soil—a discovery that seemed to fulfill the ancient Biblical promise: "The Lord hath created medicines out of the earth; and he that is wise will not abhor them." Streptomycin was especially important for it meant the first new triumph over tuberculosis, and startling results were achieved. It has since been found that its effectiveness in treating tuberculosis is increased if it is used in combination with one of several synthetic drugs, particularly isoniazid and para-

aminosalicylic acid (PAS). Streptomycin proved useful also in treating colon infections, plague, brucellosis and other ailments. Dr. Waksman's discovery brought him the Nobel Prize in Physiology and Medicine in 1952; it also set researchers everywhere to hunting for more miraculous medicines in soil, fungi, molds and various plant growths.

In 1947, Dr. Paul Burkholder, then of Yale University, discovered chloromycetin, which proved amazingly effective in treating typhoid fever and various dysenteries. Its molecule is the smallest of all the antibiotics in use; its synthesis is easy and economical. In 1948, Dr. Benjamin Duggar, a retired Botanist, discovered Aureomycin. This is one of the least toxic of all the antibiotics, perhaps because its molecule has eight oxygen atoms and the body oxidizes it readily. Its uses include treating Asiatic cholera and brucellosis. In ointment form it is being used throughout the world to fight trachoma, a dread virus disease that causes blindness.

In 1949, Dr. Waksman added neomycin—effective in skin diseases and infections of the eyes, ears, nose,

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throat and gastro-intestinal tract. It recently has been found useful in helping to reduce toxic accumulations in some cases of liver disease, heart trouble and shock. In the early 1950's Achromycin and Terramycin joined the family of broad-spectrum antibiotics, so-called because they attack a wide variety of invading bacteria. Recently cycloserine was added, and it has made impressive attacks on tuberculosis. In fact, some 300 antibiotics have been isolated and about a dozen are in use, with new discoveries and new uses of the older ones reported frequently. Some are combined with each other or with other drugs for greater effectiveness or in some cases to help counter undesirable effects. The antibiotics have become indispensable in surgery, in preventing or controlling infection.

To the American people the use of antibiotics has meant — to give only a few examples — a sharp reduction in the death rate from influenza (77 percent), tuberculosis (75 percent), appendicitis (69 percent), nephritis and other kidney diseases (40 percent), syphilis (56 percent), and rheumatic fever (66 percent).

A medical milestone was reached in America in 1948 with the discovery of synthetic cortisone. This hormone was exceedingly difficult to synthesize, and it was not possible to create a completely synthetic product. Dr. Lewis H. Sarett and his colleagues in the research laboratory of a large pharmaceutical firm began with ox bile and worked out a complicated 37-step synthesis. They produced enough of the compound to use for testing in human illness. In September 1948, Dr. Philip Hench, of the Mayo clinic, injected some of the compound into a young woman patient who had been helplessly bedridden with rheumatoid arthritis for over four years. A week later she went out on a three-hour shopping trip.

The next year, Dr. Hench showed before a medical convention a before-and-after film that revealed what cortisone injections had done for fourteen rheumatoid arthritis patients. The amazed doctors watched as a miracle unfolded — and cortisone was launched for the world effective in many cases but not always in others. Later it was found that another hormone, known first as ACTH and now as corticotropin, used in combination with cortisone, can bring dramatic relief from rheumatoid arthritis pain and enable the victim to move about. Researchers are now experimenting with using these two hormones to treat schizophrenia, on the premise that glandular unbalance may contribute to mental illness.

A single hydrogen atom added to cortisone has produced hydrocortisone, which gives faster relief than cortisone. It is effective also in easing bursitis pain and in helping to loosen stiffened joints in elderly persons; it relieves acute bronchial asthma; it has proved useful in treating baffling skin diseases and irritations; and it has brought under control 90 percent of cases of acute rheumatic heart disease. But the search continues for a drug that will give lasting help to the millions suffering from rheumatoid arthritis. Two new compounds, metacortandracin and metacortandralone, appear to be effective, and some hope has been found in the use of the antibiotic Achromycin.

Some of the best known of other hormones in use are the sex hormones, the estrogens (female) and the androgens (male). They often are made synthetically and have various uses. Notable is their effectiveness in treating certain types of cancer. Both are used for breast cancer, and the estrogens for cancer of the prostate.

An important step in hormone knowledge was made in 1953 when Dr. Vincent du Vigneaud achieved the first synthesis of one of the mysterious pituitary gland hormones. Dr. du Vigneaud and his associates at the Cornell University Medical School produced the most complex material of its kind yet produced by humans — a hormone composed of eight of the different amino acids which are the building blocks of protein material. The hormone was oxytocin. It causes the mother's womb to contract at the time of birth and stimulates the flow of mother's milk. Obstetricians now using this hormone find that it shortens labor's duration to an average of three and a half hours for delivery of first-born babies, and to an hour and forty-five minutes for subsequent children. For his discovery and also for his work done on insulin and penicillin, Dr. du Vigneaud received the 1955 Nobel Prize in Chemistry.

American chemists have made an important contribution to world knowledge in the conquering of malaria. As late as 1945 there were 63,000 malaria cases reported in America. Today it is almost extinct. The development of anti-malarial drugs, such as Atabrine, chloroquine and primaquine, has been in part responsible. Primaquine is both cure and preventive and destroys the malaria parasite in the tissues, lowering the relapse rate to less than one-tenth of one percent. Sweeping progress in

malaria control has been achieved through extensive sprayings with DDT and powerful new insecticides that destroy the malaria-bearing mosquito.

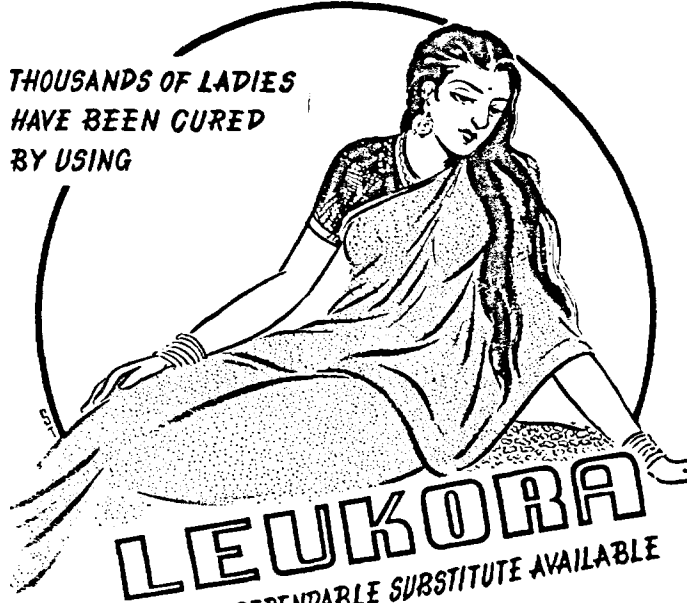
Thus American science has found that it is possible to wipe out malaria, that it can be controlled. The present global toll of this scourge is estimated at 150,000,000 cases a year with 1,500,000 deaths, the survivors often being left with life-long debilitating effects. A coordinating program of the World Health Organization and various nations is seeking to eradicate malaria in a five-year \$521,000,000 effort. The United States is contributing \$114,000,000 towards this project.

In the past, certain vaccines have proved effective in obliterating serious diseases in America. Many vaccines have been developed, some very recently such as one for the so-called Asiatic influenza. But to many Americans the vaccine against poliomyelitis, devised by Dr. Jonas E. Salk of the University of Pittsburgh, ranks as one of the great discoveries. Until 1955, polio killed more children in the five to fourteen-year old group than any other communicable disease. Some 138,000,000

doses of the vaccine have been given in America, resulting in a sharp drop in the number of cases. The vaccine formula was made available immediately to the world by President Dwight D. Eisenhower.

While certain virus diseases such as polio, smallpox and yellow fever can be controlled by vaccines, the cure of virus-caused diseases remains puzzling. An important advance was made when Dr. Wendell Stanley, of the University of California, discovered that a virus actually is a chemical molecule. He found it to be a living organism that can reproduce itself, but that it also can exist in crystalline form like a grain of salt — a link between non-living chemicals and life itself. Because of his findings the properties and behaviours of viruses can now be studied with systematic chemical methods. His discovery brought him the 1946 Nobel Chemistry Prize. And while most persons consider the virus a dread enemy, Dr. Stanley does not agree. Recently he said: "This may sound strange to you, but in the laboratory we look upon the virus as a potential source of great good, for it is the container of man's greatest secret—the nature of life itself."

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Chemists believe that a virus is made of nucleoproteins—proteins found in the nucleus of body cells. Dr. Linus Pauling, of California Institute of Technology, was awarded the 1954 Nobel Chemistry Prize for his research in describing the physical characteristics and structure of protein molecules. His discovery was hailed throughout the world as a land mark, and is expected to lead to information on how genes determine hereditary characteristics.

More and more is being learned about chemical reactions that take place within the body. Enzymes, which chemists consider the chemical spark plugs of life's processes, are being studied extensively. Basic research on them has brought Nobel Chemistry Prizes to two Americans. In 1930, Dr. James B. Sumner isolated urease; four years later, Dr. John H. Northrop obtained pepsin in pure crystalline form and later, with Moses Kunitz, isolated trypsin. Half of the 1946 Nobel Prize went to Dr. Sumner, and the other half was shared by Dr. Northrop and Dr. Stanley.

Vitamins are believed to be tiny parts of enzymes that play a catalytic role in the body. Some speed up the process which enables body cells to get energy from fuel available in food. The vitamin discoveries of the past twenty-five years are well known; more than a dozen have been produced that are known to be necessary for adequate nutrition and healthy functioning of the body. The most recent discovery is Vitamin B12, which among other uses has proved a blessing to pernicious anemia victims. Minute injections taken regularly do not cure the disease but act to keep the patient in good health.

A family of drugs recently discovered are the coumarin compounds, anti-coagulating agents used in preventing thrombosis and after surgery. The first to be discovered was Dicoumarol—and in a curious fashion. A number of cows in scattered areas of the American Middle West began to die of a mysterious ailment in which they bled to death from copious internal hemorrhages. One day a farmer brought a cow's carcass and blood samples to the laboratory of Dr. Karl P. Link of the University of Wisconsin, asking him if he could determine what was wrong. The source was found to be spoiled sweet clover. The coumarin molecule, which gives the clover its sweet fragrance, was studied extensively, and Dicoumarol was the result. Given in proper amounts it can prevent blood from clotting when and where it should not. By changing a few atoms of the coumarin molecule,

Tromexan and Pelentan were created, which work more rapidly. Rutin, a drug now made from buckwheat, often is combined with Dicoumarol to treat diseases tending toward capillary hemorrhages. Heparin is another of the new anti-coagulating agents in use; another drug, polybrene, recently developed at the Northwestern University Medical School, is used in cases of excessive bleeding to counteract the anti-clotting effects produced by the other drugs.

Plants always have been the source of many medicines. Today, reserpine and other drugs from such plants as *Rauwolfia serpentina* (Indian snakeroot) and *Rauwolfia heterophylla* (a Central American plant) are helping to keep high blood pressure under control.

Other drugs, the hexamethonium compounds, treat high blood pressure by performing a kind of chemical nerve-cutting surgery. The nerve-severing operation sometimes is used as a "last resort" in high blood pressure cases. A new drug, chlorothiazide, discovered by Dr. Robert W. Wilkins and Dr. William Hollander at Massachusetts Memorial Hospital, has been found effective in lowering blood pressure.

Reserpine also was one of the first "tranquilizing" drugs, along with chlorpromazine and others. These have been used effectively in mental hospitals in treating mental and emotional illnesses, lessening the need for electro-shock treatments and restraints, and in some cases effecting cures. Other milder drugs, such as the meprobamates, relieve anxiety. Chemical research has created drugs that kill pain, quiet nerves, induce sleep or keep one awake, all of which when used intelligently and under medical guidance have their uses and blessings. New anesthetics have been developed that permit new types of surgery; others reduce difficult after-effects.

The antihistamine drugs, useful in combating various allergies, were introduced first in France but have been developed extensively in America. They bring relief to many sufferers of such common allergies as hayfever. And unexpected uses have been found. One is dramamine, popular as a preventive for seasickness and airsickness, while other antihistamines relieve the nausea so often experienced in early pregnancy.

American chemists deliberately created a group of drugs known as the nitrofurans. Intrigued as to why soy sauce does not spoil, they traced the reason to the furan compound. By adding nitrogen, oxygen

and other molecules to furan they produced a powerful antiseptic known as furacin, the first of the nitrofurans.

New inroads are being made on epilepsy through chemistry. *Grand mal* attacks are reduced by such drugs as Dilantin and Mesantoin, and the *petit mal* by Tridione or Paradione. Many new drugs are being developed to help control this affliction.

Atomic energy is of increasing importance to American medicine. Radiation is employed to sterilize drugs, and the use of radioisotopes is common practice. The latter, once called the chemistry of phantoms, can trace the path of an element in the body. That is, a drug, hormone or vitamin is labelled with a radioisotope and followed in the body as it travels from one organ to another. Isotopes such as Phosphorus-32 treat blood diseases, even some leukemias. Iodine-131 helps to diagnose thyroid conditions and treat thyroid cancer. Other isotopes determine the number of red blood cells or treat effectively some types of cancer. Radiogold is used for some cancers such as prostate, bladder and uterine cervix: cobalt-60 is used most frequently for external radiation in cancer therapy.

A new development is the use of high purity ion exchange resins similar to those used in industry—but this time the chemical fishing is done within the human body. The technique has been used successfully on cardiac patients who must have a salt-free diet. The proper exchange resins, taken along with normally salted food, aid in the removal of excess salt from the body.

Even nylon, silicones and polyethylene have medical uses. An artificial artery of nylon coated with silicones has had great success. Polyethylene is being used as a base for some salves, including those containing antibiotics and hormones. The advantage over the petrolatum base seems to be that more medicine is released over a longer period of time.

The search continues in this quest to conquer illness, abnormalities, disease and suffering with the help of chemistry. The new findings represent the knowledge, skill and dedicated effort of chemical researchers combined with production techniques developed by industry. Together they give the world drugs created by the chemist's skill and make them available in quantities large enough to meet the needs of the people.

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Chromatography and its Role in Clinical Diagnosis

BY DR. D. P. GUPTA, M.B., B.S.

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TSWETT^{1,2}, a Russian botanist was the first to be aware of the great possibilities of chromatography, in 1906. It was, however, only in 1931, when Kuhn and Lederer⁷ separated the xanthophylls and carotene on a preparative scale on columns of alumina and calcium carbonate, that the possibilities of Tswett's work were fully realised. Chromatography as described by Tswett^{1,2}, consisted in separating substances by filtering their solution through a column of a finely powdered adsorbant filled into a glass tube and then washing ("developing") the column with a solvent. The word 'chromatography' is, however, a misnomer¹. Though Tswett^{1,2} showed a visible separation of coloured compounds, the essence of the process is not a colour separation but the partition of a solute between two solvent systems, usually liquids, one of them moving with respect to the other. Martin and Synge⁸ introduced the use of silica gel as the adsorbant.

Chromatography has been exploited by many workers in the analysis of various mixtures including body fluids for the detection of different constituents; and thus several chromatographic techniques have been developed.

Some of these are:—

1. Column chromatography.
2. Paper chromatography.
3. Chromatography by frontal analysis and displacement development.
4. Liquid or flowing chromatography.
5. Gas liquid chromatography.
6. Ion exchange chromatography.

The last four techniques are of relatively recent origin.

1. *Column chromatography*: Separation by elution on adsorption columns is the oldest form of chromatography. As practised by Tswett^{1,2}, the column consisted of alumina and

calcium carbonte. Tiselius¹¹ used activated carbon as the adsorbant whereas Gordon, Martin and Synge⁸ introduced silica gel for adsorption chromatography.

2. *Paper chromatography*: In this technique, use is made of a strip of filter paper to separate two or more substances in a mixture. Substances may already be in solution as e. g. in urine or be dissolved for application as a small spot or narrow band or streak. The spot is then dried, thus embedding added components in a small region.

Paper chromatography as practised today derives from the work of Consden et al³, who described an apparatus in which the strip was suspended in a trough to which solvent was then added. This solvent flowed down the paper, by gravity, to produce a one way descending paper chromatogram, the chromatogram being removed and dried after the solvent had flowed a sufficient distance.

Because of the original difficulties in constructing satisfactory apparatus, Williams and Kirby¹³ modified the technique so that the solvent flowed up the strip instead of down (Ascending chromatography). Ascending and descending chromatographic techniques may be combined⁴ by hanging a paper over a rod so that solvent passes up and then down, thus nearly halving height of the tank required. In the radial method, a spot is at or near the centre and passes radially to evaporate at the free edge.

Martin and Synge⁸ and their colleagues were the pioneers of modern paper chromatography. They regarded the process as a partition of components between water held as a stationary phase in paper fibres (filter paper contains about 15% of the weight of water) and the moving solvent or mobile phase and showed that mobility of two components paralleled their partition coefficients. They showed that under specified conditions, from the starting

lene or spot, $\frac{\text{Distance travelled by component}}{\text{Distance travelled by solvent}}$, is

constant for each component for a stated solvent, temperature, and filter paper. This ratio they called R_f of the component. R_f values are said to be as characteristic as boiling points or melting points. It is usual to run control spots of known substances on the same paper at the same time in the same tank. In clinical work, paper chromatography is undertaken most often for urinary amino acids and reducing substances, especially when the components are present in high dilution undetectable by other known methods. The great assets of this analytical technique are the minute amounts of material required and its extraordinary versatility.

Paper chromatography should, however, be distinguished from paper electrophoresis. In chromatography, the components are embedded in paper and dried. A solvent is passed through them to cause separation. In electrophoresis, many substances, if dried, could be damaged (e. g. proteins). The paper is wetted with a salt solution to carry the current and not to move components⁴.

A paper chromatogram is prepared as follows¹⁰: A drop of the solution containing the compounds to be separated is placed near the end of a strip of paper (most commonly used is Whatman No. 1,—special for chromatography) and allowed to dry. The strip is then placed so that a few millimeters of it dips into a solvent but it is essential that the dried spot is not immersed in it—otherwise it will dissolve off into the solvent and be lost. The special solvent must be one in which the components to be separated are only slightly soluble. If freely soluble, they would move at the same rate as the solvent; if insoluble, they would not move and obviously in neither case would there be separation. The solvent commences to flow along the paper, over the spot and towards the far end of the paper and when it reaches this end or when some convenient time has elapsed, the strip is withdrawn and rapidly dried. In order to prevent evaporation from the surface of the paper, the operation is conducted in an air-tight container. Thus a one way or one dimensional strip chromatogram has been prepared. As the majority of compounds of biological importance are colourless and so not visible on the paper, the problem of locating them still remains. The most widely used method is that of applying to the dry chromatogram a chemical reagent which will react with some or all of the compounds of interest to produce a colour—this being done by dipping the chromatogram through a bath of the

reagent followed by some appropriate treatment such as allowing to dry in air or heating until the colours appear. The location reagent may be a general one i. e. one which will locate all the components of interest or a more specific one i. e. one which reacts with only one component in the original mixture. Until recently, it was necessary to prepare a separate chromatogram for each reagent but by use of the "multiple dipping" technique of Jepson and Smith⁶, it is now possible to apply a sequence of three or four reagents to a single chromatogram with the result that a great deal more information can be obtained with very little extra labour. The area of the colour spot may be measured by a planimeter.

Complete separation of all the components in a mixture containing many components may not be possible on a strip of finite length or two substances may run to the same position on the chromatogram. In order to overcome this difficulty, recourse has been made to the use of a number of different solvents with different properties so that components running together in one solvent will probably separate in another solvent. Thus much more information is obtained by preparing two-way chromatograms—a drop of the mixture is placed near a corner of a square or rectangular sheet of paper. Solvent is then allowed to travel up the whole sheet with the result that a one-way separation is obtained and then after drying completely, the paper is turned at right angles and run in a second solvent which performs a further separation and causes the components to be distributed on the paper in two dimensions instead of the previous one dimension.

For the quantitative estimation of a substance, the substance is eluted and determined in the resulting solution. Two identical chromatograms are prepared and run simultaneously. One chromatogram is located with a reagent and placed alongside the other if one-way chromatograms have been prepared or directly on top of the other if two-way chromatograms were made. The area occupied by the substance on the untreated paper is marked with a pencil and the small area of paper is cut out. The paper is extracted two or three times with a suitable solvent, filtering and centrifuging in between extractions and then the compound is estimated in the solution so obtained.

3. *Chromatography by frontal analysis and displacement development*: Frontal analysis

is a special method of adsorption chromatography developed by Tiselius, though it need not be restricted to the absorption mechanism. In this technique, the mixture of solutes in solvent is applied to the top of the column continuously. The first samples of effluent are pure solvent. After the column has been running long enough to become saturated, the effluent samples are identical with the ingoing solution. In between these two stages, however, the different solutes are adsorbed to different degrees and the first solute to appear is that which is least adsorbed by the column.

In the displacement technique, the mixture to be resolved is applied to the top of the column but instead of eluting the column with pure solvent, a 'developing' solution is applied. This solution contains a solute which is more strongly adsorbed on the column than any of the solutes in the mixture; therefore, it "displaces" the original solutes as it flows down the column.

4. *Liquid or flowing chromatography*: This analytical method was introduced by Reichstein⁹, in 1938. The method consists in washing the column successively with a series of solvents of stronger and stronger eluting power (e. g. light petroleum, benzene, ether, acetone, alcohol or appropriate mixtures of these solvents); each filtrate is collected separately.

5. *Gas liquid partition chromatography*: This method was described by James and Martin⁸ in 1952. The column consists of keisulguhr to which silicone has been added to form a liquid phase. The gas phase is a current of nitrogen and the substance to be analysed is vaporised and carried along the column by the stream of nitrogen. The separated constituents issue from the column in the stream of nitrogen which bubbles through the liquid in a titration cell.

6. *Ion-exchange chromatography*: Chromatography on ion-exchange resins is of comparatively recent origin. Ion-exchange resins were introduced as an alternative material to the zeolites used in water-softening; but when

their usefulness in chromatography became apparent, special resins were developed. Anion and cation exchange resins, which are now available commercially, are chemically stable and have high adsorptive capacities. The method of using them has been either the displacement method or the elution method.

Clinical applications: Chromatography is used most commonly in the diagnosis of disorders involving the following substances:—

1. Amino acids. 2. Sugars and 3. Steroids.

1. *Amino acids, amines and related compounds*: Techniques for extracting amino acids are relatively simple because the compounds are very stable and are readily soluble in water or dilute acid and in ethanol containing 5-20% water or dilute acid. Tissues, organs, whole organisms etc. can, therefore, be macerated in simple aqueous or ethanolic solvents or in trichloroacetic acid in order to precipitate proteins and after centrifuging, a clean extract is obtained. It is always essential to desalt solutions if they contain much salt as this interferes with the subsequent chromatography (Desalting is the process which results in the removal of inorganic ions or salts while leaving the organic ions and molecules either in the original solution or in a condition where they can be quantitatively recovered free from inorganic compounds.)

Abnormality is usually associated with the appearance of amino acids that are not normally present in sufficient concentration in the urine to show on the chromatogram. Urine has been the most widely studied body fluid as far as the pathological variations in amino acid composition are concerned. In a normal urine amino acid chromatogram, glycine usually stands out as the dominant spot. On a much lower scale follow alanine, serine and glutamine; taurine, histidine and methyl histidine may also be identified. Clinical conditions in which urinary amino acid chromatograms may help in diagnosis are, (a) *Liver disease*: amino acids, in addition to those normally present include cystine and methionine. These usually appear in hepatic coma and massive hepatic necrosis. During the regenerative phase of liver disease, ethanolamine has

been observed as the dominant amino compound on the chromatogram. (b) *Phenylketonuria*: Two-dimensional chromatogram should be prepared and this shows a single isolated spot in the upper left quadrant of the paper due to phenylalanine. The rest of the paper shows the normal amino acids. (c) *Wilson's disease*: The chromatogram shows a fairly generalised aminoaciduria with notable increases in threonine, cystine, lysine, serine and tyrosine; glycine, glutamine, histidine and alanine show up more strongly than on the normal chromatogram. (d) *Acute renal tubular necrosis*: In this condition, arising from whatever cause, there is marked aminoaciduria with dominance of cystine, the basic amino acids, threonine and leucine. On the whole, it has been held that amino aciduria is not a reliable criterion by which to judge the patient's condition, glycosuria and other renal function tests being a better guide to treatment and prognosis. (e) *The Fanconi syndrome*: The picture is varied and the pattern has features that are common to the aminoacidurias of rickets and galactosaemia. However, once the diagnosis has been made on a composite clinical picture, amino acid chromatograms are useful to follow the course of treatment. (f) *Hartnup disease*: This, like the Fanconi syndrome, is a genetically determined disease and is accompanied by generalised aminoaciduria which can, however, be distinguished from other generalised aminoacidurias by the absence of proline and the presence of asparagine, the latter being easily identified by its brown ninhydrin colour. There is also high excretion of tryptophan and indol derivatives and this feature differentiates this disease from pellagra with which it may simulate clinically. (g) *Pernicious anaemia*: A characteristic aminoaciduria has been reported in cases of untreated pernicious anaemia and subacute combined degeneration of the cord. The urinary pattern shows taurine as the strongest spot and in addition to the amino acids normally present small amounts of lysine, leucine and cystine may be present.

Chromatograms of deproteinised plasma and cerebrospinal fluid show more striking changes than the corresponding urine chromatograms when the plasma rise involves largely those amino acids which have low renal clearance.

2. *Sugars*: The sugars which have so far been found in specimens of abnormal urine are few in number viz: glucose, galactose,

(Continued on page 100)

fructose, ribose, glucuronic acid, sucrose and lactose and it is rare to find more than four present in any particular case. Thus chromatographic identification of urinary sugars can be achieved by one-way chromatogram. The clinical circumstances usually restrict the search to a couple of sugars, thus facilitating interpretation e. g., in pregnancy, one is interested in the relative amounts of glucose and lactose that may be excreted; in suspected galactosaemia, galactose must be identified, and differentiated from glucose and in pentosuria, one seeks to confirm the absence of glucose and to identify the pentose(s) in the urine.

3. *Steroids*: Chromatography has played a fundamental part in the development of our knowledge regarding steroids. In pathological material abnormal steroids may be missed if they act like normal compounds in the "collective" methods such as employed for the estimation of 17-ketosteroids. Individual compounds can be isolated and estimated only by chromatography; whether this is necessary or not depends upon the problem under investigation. Pathological changes in the glands may bring about either a quantitative or qualitative change in secretion. Aldosterone can only be identified and estimated in urine by the use of chromatographic methods.

Analysis of complex mixtures including body fluids by chromatographic techniques, though of more value in research, can be of real help in the diagnosis of some obscure and difficult cases, particularly those cases due to congenital errors of metabolism. In others, the various chromatographic techniques, though not aiding in diagnosis, may render valuable information regarding the day to day progress of the patient or the effect of treatment on the course of disease.

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Community Hospitals Serve American Health

ALEXANDRIA, Virginia—Maintaining the health of a community is one of the responsibilities of a modern society that many people believe should be a major concern of all elements of the community.

Sometimes this is done through programs, clinics and hospitals maintained by federal, state or local government, or privately with governmental support.

More often, however, it is accomplished through the cooperative effort of the people themselves. When this is the case it usually is an effort led by individuals and groups who give their time and energy, and money, considering the physical welfare of their follows the best contribution they can make for the community's good.

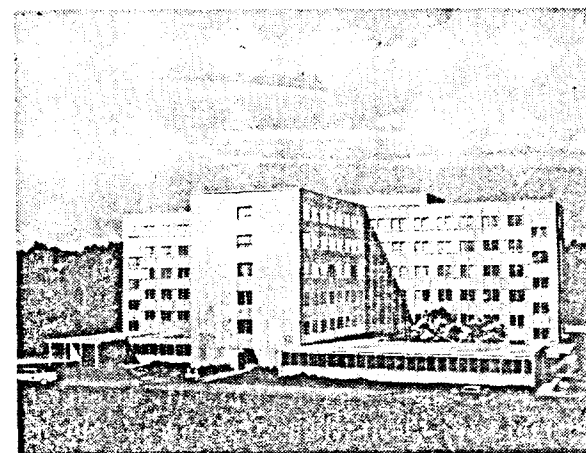
This expression of concern over maintaining the health of the community has its most frequent expression in the non-profit community hospital of a type that provides needed services at a minimum cost to those requiring it. Such hospitals are, generally, the major centers for all public health activity and effort for the areas they serve.

Such an institution, representing the medium-sized hospital in an average United States community, is the Alexandria Hospital in the city of Alexandria, Virginia, close to Washington—the national capital. It is operated by a corporation composed of a large number of citizens of the Alexandria area.

The original organizers and those who have followed them have been notable for their active interest in the welfare of their community and its people.

With other American hospitals, Alexandria's recently finished the observance of National Hospital Week, an event that attracted millions of Americans to personal tours of their hospitals. Thousands of visitors came to inspect the Alexandria hospital thus obtaining a closer view of their hospital's services and a chance to study the need for facilities that might permit it to give more and better services. One of the more colorful of several special events of the Alexandria week was a "reunion" of its "Baby Class of 1953." This attracted a huge gathering of five-year-old children, who had been born in the hospital in 1953.

The Alexandria hospital, at present, is an institution with a capacity for 285 bed patients and with demands that strain that capacity, its out-patient services, surgical facilities and other divisions. All are trying to cope with a tremendous service demand. With a dedicated staff, it has managed somehow to meet most of the demands made on it in its 24-hour-a-day operation. However, mindful of the need for expanded services, members of the hospital corporation and other community-minded volunteers are creating a fund for a new and more adequate building and greater facilities. This also is a situation typical of many American communities.



The New, modern structure for the Alexandria Hospital.
(Virginia - U.S.A.)

The fund-raising drive for the new building is nearing completion and a new structure, with more than 365-bed in-patient capacity and far greater space for present and prospective facilities will be started soon. Public-spirited citizens and many local organizations have responded generously with cash gifts and pledges for more.

The fund-raising effort is headed by a volunteer group that is notably representative of the community's progressive elements—men and women from the Alexandria area's businesses, professions, homes, fraternities and its social and civic improvement organizations.

Some of the organizations consider it as part of their regular expenses and have set up their contributions in their budgets, or make direct drafts on their treasuries, others solicit voluntary gifts from members. Still others give benefit events for which members sell tickets.

Contributions by individuals have been made in as varied fashion. Some persons have turned over property for sale to add to the swelling building fund. Some have given the income from properties for a set term. Some with modest incomes are making small periodic donations or have drawn lump sums from their savings. Wealthier Alexandrians have subscribed to the fund in methods just as varied.

Alexandria Hospital history dates from 1872, when the Virginia Assembly (legislature) granted a charter to 28 citizens of the then tiny city of Alexandria

to incorporate the "Alexandria Infirmary." From a very unpretentious beginning in a few rooms in the home of the small town's leading surgeon, the hospital grew and its quarters expanded to occupy the present five-story, well-equipped structure near the business center of Alexandria. Its prospective new, completely modern and much larger hospital building will be some distance from the present location and the business district, but will be even closer to the center of the population area it must serve. It will provide more rooms, larger floor space for other hospital services, voluntary, non-profit institution in the United States, is financed by fees for patients' treatments, gifts from generous citizens and organizations and support of the United Givers Fund. The latter is a nation-wide organization that bands many worthy charitable and quasi-public projects into an over-all group to which public spirited citizens contribute.

The corporation that governs the hospital now includes more than 300 leading citizens interested in its progress, and service. This group elects the board of directors that is accountable for actual administration of the hospital and who serve without pay as a civic duty. Coming from many professions, businesses and occupations, these give wide community representation and bring broad and varied experience and view points to aid hospital administration.

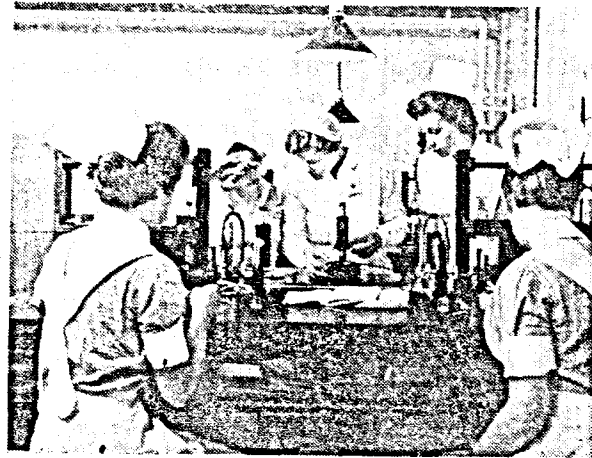
Many other local residents voluntarily give countless hours toward hospital services and thus provide services at much lower costs. Several women's auxiliaries, particularly, are active in work which ranges from fund-raising projects and equipment purchases to bedside services for patients and assistance in social activities for nurses.

An adjunct to the hospital is its School of Nursing, one of the oldest hospital schools in the country. It was chartered in 1872. Fully accredited by the National League for Nursing and the Virginia State Board of Nurse Examiners, its program is also approved by controlling agencies of the American Medical Association. Annually its three-year training course turns out a group of young women with training equalled only by the best nursing schools of the large universities and private colleges. In their training programs student nurses also give valuable service to the hospital and its patients.

Its faculty includes eminent physicians and surgeons, nationally known leaders of the nursing profession and

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Students of the Alexandria Hospital School of Nursing serve the cause of human welfare as they gain knowledge and experience in their profession. Here a quartet of student nurses receive instruction in clinical procedures from an instructor who is a capable graduate nurse of considerable experience.

highly qualified instructors in the more academic fields. Twenty-three courses are included in the curriculum. Some young women are assured of their education in nursing by organizations that sponsor them and pay their tuition charges and sometimes other expenses.

An international exchange program brings capable men and women from overseas in the fields of medicine, surgery and the allied professions in an unusual phase of the hospital's activities.

Presently there are 16 men and 2 women—all holders of doctors' degrees and some notable specialists in fields of medicine and surgery—in this group. In it is a husband and wife team from Germany, the wife a noted obstetrician, the husband well-versed in internal medicine and radiology. Other countries represented at present are Greece, Mexico, China, Korea, Argentina and Italy. Three are refugees from Hungary's revolution against Communist oppression.

All members of this exchange group are fully qualified for practice in their own countries. They apply for the exchange program, conducted under the auspices of the U. S. Department of State, to broaden their professional experience. Their applications specify the hospitals to which they would go and the hospitals also have a voice in the selective process. American medical men take the places in the countries from which all but the refugees came. The Alexandria

hospital has more than its full share of this talent from abroad.

The exchange doctors study modern American hospital techniques and practices, highly developed in the Alexandria Hospital. They also have the opportunity to study different phases of medicine and surgery under several specialists of repute who are members of the hospital's medical and surgical staff.

Services of the hospital are numerous and complete. Its Emergency Rooms maintain a 24-hour readiness and provide emergency treatment for an average of 51 accident victims and sufferers from critical ailments daily. About 38 patients are admitted to the hospital each day. In 1957, for example, 5,791 surgical operations were performed. The dietary service serves nearly 30,000 meals a month, and writes menus for and prepares 143 special diets a day.

A new life begins about every 2½ hours at the hospital and 3,284 babies were born there during the last 12 months.

X-Ray examinations averaged about 52 a day and totaled 15,137 during 1957. In this field operations have expanded rapidly in recent years to indicate notable advances in both the scientific detection of various diseases and for better treatment of injuries. Over 3,365 such examinations took place in 1945.

Complete records are kept for each patient treated at the hospital, and often serve as valuable bases for future treatment. A total of approximately 164,000 medical histories is included in the Medical Records department.

The hospital's inventory of equipment is worth several hundred thousand dollars and could have been established only through the extremely good support it has received from residents of the community. This may be easily understood when it is known that a single modern X-Ray machine costs \$15,000 and the autoclaves used to sterilize instruments are worth \$2,000 to \$3,000 each.

Numerous personal services are set up within the hospital by its staff and by a number of community organizations to add to the comfort and convenience of patients.

A comparatively large number of volunteers, some

(Continued on page 103)

FAT IN NUTRITION

Vanaspati (Hydrogenated fat)

By

SURESH CHANDRA BANERJEE

FAT is the most concentrated form of energy. To obtain the energy to produce 2500 calories which the person of average stature expends daily, one should require 240 gms (about 8 ozs.) of fat if it is to supply all the heat, since fat has an energy value of 9.3 calories per Gm. Were carbohydrate to serve as the sole source of this 90% of the daily calorie requirement about 559 gm. (more than 18 ozs.) would be used, as this foodstuff has a heat value of only 4.1 calories per gm. More-over since carbohydrate is usually present in foods along with considerable quantities of water, the fatty foods may be largely free from water, the discrepancies between the weight of food required to satisfy the calorie needs of the animal far exceeds the 2.3/1 ratio of the calorie values of & carbohydrates.

More over fats are the best vehicles for dissolving the fat soluble vitamins A, D, E & K. From that stand point, one might regard the fats as an essential foodstuff since they afford a simple medium to assure the absorption of these required vitamins. Now the question which vitally interests all of us is whether we need to feel undue alarm from a health stand point at the present day scarcity & dearth in butter fats (Ghee).

An examination of the dietary habits of animals gives us definite evidence that milk fat is not

required after infancy. Wild animals have continued a normal existence over centuries without milk or butter fat after weaning. Except for cat, dog & pig the same is also true for domestic animals. Man has attained his physical and mental stature largely without milk fats after weaning. Certain tribes in our country have been known to live satisfactorily after the nursing period on diets which are completely devoid of milk or butter fat. We come back now to the question as to how effectively hydrogenated fat (fortified with vitamins) can do the job of butter fat.

The relative nutritive values of butter fat and other edible fats have constituted the subjects of much controversy. Recent investigation in this field have been principally concerned with the rate of growth of weanling rats on different fat diets. Superior growth on a butter fat diet has been reported by many scientists. On the other hand other scientists reported butter fat to be inferior to hydrogenated fat. The superiority of butter fat was evident only when the carbohydrate in the diet consisted mainly of lactose. In dealing with the comparative merits of butter and hydrogenated fat in the human diet, it is pertinent to consider that human milk fat and the milk fat of the cow differ greatly in composition and that the former actually resembles a typical hydrogenated fat more closely than it does butter fat. It has been shown that iso-oleic acid in hydrogenated fats and that the

(Continued from page 102)

members of auxiliary organizations such as the Red Cross and nurse's aid groups and private citizens offer their services individually to enlarge the benefits the hospital and its staff can give patients. Secretarial workers, for instance, write letters and handle other affairs for patients, or keep medical and personnel records of types suitable to their experience.

Some, with a measure of technical knowledge, keep or help to keep medical and personnel records, help in the medical library or electrocardiograph department. Others handle individual tasks that satisfy small needs

of patients or even help with domestic or welfare problems the patient cannot solve from his hospital bed. The life of nurses is eased with social activities planned by volunteers. Hardly a field touched by the hospital does not have some voluntary aid. Thus, it will be seen that a hospital of this type from its inception, through its management and down to some of the most minute details of day-to-day operation, is largely the product of voluntary community cooperative effort.

(Photos: Courtesy - United States Information Service)

mono—and di-glycerides produce good growth in rats at reasonable levels of ingestion. An argument for the superiority of butter over hydrogenated fat was advanced in 1913, when it was found that the former was a good source of vitamin A, since it was soon determined that this vitamin, so essential for growth and for life, was absent in most vegetable oils. There would then appear to be some justification for the preference of butter to hydrogenated fat on nutritional grounds.

However as soon as colourless vitamin A concentrates were available, it became the practice to add sufficient of the vitamin A concentrate to counter balance its deficiency from an average butter. At present hydrogenated fat is fortified with 700 I. U. of vitamin A per ounce of the fat.

Extensive experiments carried out in India and abroad revealed that corn, cotton seed, olive, peanut and soybean oils as well as hydrogenated fat were equally efficacious in promoting growth as were butter fat on diets of mineralized skimmed milk powder which were fortified with the fat soluble vitamins. The diets were all shown to be equally well utilised as demonstrated by the fact that the same amount were required to cause equivalent growth. In further experiment it was reported that the vegetable oils were equally satisfactory components of the diet as butter fat in furnishing adequate nutrition for normal pregnancy and lactation. In a large number of tests on various vegetable fats, hydrogenated fat and butter fat there was no evidence of superiority in any dietary group. Dr. H. C. Sherman of Columbia University, America, has maintained a colony of rats for 50 generations on a diet consisting of one third of whole milk powder, two thirds of whole ground wheat and a little salt supplemented with small amounts of lettuce and lean meat once a week. They were maintained on a diet identical with Sherman's except, skimmed milk powder and amount of hydrogenated fat was added corresponding to the normal content of butter fat in the whole milk powder. The following generations of rats were in much better physical condition than the first generation.

From the analogy between rat and man, it is not too much to expect that a diet which is nutritionally satisfactory for the rat would also be beneficial for man and vice versa. Conclusions on the nutritional value of diets for humans based on rat experiments would seem to be entirely justified as far as fats are concerned.

The Vanaspati industry in India is of recent origin. Production was first started on a small scale in 1930. Sanction was accorded to the establishment of 50 or more factories in different parts of the country, thus bringing the total production capacity to 4,50,000 tons per year. There was however a considerable volume of opposition to the proposed expansion. The ghee manufacturers felt that increase in Vanaspati production would affect the interest of the Ghee industry.

Evidence of poor storage of vitamin A in the liver, as also of symptoms of vitamin B deficiency consequent on prolonged feeding with vanaspati, as the main source of fat, were reported by the experiments carried out at the Indian Veterinary Institute, Izatnagar. These results led to misgivings about the use of Vanaspati as an article of human food.

The nutritive value of Vanaspati was taken up for discussion by the department of Food and it was urged that a comprehensive and critical scientific investigation of the subject should be undertaken to obtain definite and conclusive evidence, on the basis of which Government could take a decision in regard to the future of the industry.

In comparative feeding experiments carried at 4 different research centres, on rats for 3 generations, it was found that there is no deleterious effect produced by vanaspati as compared with other edible oils. Human feeding trials carried out at 4 different centres also indicate that Vanaspati of melting point 37 C, has no harmful effect as compared with raw groundnut oil. The recent available scientific evidence indicates that when fortified hydrogenated fat is used in place of butter fat as a source of fat in a mixed diet no nutritional difference can be observed. Although important difference can be demonstrated between different fats in special experimental diets these differences are unimportant when a customary mixed diet is used. The above statement can only be made in respect to fortified hydrogenated fat and it should be emphasised that all hydrogenated fat should be fortified.

The most obvious result of the introduction of hydrogenation on a wide scale has been the establishment of liquid oils such as cotton seed oil and other vegetable oils carefully refined and bleached, as adequate substitute for originally more expensive edible fats. The object of refining and bleaching is

to remove the objectionable impurities in the oil with the least possible damage to either the glycerides or the tocopherols. It is a mistake however, to think of hydrogenation merely as a means of producing substitute product, in as much as hydrogenated fats may be superior in important respects to any of the natural plastic fats.

As regards the comparative nutritive values of (1) pure Ghee, (2) raw groundnut oil, (3) refined groundnut oil, (4) Vanaspati, the balance of experimental evidence places Ghee as the best, groundnut oil and Vanaspati fall into one group and next to pure Ghee. We can scarcely view with concern the increasing use of hydrogenated fat in the diet, if

that means that larger amounts of whole milk become available at a reasonable cost for human consumption.

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Urine Estrogens Predict Ovulation

Measurement of urinary estrogen levels pinpoints ovulation time almost four days before the basal temperature rises.

This finding was reported at a conference on the endocrinology of reproduction, held by the State University of New York.

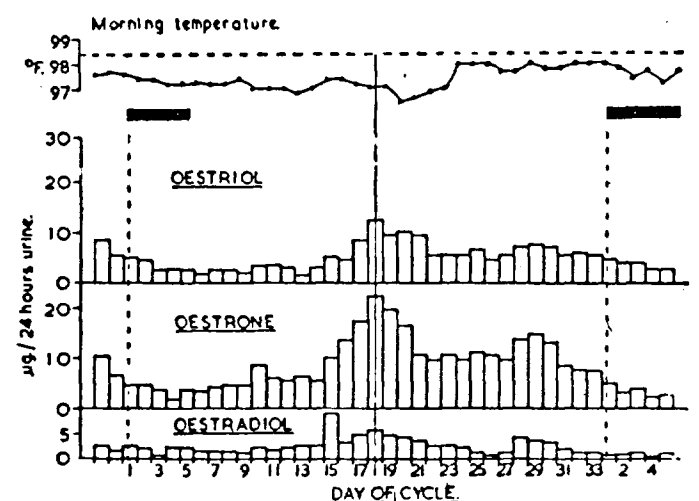
A characteristic peak in estrogen levels at about the middle of a normal cycle is "always associated with ovulation," said Dr. James B. Brown of Edinburgh University, Scotland. Levels remain more or less constant during anovulatory cycles.

LEVELS MEASURED

In nine women, ranging in age from 18 to 41 years, levels of pregnanediol, gonadotropin and three estrogens—estriol, estrone and estradiol—were measured by Dr. Brown and his associates, Drs. A. I. Klopfer and J. A. Loraine of the Clinical Endocrinology Research Unit at Edinburgh. Basal temperature was also recorded daily.

Seven of the women were in normal health and two were hospitalized for mammary carcinoma; none had any history of abnormal menstruation or ovarian disturbance.

A sharp increase in estrogen levels preceded the rise in basal temperature and pregnanediol levels by one to



INCREASED LEVELS of three urinary estrogens signal approach of ovulation. Rise precedes usual climb in basal temperature.

four days, Dr. Brown said. And gonadotropin levels rose about one day after the estrogen peak.

"In our cases," he continued, "menstruation followed the estrogen peak by an average of 14 days; the gonadotropin peak, by an average of 13.2 days; the pregnanediol peak, by 11.7 days; and the rise in basal temperature, by 11.2 days.

"We can therefore conclude that this estrogen peak is one of the earliest and most reliable indications of ovulation," the Edinburgh investigator said.

PROTEINS

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OF the three major constituents of the food, the proteins not only give the 'structural frame work' but also serve as the controlling power of the metabolism through the different hormones which are proteins in nature. The importance of the protein in the diet is best understood by the fact that the cells can survive without carbohydrates and fats for some time but if the supply of the protein is cut down from the diet, the cells die. Mulder in his "The chemistry of vegetable and animal physiology" (translated by Dr. Hromberg, Berwick, 1845) rightly remarked, "It is unquestionably the most important of all known substances in the organic kingdom. Without it no life appears possible in our planet." Mitchell et al (1945) analysed the composition of the human body and have found that the inorganic constituents amount to 73% of which 68% is water, while about 13% is protein, 12% is fat and about 1/2% is carbohydrate. The protein not only serve as the frame work of the body and regulator of the metabolism but also provide us with the clothes, silk, wool, furs etc. The use of the protein (hair of sheep into fabrics, manufacture of silk) in these purposes are known to the human being as early as to the Neolithic age (Tracey—1948). The enzymes are made up of the protein. The antibodies are also nothing but protein. Moreover, the protein maintains the osmotic pressure of the extracellular and intracellular fluids to some extent. The use of the enzyme namely the rennet for the purpose of the curdling of milk is known to the human being for nearly the same period. Homer in his immortal writing Odyssey (book 9, lines 349—351) has mentioned the use of the sap of the fig tree which is an important plant enzyme for the purpose of the curdling the milk. The use of different protein adhesive like egg, milk, ox-gall etc. are also known to the painters from the time immemorial. The coagulation properties of the protein was used in the ancient time for clarification of the liquid e.g. the white of an egg and blood to clear the wine.

Though the use of the protein was known from the Neolithic age the scientific knowledge of the

substance began in the middle of the eighteenth century. Though it was also known that ammonia was evolved on heating the protein but the discovery of Nitrogen by Daniel Rutherford (1772) and by Cavendish (1774) both independently and Berthollet's discovery of the composition of ammonia (1785) led to the conclusion that the protein contained Nitrogen. Cavendish was the first to observe, vegetables seem to consist almost entirely fixed and phlogisticated air (CO_2 & N_2) united to a large proportion of phlogiston (H_2) and some water." (Nicholson—1795)

The modern concept of protein chemistry begins with Vauquelin and Robiquet (1806) who isolated an amino acid derivatives from protein and also demonstrated the presence of Nitrogen in it. Wollaston (1810) was the first to discover the first amino-acid cystine. Braconnot in 1820 obtained the glycine by the breakdown of the gelatin and thus it was first postulated that the proteins are composed of amino-acids. Mulder after analysis of fibrin, serum albumin, egg-albumin, silk, etc. gave the formula for them as $2\text{C}_4\text{H}_{12}\text{N}_2 \cdot 5\text{O}$ and later he first used the term protein to the $\text{C}_{40}\text{H}_{82}\text{N}_{10}\text{O}_{12}$ radical which combined with varying amount of Sulphur and Phosphate. Protein is a Greek word and it means "pre-eminent". Simson in his "Animal Chemistry" gave an idea about the discovery of Mulder's theory regarding the protein. He observed, "Two most important discoveries have recently made regarding these substances (Albumen, Fibrin and Casein). The first is the discovery made by Mulder that albumen, fibrin & casein are nothing more than modifications of one compound to which he has given the name protein,..... which may be regarded as the commencement and starting point of all tissues; the second is, that protein, in every respect identical with that which forms the basis of the three aforesaid animal principles, may be obtained from similar elements in the vegetable kingdom. "Though Mulder's theory was much appreciated but soon term protein did not remain confine to the Mulder's radical part only. To-day protein is defined as "compounds of high molecular weight, consisting

largely (or entirely) of chains of amino-acids united in peptide linkage." (Cantarow & Schepartz—1954). The amino-acids are derived after hydrolysis of proteins. These amino-acids are the "building-stone" and about 23 different amino-acids have been definitely identified as the constituent of the protein molecule; but only a few proteins contain all the amino-acids. The enzymic method of hydrolysis of the protein is used to avoid destruction or racemization of the aminoacids; but the hydrolysis by the enzymes is seldom complete, it takes a longer time and often the enzymes themselves are autolysed raising difficulties or inaccurate estimation of the aminoacids. To overcome these difficulties of the enzymatic hydrolysis Redfield & Anfinsen (1956) used the combined application of enzymatic and chemical hydrolysis. The method is more useful for the proteins with longer chains. The strong alkalis like NaOH , $\text{Ba}(\text{OH})_2$, KOH etc. completely racemize the amino-acids associated with partial or complete destruction of the arginine, cystine, threonine and certain other amino-acids, but it is conveniently used in the determination of tyrosine and tryptophane. HCl , H_2SO_4 , HI , and a mixture of HCl & HCOOH are the common acids used for the hydrolysis of the acid-table amino-acids. Humin, the brown-black protein carbohydrate decomposition product is usually formed in this process of hydrolysis and to prevent the formation of the decomposition product, use of tin or SnCl_4 in the hydrolysis mixture is advocated. (Hlaziwetz & Habermann—1873) Kossel & Kutscher (1900) on the other hand used a mixture of HI and HPO_3 to get a better result. Partial acid hydrolysis is a valuable method in the study of the structure of protein with shorter chain.

The molecular weight of the proteins vary in a very wide range because of the different amount of the amino-acids. The range may be from 13,000 to many millions. An idea of the approximate molecular weights of the different protein may be obtained from the Table No. 1.

It is rather difficult to determine the exact molecular weight of a particular protein, but the average elementary composition of the proteins like albumin and globulin is as follows:— Carbon—54%, Hydrogen—7%, Nitrogen—16%, Sulphur—1%, and oxygen 22%. The structure of the serum proteins like other globular proteins is arranged in a lattice pattern. The single chain of the serum albumin is cross-

TABLE I

Sources and approximate molecular weights of proteins

Protein.	Sources.	Estimated Molecular weight.
Insulin	Pancreas	35,000 or 46,000
Pepsin	Gastric Juice	35,200
Benece-Jones Protein	Urine	35,200
Beta-Lactoglobulin	Milk	42,000
Ovalbumin	Hen's egg	43,000
Zein	Corn	50,000
Hæmoglobin	Human Blood	70,000
Serum albumin	Human Blood	70,000
Gamma-globulin	Human Blood	156,000
Urease	Jac-bean	422,000
Thyroglobulin	Thyroid	650,000
Antipneumococcus serum Globulin	Horse Blood	845,000
Bushy stunt Virus	Tomato plant	7,600,000
Tobacco Mosaic Virus	Tobacco plant	40,000,000

linked through approximately 17 disulfide bonds. The structural rigidity of the serum albumin is attributed to the presence of the tyrosine hydroxyl-carboxyl. There is a single sulphhydryl group in serum albumin. (Hughes—1947).

The proteins in the body may be present in the free state as for example serum albumin, serum globulin or may also be present in combination with the carbohydrates and lipids e.g. Mucoprotein and lipoprotein respectively. The serum or the plasma albumins are called albumins because of their close resemblance to the white of an egg. This resemblance has been studied as early as eighteen century by Hermann Boerhaave who has given one of the most earliest and complete description of the serum proteins.

The serum albumin is not a homogenous one and consists of two parts or two fractions,— fraction A and fraction B as obtained from the horse serum by Kekwick (1938). Fraction A was more soluble than fraction B and both contained the hexose. In fraction A the amount of hexose as determined by oreinol was 1.95% and in

fraction B it was 0.083%. The fractions obtained by Blix, Tiselius and Svensson (1941) by the process of electrophoresis also contained 1.1 & 1.2 p. c. of hexose and 0.45 and 0.56 percentage of hexosamine respectively. The concentration of albumin in the blood is more affected by the nutritional factors than the other fractions of the blood protein; and if the dietary intake of the protein is less, the concentration of the albumin in the blood decreases and vice versa. The molecular weight of the albumin is much less than the globulin and, therefore, the albumin is more permeable through the capillary walls than the globulin; and that is why the exudate contains mostly the albumin as protein component. In the majority of the diseases, wherever, there is alteration of the total serum protein percentage there is decreased of the albumin component and increased of the globulin component. The different major causes that are responsible for the decrease of the albumin are:—

- (1) loss of albumin through the different channels of excretion e. g. urine, ascitic fluid etc.
- (2) insufficient supply of the dietary protein.
- (3) impairment of the protein synthesis.
- (4) sudden plasma dilution following a sudden recovery from dehydration.

If the concentration of the albumin becomes very low œdema may develop. The study of the concentration of albumin has clinical importance and it gives a general idea of the state of the liver.

The serum albumin has got the specific power of reversible combination with other molecules like the anions of fatty acids & alkyl sulfonic acids, many aromatic carboxylic acids and acetylated amino-acids, sulfonamide derivatives, many types of naphthoquinone derivatives etc. These substances combine with the albumin upto a definite saturation and then these substances either combine with the globulin part or remain in the free state in the blood. The combined substances have a far reaching biological importance (Bennhold-1932-1938) and because of these substances, specially the anions of fatty acids, acetylated amino-acids the stability of the albumin is greatly enhanced.

The credit for the discovery of the fibrinogen goes to the English Physician William Hewson who did a series of experiment and observed that a portion of the proteins, now known as fibrinogen, is responsible for

clotting of blood. He observed that, "by agitating fresh blood with a stick, so as to collect this substance on the stick...the rest of the blood remains fluid." Even then the detail of the fibrinogen is not known. The molecular weight of the fibrinogen is 400,000 and their dimension perhaps is the biggest. This fraction of the blood is the most easily precipitated globulin fraction and can be removed from the plasma by any one of the three methods viz:— (a) ionized calcium helps in the spontaneous coagulation, (b) on heating at 50° it coagulates, and (c) it can be precipitated more easily than the other plasma protein by addition of salts. The fibrinogen originates from the liver (McMaster & Drury-1919, Whipple and co-workers-1922).

Denis (1859) termed that fraction of plasma protein which is precipitated on dilution and redissolved on addition of salts as globulins. The globulin part of the blood protein is also not a homogenous one and all serum globulin fractions also contain carbohydrate. According to Tiselius (1937) alpha-globulin contains 0.4% of hexose, Beta-globulin 2.2% and gamma-globulin 0.7% of hexose. This study was carried on horse serum. Blix et al (1941) gave a much higher values of hexose content in the two normal sera:—

	alpha-globulin	Beta-globulin	gamma-globulin
Normal I	—	8.3%	3.6%
Normal II	6.0%	6.2%	3.0%

The alpha one and Beta one globulins are the lipids carrying part of the globulin. The molecular weight of alpha one globulin is 200,000 and of alpha two globulin is 300,000. In the alpha one globulin part there is 35% of lipid content and in the beta one globulin the lipid content is 75%. The alpha two globulin is the glyco-proteins, muco-proteins and esterase carrying part. The molecular weight of the gamma-globulin is 160,000 (Porter (1950) and probably the structure of the gamma-globulin consists of a long chain of over a thousand residues. Porter's observation also suggest that antibody and gamma-globulin are similar chemically and this leads to the conclusion that antibodies are formed by the simple rearrangement of the pre-existing serum globulin but that hypothesis has now carried no weight as the present study by the radio-isotopes techniques has clearly shown that the antibodies are newly formed proteins and not a derivatives of the

precursors that circulate in the body. (Green and Anker 1954) The globulins can be easily precipitated out from the plasma or the serum by lowering the P_H to the neighbourhood of the isoelectric point (P_H 4.5) or by lowering the salt concentration through dilution or dialysis. Sorensen (1924-25) has determined the molecular weight of globulin to be 100,000 whereas Cohen et al (1925) after determining the molecular weight of serum albumin and serum globulin by different methods have concluded that the molecular weights of albumin and globulin are 45,000 and 81,000 respectively. Govaerts (1927) has observed that the weight of the albumin molecule is only one fourth of the globulin. The gamma-globulin in human is about 11% of the total protein percentage and approximately 3% of the normal human plasma is the beta-two globulin. The antibodies are mostly associated with the gamma-globulin but some antibodies are also present in the beta-two-globulin. Physiochemically the beta-two and gamma-globulins have much similarity and the molecular weight of both are near about 160,000; but a portion—about 10 to 15% of these two fractions have a higher molecular weights. Simple sugar, amino-acids, tartrate and succinate react with the gamma-globulin and make it more stable and these chemical also modify the solubility of the gamma-globulin. It is difficult to distinguish the gamma-globulin from the beta-two globulin precisely (Oncley-1953). The gamma-globulin mobility in P_H 8.6 and 0.1 ionic strength barbiturate buffer may be as low as -0.8×10^{-6} and that of beta-two globulin in the same identical condition may be as high as -2.2×10^{-6} . The gamma-globulin is separated from the beta-two globulins by adding sodium chloride to the solution dissolved in 0.04 to 0.06 mole fraction ethanol (Oncley-1953). Sulphate, nitrate and specially the tartrate were more effective than the chloride in such fractionation (Gord & Gordon). Kirkwood and his colleagues used the method of electrophoresis to fractionate the two components of the globulins. It has been observed by Petermann (1946) and Bridgman (1946) that even though the half of the molecule of the gamma-globulin be destroyed by the enzymatic action, the various antibodies linked with gamma-globulin is still not destroyed and remain as active as before. Because of the close association of the antibody and gamma-globulin it has been suggested that the macrophage is the principal fabricator of serum globulin. Sabin (1939) was of opinion that the serum globulin originated from the macrophages by the process of "shadding of surface films or cytoplasmic material". She concluded, "that the

cells of reticulo-endothelial system normally produce globulin and that antibody globulin represents the synthesis of a new kind of protein under the influence of an antigen." Sabin's opinion on the origin of serum globulin specially the gamma-globulin was soon modified and it has been advocated by Rich (1944) that the antibodies originate, not from the macrophages alone, but also from the lymphocytes. Rich has expressed that, "the lymphocytes is concerned in some way with the earliest reaction of the body to foreign proteins warrants its consideration in relation to the problem of the cells concerned in antibody formation." Ehrich et al (1942 to 1945) have also thought in the same way and have suggested that, "the lymphocytes either produce antibodies or take them up from the lymph plasma." Dougherty et al (1944) have thought that the antibodies do not originate from the lymphocytes rather the lymphocytes act as "a store-house of antibody protein." They have regarded the lymphocytes as the carrier of the antibody protein and are of opinion that the antibody protein may be released at an increase rate "in circumstance augmented adrenol cortical secretion."

The exact chemical composition of the globulin is not known; but the evidences are there that it contains several amino-acids essential for the growth in the experiment carried on rat; and in human body essential for nitrogen balance. Calvery (1938) did the analysis of the globulin and though his analysis was incomplete but he isolated 14 amino-acids from the serum globulin in the following orders:

Glycine	..	3.5%
Alanine	..	2.2%
Leucine & Isoleucine	..	18.7%
Histidine	..	0.9%
Arginine	..	5.2%
Cystine	..	1.0%
Proline	..	2.8%
Phenylalanine	..	3.8%
Tyrosine	..	6.7%
Tryptophane	..	2.3%
Glutamic Acid	..	8.2%
Aspartic Acid	..	2.5%
Lysine	..	6.2%

Brand, Kassel and Saidel (1944) have analysed a specimen of purified gamma-globulin and have found 12 amino-acids. In both the analysis it has been found that seven out of eight amino-acids essential for nitrogen equilibrium in man were present; and also the fact that all the amino-acids present in the serum cannot be synthesised by body but is to be substituted in the diet. That the serum globulin is composed of 3 different fractions namely alpha, beta and gamma and the latter is only associated with antibodies is the result of Tesilius who fractionated the serum by electrophoresis. The evidences, that support the fact that the gamma-globulin is associated with antibodies are many and one of these is that in the new-born calf there is deficient of gamma-globulin and after 18 to 24 hours after the ingestion of the colostrum the gamma-globulin appears in the serum. It has also been found that there is an increase of gamma-globulin content in the hyperimmunised individual. The close association of the antibodies and the gamma-globulin or a fraction closely resemble to gamma-globulin fraction is not definite as yet; but the studies and investigations that have been carried out so far by the different investigators on the rabbit, horse, rat, monkey, and man all are in support of the fact that the antibodies are carried in the slow mobile fraction of the globulin. The gamma-globulin in normal individual is one third of the total concentration of the serum globulin; the increase of globulin or alteration of albumin/globulin ratio may, therefore, be affected by the other two-thirds of the total serum globulin concentration and these two-third of the total serum globulin is constituted by the alpha and beta component.

The plasma protein has got the power of regeneration and it has been found that the globulin regenerates more rapidly than the albumin (Kerr, Hurwitz & Whipple—1918, Smith, Belt & Whipple 1920). The observation of Bodansky et al (1927) and Fishberg (1929) that after hæmorrhage the globulin is restored more rapidly than the albumin is also in conformity with the previous observation. In an average in man 25 Grams of albumin can be regenerated in 24 hours (Peters & Van Slyke—1931). The different proteins behave differently so far the regeneration is concerned and they have the different influences over the regeneration of the proteins; e. g. serum proteins, liver proteins have the capacity of decreasing the potency in influencing regeneration of plasma proteins. It has

also been observed that the administration of certain types of proteins promotes the regeneration of a certain type proteins only; to give an example it is found that lact-albumin stimulates the synthesis of plasma-albumin and not plasma globulin.

The determination of nutritive value of protein is essential not only from the point of Biochemists but is also a problem to the Nation as a whole, particularly to the Economist and the importance can be well understood by the fact that Britain annually imports 1,048,000 tons of animal protein and that costs near about £ 38,129,000. A considerable amount of this money could have been saved by the proper use of them "to balance the ration." (Cuthbertson—1957). All the proteins are not of equal biological value; though it has been considered that the animal proteins, as they are structurally similar and hence easily assimilable to the human body are of high

TABLE No. II
Comparison of the "biologic value" and digestibility of the different proteins.

Food.	Quality of protein		Protein value of food on fresh basis
	Digestibility P.C.	Biologic Value P.C.	P.C.
Whole cooked egg	100	94	12.0
Milk	100	85	2.6
Egg white (cooked)	100	83	10.0
Beef liver	90	77	14.9
Beef kidney	99	77	12.3
Beef heart	100	74	11.3
Beef Round	96	69	13.7
Pork ham	100	74	17.9
Veal	100	62	12.4
Rolled oats	90	65	9.8
Whole wheat	91	67	7.1
White Flour	100	52	4.3
Whole corn	95	60	3.0
Potato	78	67	0.8
Navy beans (cooked)	76	38	4.2

(after Mitchell & Hamilton)

biological value or first class protein; but actually the classification of proteins depends upon the availability of the essential amino-acids and also partly to the accompany vitamins; and not upon the power of simple assimilability alone. The nutritive value of protein depends upon the two factors, viz :— (a) digestibility and (b) the availability of the amino-acids specially the proportion of the essential amino-acids for the construction of the tissues protein and, hence, "the biologic value" or "the protein efficiency ratio" does not completely give the full picture of the protein as two proteins of same biologic value may contain different proportion of the essential amino-acids availability. "The biologic value" of the protein is assayed by (I) the efficiency for growth and (II) the amount of absorbed Nitrogen retained in the body as measured by the Thomas Mitchell Method (Bender—1957). The animal protein have got highest digestibility ranging from 95 to 100 percent; the digestibility of potato is near about 80% and the biologic value and the digestibility of these different proteins are compared in Table No. II.

Because of these varying digestibility and biologic value the usual normal requirement for the human body is also varying. It has been observed that certain protein that is quite sufficient for the adult to repair the damaged tissues may not be sufficient for a young where the function of the requirement and the function of the growth are to be carried on by the protein. Moreover, certain functions like replacement and building up of specific plasma protein, hæmoglobins and enzymes may be quite different from that for the repair of the body tissue as a whole (Henry—1957). Sherman (1920) after repeated experiments with human beings has come to the conclusion that, "a standard allowance of 1 Gms. of protein per Kilo of body weight per day appears, therefore, to provide a margin of safety of 50 to 100 p. c. as far as requirements of adult maintenance are concerned." The Food and Nutrition Board of National Research Council has advocated a quota of 70 Gms. of protein daily for a man weighing 70 Kilograms and 60 Gms. to a woman weighing 56 Kilograms. It must be remembered that those recommendations are designed for the maintenance of good nutrition of healthy persons in U.S.A. and allowance must be considered for the persons living in different climatic condition, stature of the body etc. Keys (1948) has, therefore, advocated that this recommendation of the National Research Council "could be reduced to 50 Gms. and still provide approximately 30 p. c. margin above require-

ments." He has come to this conclusion after much careful studies and observations. He has found that no advantage is obtained if greater than two-third Grms. of protein per kilogram of body weight is given to young man doing hard work. He has expressed himself with the words, that, "in studies on young man doing hard work in the open no advantage was found for intakes greater than about two-third this amount, (1Gm. of protein per kilogram of body weight for adult) even when much of the protein was from the vegetable sources."

THE HISTOLOGICAL EFFECT OF LIQUORICE EXTRACT ON EXPERIMENTAL GASTRIC CINCHOPHEN ULCERS IN DOGS

In cases of gastric ulcer the disappearance of symptoms is attained more rapidly by the use of liquorice extract than by any other usual medicamentous treatment. In previous investigations of experimental gastric histamine erosion in rats they employed liquorice extract with good results. Changes shown by cinchophen ulcers during therapy with liquorice extract have been observed in experiments on 37 dogs. In the course of treatment gastric mucous secretion was found to increase, a phenomenon interpreted by the authors as a defensive reaction of the organism against the cinchophen. Mucous secretion was seen to be more copious in the regions of the lesser curve and of the pylorus than in the duodenum. This explains why treatment of humans with liquorice extract brings more favourable results in gastric ulcer than in duodenal ulcer.



"You will spread virus disease by emptying your flute on the stage...."

Section of the Pituitary Stalk for Secondary Cancer

By DR. F. L. DAVIES, M.B., B.S., F.R.C.S.

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Hurstwood Park Hospital, Haywards Heath, Sussex, England.

HYPOPHYSECTOMY is an established surgical procedure in the treatment of advanced cancer. Results of this operation have been reported by Perrault et al (1952), Shimkin et al (1952), Luft and Olivecrona (1952) and by Pearson et al (1952).

Luft and Olivecrona (1953, 1954) have shown that when hypophysectomy is complete a remarkable regression of the carcinoma of the breast may occur.

All the available evidence indicated that only those cases of breast cancer which are hormone dependent benefit from removal of the pituitary. The present difficulty in selecting patients with breast cancer for operation is in determining those whose growths are in fact hormone dependent.

Two possible tests are available, in one (Pearson) oestrogens are given and the effect on the mammary cancer noted, an increase in activity indicates that the growth is influenced by oestrogens and that hypophysectomy might be of value. The second test (Hadfield) is the estimation of the mammatrophins in the urine by injection into mice. Further work on these methods is awaited with interest. It should be noted, however, that while patients who have had a favourable response to oophorectomy or to androgen therapy are likely to have a favourable response to hypophysectomy, failure to respond to androgen or oestrogen therapy does not necessarily mean that the patient will fail to respond to hypophysectomy.

Following the publication by Rothenberg et al (1955) of their method of pituitary destruction by the injection of radioactive chromic phosphate, we gave this method a trial at the Middlesex Hospital. Davies (1956), Davies & Buxton (1957)

This procedure appeared from the published report to be a relatively simple operation compared with that of hypophysectomy, which in severely ill patients can be a major undertaking. Furthermore, we decided it would be of value to compare the

results of injection alone with that of injection plus stalk section and with stalk section alone. Davies & Buxton (1957), Nabarro et al (1958).

We were unable to confirm the satisfactory results as described by Rothenberg et al. and in no case that had undergone injection of radioactive substance was there any clinical or endocrine evidence of effective pituitary destruction. In one case, however, there was profound disturbance of endocrine function soon after operation. In this case, there had been some damage in the region of the pituitary stalk and it was decided to section the stalk deliberately in future cases. In three cases the stalk was sectioned and radioactive chromic phosphate was injected into the gland. All three cases showed profound endocrine change. It seemed that the important part of this procedure was the stalk section and so further cases were subjected to this procedure alone.

Thirty cases of secondary cancer have been treated by section of the pituitary stalk. In twenty seven cases the primary was in the breast, in one the prostate, in one the nasal cavity and in one the uterus. (See diagram).

INVESTIGATIONS (PRE-OPERATIVE)

A complete investigation of pituitary function was carried out pre-operatively. A complete blood investigation—(Hb, R. B. C., W. B. C., blood urea, serum electrolytes, cholesterol, blood sugar, electrophoresis, and proteins) was made.

The B. M. R. and radioactive iodine uptake and excretion was estimated. The urinary 17 ketosteroids and glucocorticoids (cortisone metabolites) were estimated as well as the daily calcium output. A complete radiological skeletal survey was made.

OPERATIVE PROCEDURE

This has been previously described. [Davies (1956) and Davies & Buxton (1957).]

In summary, a coronal scalp incision is made or a small unilateral frontal flap is turned down, a trephine opening $1\frac{1}{2}$ inches in diameter is made above the superior orbital ridge, the frontal lobe is elevated, the olfactory tract is cut and the pituitary stalk is then seen beneath and behind the optic chiasma. It is held with a blunt hook and gently coagulated and cut. The superior part of the pituitary gland is then coagulated with a low current, a piece of cellophane is placed on the diaphragm over the gland and the wound closed by replacing the disc of bone and scalp. A general anaesthetic is used.

POST-OPERATIVE COMPLICATIONS

These have been of a minor nature. All patients have complained of slight headache for the first forty eight hours or so. Others complained of a feeling of fullness behind the eyes for a few days, nausea and loss of appetite. In one patient there was a temporal field defect, but this cleared up after a few weeks. There were no permanent visual abnormalities. Several of the early patients collapsed post-operatively, showing a very rapid pulse, low blood pressure, having a pale skin and being very drowsy. In these cases the intravenous injection of Hydrocortisone 100 mgm. in 100 c.c.s. of water produced dramatic improvement.

Diabetes insipidus was present for varying lengths of time in all patients. In the majority it made its appearance about the second or third day and tended gradually to improve after a few weeks. In two patients, however, who have survived the operation for over a year and a half, diabetes insipidus has persisted, necessitating twice weekly injections of Pitressin tannate (10 units).

POST-OPERATIVE TREATMENT

100 mgm. of Cortisone acetate is given intramuscularly to all patients while the operation is in progress, unless the pre-operative investigations have shown depression of adrenal function. In those cases, the Cortisone is started a few days before operation.

When the patients return from the theatre to the ward, they are given 25 mgm. of Cortisone acetate six-hourly for the first few days. After two days the dose is gradually reduced until at the end of ten days the patient is usually on a maintenance dose of 12.5 mgm. twice daily. Later, it is usually found possible

to reduce the Cortisone to a dose of 12.5 mgm. daily.

Several weeks to two months after operation, most of the patients show signs of hypothyroidism. These are then given Thyroid extract gr. $\frac{1}{2}$ twice daily.

It should be emphasised that this is just a typical post-operative regime, but that each patient reacts differently and the programme has to be modified accordingly.

RESULTS

All these patients, with the exception of one, have shown an immediate and profound depression of endocrine function following operation.

The radioactive iodine uptake was considerably reduced in all cases and the 17 OH and 17 KS rapidly decreased in all cases post-operatively.

In those patients with skeletal metastases, the twenty-four hour urinary calcium excretion showed marked reduction. Example: from 42.52, 36 to 14, 19, 24 mgm. per 100 ml. respectively. These figures suggested marked reduction in the activity of the bony metastases. This was further shown by post-operative X-ray control.

Cases 9 and 10 had been bedridden with pathological fractures of the femora before operation. They were improved to the extent of being able to walk out of hospital after operation.

In two cases there has been marked relief of bone pain and, except in the one patient who died immediately following the operation, all patients have shown subjective improvement, even though a few had no radiological changes in the skeleton.

Case 11 had multiple secondary deposits in the lungs, with bilateral pleural effusion. She showed remarkable improvement after operation, the pleural effusion did not recur, the lung deposits and the cutaneous metastases showed regression. This patient is now back in her home in South Africa and writes that she is very well three years after operation.

CONCLUSIONS AND SUMMARY

1. Complete destruction of the pituitary gland was

- not attained in any of the six patients in whom radioactive chromic phosphate was injected into the gland.
2. Three cases in which injection of radioactive material plus section of the pituitary stalk was carried out showed marked endocrine depression and subjective improvement—even if temporary.
3. Of the thirty cases of secondary cancer which have been subjected to pituitary stalk section, one patient has been in remission for three years and is still alive and well without any symptoms; two patients (both with secondaries in the lungs, an effusion and bony metastases) are alive and well with marked radiological improvement in the appearance of the bones one and a half years after operation; five patients have shown marked improvement and are still alive from periods of one to four months after operation; there has been no operative death, the patient dying on the table (but as large bilateral pleural effusions were present and had not been aspirated, it was felt that her death was due to respiratory embarrassment while under the anæsthetic).
4. Post mortem examinations have been performed on a considerable number of these patients and it is interesting to note that in no case has there been 100% necrosis of the anterior lobe of the pituitary gland. A various amount of viable tissue has been found, but as all these patients had shown marked endocrinological changes, such as depression of the iodine uptake and very low ketosteroid excretion, it is felt that it is not essential to remove all the pituitary gland in order to obtain a satisfactory clinical result.

In the pathological material which we have, there is no evidence of any revascularisation of the pituitary stalk or of the infarcted areas of the pituitary gland. It is therefore felt that the technique of the operation described for section of the pituitary stalk through a small trephine hole without major craniotomy is a relatively simple procedure and is much safer when used for seriously ill patients.

It is certainly true that when the beneficial effect of

stalk section appears to have worn off, the patient shows evidence of reactivation of the secondary deposits and rapidly goes downhill. This, however, occurs after hypophysectomy and so is not a valid objection to stalk section.

The main problem is the selection of cases of malignant disease in which regression of the tumour may be expected. So far, we are not able to do this, and in this small series fourteen patients have shown no change, and it is reasonable to assume that their cancer was not hormone dependent.

I wish to thank the following colleagues who have collaborated in this work :—

Dr. J. D. N. Nabarro, Dr. G. Walker, Dr. A. M. Jelliffe, Dr. P. B. Buxton and Professor B. W. Windeyer, of the Middlesex Hospital, and Dr. C. Riley, Pathologist to Hurstwood Park Hospital.

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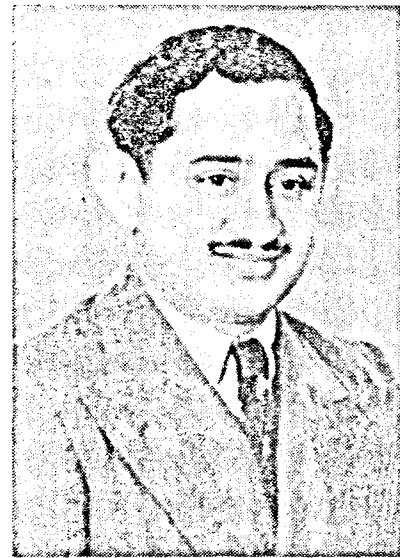
CASES TREATED BY SECTION OF THE PITUITARY STALK

Case	Age	Sex	Site of Primary Tumour	Effect on Tumour	Post Operative Survival
9	57	F	Breast	Relief of Bone Pain	
10	58	F	Breast	Relief of Bone Pain	Died at 14 weeks
11	42	F	Breast	Regression of Cutaneous & Pleural deposits	
12	63	M	Prostate	Marked Fall Acid Phosphatase	
13	46	F	Breast	No Change	Died at 10 weeks
14	42	F	Breast	No Change	
15	72	F	Breast	No Change	Died at 1 week
16	69	F	Breast	No Change	Died at 12 weeks
17	49	M	Nasal Cavity Fibrosarcoma	Relief of Pain Superficial Necrosis of Tumour	Died at 8 weeks
18	75	F	Breast	Regression of Primary and Secondary Growths	Died at 16 weeks
19	74	F	Breast	Regression of Primary and Secondary Growths	Alive at 60 weeks
20	23	F	Breast	No Change	Died at 6 Hours
21	56	F	Breast	No Change	Died at 12 weeks
22	38	F	Breast	No Change	Died at 2 weeks
23	62	F	Breast	No Change	Alive at 55 weeks
24	49	F	Breast	Regression of Primary and Secondary Growths	Alive at 54 weeks
25	42	F	Uterus	No Change	Died at 4½ weeks
26	50	F	Breast	No Change	Alive at 9 weeks
27	41	F	Breast	No Change	Alive at 8 weeks
28	48	F	Breast	Slight Regression	Alive at 7 weeks
29	51	F	Breast	Slight Regression	Alive at 6 weeks

MEDICAL NOTES & NEWS

DOCTOR OF MEDICINE—CAMBRIDGE UNIVERSITY

"WE offer our warmest congratulations to one of the members of our Editorial advisory board, Dr. Vishnu Sarma for having been admitted to the Degree of Doctor of Medicine—M. D. (Cantab)—by the University of Cambridge.



Dr. Vishnu Sarma

Dr. Vishnu Sarma took the Natural Science Tripos at Emmanuel College, Cambridge and was then as St. Bartholomew's Hospital for his clinical studies. At this oldest hospital in London, he won the Matthews Duncan Prize in Obstetric Medicine: the first Indian to win this coveted prize. Student of the late Wilfred Shaw, he took up Obstetrics and Gynaecology for a specialty. After taking the conjoint diplomas of the Royal College of Physicians and Surgeons (M.R.C.S., L.R.C.P.) he took his medical degrees at Cambridge. After qualification he held a number of appointments in the National Health Service obtaining experience in Surgery, Anaesthesia and Gynaecology. In 1953 he was elected a Fellow of the Royal Society of Medicine, England.

Returning to India he joined the Madras Medical

Service and had an opportunity to work in the maternity hospitals of the city. For independent and outstanding research in Obstetrics during this period he was given the M. D. Degree. This recognition from one of Britain's foremost Universities comes as a great honour. Working for a year as a postgraduate student in the Institute of Obstetrics and Gynaecology he obtained the Diploma in Gynaecology and Obstetrics from Madras University. Greatly interested in medical illustration, photography and other visual aids in medicine, he illustrates his own articles. He has published more than 75 papers in various journals relating to the speciality. Two of these have been abstracted and republished in "Obstetrical and Gynaecological Survey" of New York.

We are surprised that the Govt. of India has not already absorbed this doctor in their teaching personnel for the All India Institute of Obstetrics and Gynaecology. Unless we make use of qualified men and encourage them the country stands to lose their services.

* * *

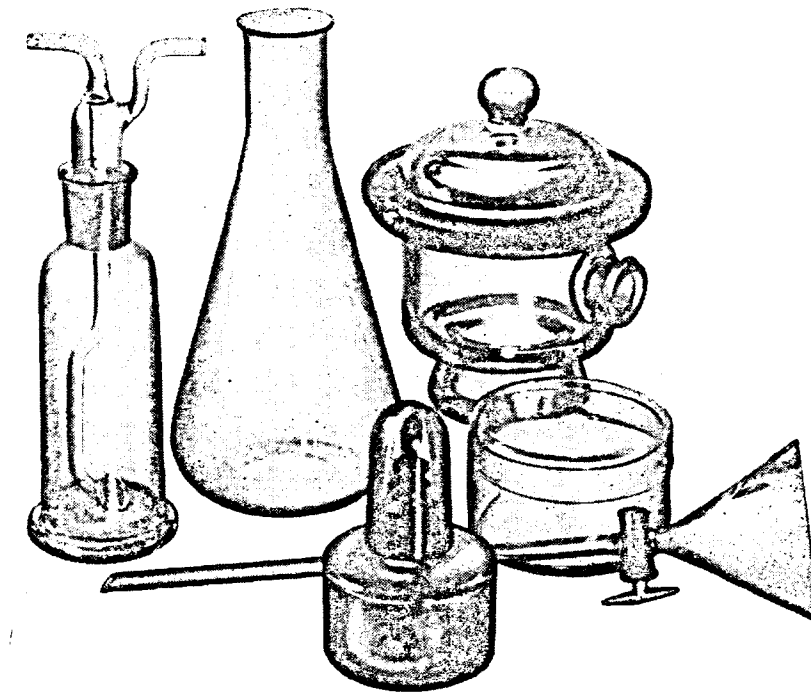
LEDERLE LABORATORIES

NEW YORK—More prescriptions were filled in the United States last year for Lederle Laboratories' Achromycin tetracycline than for any other prescription drug, states a study just made public.

The total for Achromycin came to 18,392,000—7,184,000 for Achromycin V, a newer and faster acting form of the drug, and 11,118,000 for the original Achromycin. This was the third straight year that Achromycin has outdistanced every competitor.

The study also revealed that there were 115 different drug products for each of which more than 1,000,000 prescriptions were filled in 1957 in the United States.

* * *



WHY JUST PETRI DISHES AND TUBES?

1. BECAUSE they are manufactured by a special method — a special pressing. This method guarantees the outside bottom surface as it is in the case of hollow dishes but mainly the bottom smoothness free from the microscopic pits and scratches which the microorganisms find it so easy to settle in.

2. BECAUSE they are made of the best quality glass — the best selected Czech glass.

3. BECAUSE they are perfectly sterilized by autoclaving, and their smooth surface and perfectly even edges prevent any contamination.

4. BECAUSE they are made of the best quality glass — the best selected Czech glass.

5. BECAUSE they are not more expensive than glass which are not of such a good quality.

GLASSEXPORT
PRAHA - CZECHOSLOVAKIA.

SIMAX - SIAL - KAVALIER

LABORATORY AND MEDICAL GLASS HAS BEEN SERVING WELL AND RELIABLY FOR MORE THAN 120 YEARS.

IT IS POPULAR AND IS SUPPLIED TO ALL PARTS OF THE WORLD.

GLASSEXPORT

PRAHA - CZECHOSLOVAKIA.

VARIDASE BUCCAL TABLETS INTRODUCED BY LEDERLE

NEW YORK (Special)—A buccal tablet form of Varidase streptokinase streptodornase which reduces inflammation and swelling due to trauma or infection has been introduced by Lederle Laboratories Division, American Cyanamid Company. Buccal Varidase is an enzyme product which provides a readily acceptable dosage form to patients and is used in the treatment of abscesses, burns, cellulitis, edema, hematoma, uveitis, sinusitis, chronic bronchitis, chronic bronchiectasis, thrombophlebitis and leg ulcers.

The new mint-flavored product is allowed to dissolve in the patient's mouth and is absorbed into the body. Unlike the injectable form, Varidase Buccal does not require regrigeration

Varidase Buccal acts, as does the parenteral form of Varidase, to activate a body process which helps dissolve fibrin deposits in areas inflamed as a result of infection or trauma and also reduce swelling, pain and discomfort. Where infection exists or may be expected, Varidase Buccal is used in conjunction with an appropriate antibiotic such as Achromycin tetracycline.

Since Varidase acts through the blood stream, it is effective in remote inflammations or infections.

The new product was recently employed in the treatment of 62 conditions in 57 patients by Dr. Joseph M. Miller and associates of the Veterans' Administration Hospital, Fort Howard, Md. Reporting in the February 1st issue of the Journal of the American Medical Association, they indicated that 55 conditions such as abscess, cellulitis, edema and thrombophlebitis responded excellently to buccal treatment while only three results had to be classified as poor. All patients were treated concurrently with antibiotics.

The usual dosage of Varidase Buccal is one tablet, four times daily for a minimum of three days, under the guidance of a physician. The average course of therapy is five days and dosage for as long as several weeks may be necessary in certain chronic conditions. Since Varidase is inactivated by the gastric juices, the tablets should not be chewed or swallowed.

Ease of administration of the buccal form is

expected to increase the usefulness of Varidase to the general practitioner. Because Varidase has been found most effective when administered several times daily, the injectable form has been used primarily in hospitals.

Clinical trials with Varidase Buccal to date have indicated a lack of mucosal irritations and an absence of side effects including allergic manifestations.

Each Varidase Buccal Tablet contains 10,000 units of streptokinase and 2,500 units of streptodornase. The product is supplied in bottles of 24 tablets.

* * *

NEW SULFA IS EIGHT TIMES MORE EFFECTIVE

A new sulfa drug, permitting considerably lower dosage, is substantially altering sulfa therapy and contributing, in the process, to renewed interest in these oldest of 'wonder drugs.'

The new comer is Lederkyn, known to chemists as sulfamethoxypyridazine. It has come into use throughout the world in recent months.

Its action is so much longer lasting than that of any previous sulfa, that amounts, as small as one-eighth of those hitherto required, accomplish the same results against infection. Maintenance dosage, for instance calls for only one-half gram a day, whereas four grams of other sulfas are necessary for the same purpose.

The new drug remains in the blood for days, compared to only a fraction as long with other sulfas. Consequently only one dose, instead of several, is necessary every 24 hours.

Lederkyn underwent two years of clinical testing before being generally introduced not long ago. At a Conference on Sulfonamides sponsored by the New York Academy of Sciences six groups of investigators reported their findings.

They described with special interest the value of the new drug against long-lasting infections. Stubborn genito-urinary infections were mentioned in particular, as well as rheumatic fever, where the

patient must be protected for extended periods from streptococcal infections. In addition to these, Lederkyn has been found effective in most of the diseases which yield to earlier sulfas, such as bacterial dysentery and upper respiratory infections. It is absorbed rapidly across the blood-brain barrier.

Side effects are reported minimized by Lederkyn because of its considerably greater solubility in the body and the lower dosage requirement. It thus tends to make available to physicians the therapeutic power of the sulfas without some of the problems hitherto associated with their use.

This latest and furthest sulfa advance climaxes a full generation of research and development of these drugs. The first, sulfanilamide, was discovered in Germany in the mid-1930's. A partial realization of Dr. Paul Ehrlich's dream of a "magic bullet" which would hunt down and destroy specific infectious bacteria, it created a world-wide medical sensation.

Its power against pneumonia, for instance, was astounding at the time. Pneumonia had been from time immemorial one of the principal killers. In short order, sulfanilamide cut pneumonia death rates by 80 per cent.

And so it went. Against certain other infections, the new drug was not invariably quite as dramatically effective as that, but its power was still beyond any ever seen before.

Sulfanilamide was not perfect, however, and problems remained, especially those of side-effects. From the beginning, therefore, improvement was sought and was steadily achieved, step by step.

One of the chief sources of such advance was Lederle Laboratories Division, American Cyanamid Company, developers of the new Lederkyn. Lederle had been a pioneer in the original industrial production of sulfas, immediately after their emergence from experimental status. And thereafter the company steadily and successfully—pursued the search for new and better types. Sulfadiazine, which was used by the ton in the last war, and sulfaguanadine are among earlier sulfas resulting from research.

As years went by, the sulfa family grew to be one of the largest in medicine. The current edition of a standard physician's reference book lists 300 dosage

forms of sulfas and sulfa-antibiotic combinations. Some of them are sulfapyridine, sulfathiazole, sulfamerazine, sulfamethazine and the so-called "triple sulfas", the meth-dia-mer-sulfonamides. These combine three different kinds of the drug, so that the potential toxic effect of each is held to a minimum and total toxicity is less than with one type alone.

Problems of side-effects notwithstanding, sulfas have continued uninterruptedly to be one of the main reliances of the doctor. Many people suppose that penicillin, Aureomycin chlortetracycline, Achromycin tetracycline and other antibiotics have supplanted sulfa, but this is a misapprehension. United States sulfa sales for 1957 are estimated at \$ 40,000,000 the highest ever, more even than in the wartime peak year of 1943, when huge amounts were used to protect war wounded troops.

Doctors to-day regard the sulfas and the newer antibiotics as mutually complementary rather than competitive. And especially with sulfa research still steadily producing improvements, the place of these reliable standbys is considered secure in the medical world.

* * *

MEDICAL & SURGICAL EQUIPMENT FROM GERMAN DEMOCRATIC REPUBLIC IN THE LEIPZIG INTERNATIONAL TRADE FAIR — 1959

For centuries, mankind has been waging battle against the mysteries of disease and death, which for long seemed beyond understanding or control. Gradually, however, human determination and ingenuity have begun to lift the veil, and today, the area of mastery expands from year to year.

Paracelsus was the first to diagnose disease as a natural manifestation of living activity within the body; but the advent of the microscope was necessary before any advance towards a real understanding of the nature of disease was possible. The microscope was, in fact, the first major contribution to the storehouse of medical and surgical aids, which today range from X-ray apparatus and cobalt guns, and all the impressive details which make a modern operating theatre, down to sterile dressings and self-adhesive bandages.

Indeed, so great an advance has been made in the technique of medicine and surgery, that it is possible for an ever-increasing degree of attention to be devoted to preventive measures, and in the German Democratic Republic, much has been done in the last ten years to establish a health service designed to this end, although of course, cure will remain an important function of all health services for as far ahead as our imagination can reach. So many new hospitals have been set up in the G. D. R. in the last ten years however, so many sanatoria and rural clinics, and so many mobile examination centres have been brought into use; routine medical checks, regular X-ray tests and inoculation are such an important part of the work of the health services, that it has followed of necessity that there has been a tremendous development in the output of medical and surgical equipment of all kinds. This has been accompanied by intensive research in order to secure greater efficiency and higher safety factors in every direction.

It is not, therefore, very surprising that a big increase in the exports of medical and surgical equipment has been recorded, nor that the very comprehensive display of medical and surgical equipment presented by the G. D. R. at the Leipzig Spring Fair—58 was acknowledged by visitors to measure up to the highest international standards.

On the stand of Veb Transformatoren-und Röntgenwerke Dresden, for instance there were X-ray units ranging from small mobile sets suitable for outpatients clinics and travelling examination centres to fully automatic 6-valve equipment for big city hospitals. Equipment for galvanic shocks treatment was another feature of the firms stand, while particularly noteworthy was the very high frequency sound therapy unit known as the "US 2-1", which has working frequency of 800 kilocycles per second, and its adjustable for use in 13 stages. It has a radiant area of 10 square centimetres. For use with it, a VHF sound measuring instrument has been developed which has a frequency range from 200 to 3,000 kilocycles per second, and which is now the most precise measuring instrument of its kind on the market. Despite its advanced technical level, the prime cost of the whole unit is sufficiently low to bring this method of treatment within the range of every type of medical practice.

Ultra-violet, ultra-red and infra-red therapy is now much employed, and Veb Elmed of Hohenneuendorf, near Berlin will present a large range of apparatus

in this field at the Spring Fair—59. In addition, their stand will include a mobile dental X-ray unit and a mobile underwater radiation massage unit. Considerable interest would be aroused by this firms ultra-violet and ultra red irradiation chambers, designed for use in schools, factories and the overnight sanatoria which the G. D. R. has pioneered. They provide an effective substitute for solar irradiation, and encourage general resistance to contagious diseases and to rheumatism.

A new development of the "Iron Lung" will be shown by Veb Medi-zintechnik, Leipzig. It is specially designed for use with infants and children up to approximately 3 ft. 10 inches in height. The same makers new fully automatic dental anaesthetic unit, the "414", of exceptionally compact and convenient dimension. It employs a nitrous-oxide-oxygen medium, inhaled through a mask, and is provided with pressure-button mixture control.

An eight-channel electric encephalograph for recording cerebral activity will be shown by Veb Wissenschaftlich-Technische Büro für Gerätebau of Berlin, while the display of the ophthalmological department of VEB Carl Zeiss Jena will include numerous exhibits of interest. Microscopes will be the main feature, just as they were when Carl Zeiss showed at Leipzig Trade Fair 100 years ago. The 1959 exhibits, however, will include development that were unimaginable; for example, a retinal camera enabling direct colour photographs to be made of the retina of the eye, and a recording adaptometer for examining the susceptibility of the eye to light. Another remarkable Zeiss development recently perfected is the interior chamber lens, designed by professor Emmrich, which completely supersedes the cataract glasses formerly used.

It has been possible in this short article to mention only briefly a few products of the manufacturers of medical and surgical equipment in the German Democratic Republic. The range on show at the forthcoming Leipzig International Spring Trade Fair to be held from 1st to 10th March 1959 however will include a representative and comprehensive cross-section of their current programme, and, to add to its value, numerous exhibits from the leading makers in the Federal German Republic, the Soviet Union, Czechoslovakia, Hungary, Poland and Belgium and many other Western countries.

* * *

EXCELLENT CONTROL OF DIABETES REPORTED WITH NEW ORAL MEDICATION

Excellent control of diabetes, even in patients who had previously required relatively high dosages of insulin, was achieved with a new oral medication, Dr. Arnold Lenhardt of the Department for Metabolic Diseases of Austria's Krankenhaus der Stadt Wien—Lainz, reported recently at Dusseldorf, Germany.

Dr. Lenhardt told the 1500 diabetic specialists attending the Third Congress of the International Diabetes Federation that he found the new drug, called Diabinese, gave him excellent results in 97 of the 136 patients he studied. Seven other patients also responded, but to a lesser degree.

He said he was particularly impressed by the fact that patients who required relatively high dosages of insulin could be satisfactorily controlled with Diabinese. Of a group of 22 patients in whom it had been necessary to give considerably more than 40 units of insulin daily, he found that it was possible to control the diabetic state in 12 with the new oral medication. Ordinarily, patients receiving such high dosages of insulin would not be expected to respond to any oral anti-diabetic agent.

Diabinese is a product of the Pfizer company, the international pharmaceutical and chemical firm. It belongs to a family of chemical substances called sulfonylureas, and possesses the ability to lower the blood sugar in patients with diabetes.

The potency of the new drug was stressed both by Dr. Lenhardt and by Professor H. A. Heinsen, Medical Director of the Waldkrankenhaus Zeven, a noted clinic specializing in internal medicine near Hanover, Germany. As a result of this strength, the two physicians said, they were able to control diabetes with far lower dosages of Diabinese than of a similar agents they had used previously.

Initially the patients received one to 1.5 grams of the Diabinese daily, with the dosage being reduced during the first week of therapy to 250 to 500 milligrams a day. These dosages are two to three times lower than those required with other drugs.

Pointing up the prolonged action of the drug was Professor Lenhardt's finding that he was able to control patients on a single daily dose. Frequently the

patients needed the medication only every other day.

During the current period of clinical investigation, more than 2,500 patients have been treated with the new drug. In general, those who respond best are middle aged or older persons who have a mild or moderate form of the disease.

* * *

INDIAN SCIENTIST DISCOVERS ANTI-TUMOR COMPOUND IN AMERICA

A Chicago report dated September 10 says that the isolation and concentration of an anti-tumor compound active against some forms of cancer in animals was reported by Dr. K. V. Rao of the Cancer Research Center operated by the Pfizer company, the international pharmaceutical firm.

The drug, designated E-73, was described before the Medicinal Chemistry Section of the annual American Chemical Society meeting here.

E-73 belongs to the same chemical family as actidione, an antibiotic which is made by the same micro-organism (*Streptomyces griseus*) which produces streptomycin. Actidione, which was in clinical use from 1952 to 1955, has some anti-cancer activity. The E-73 compound, Dr. Rao reported, is much more active than actidione, but it is also much more toxic.

Thus, though it has shown suppressive activity against animal tumors, it is expected to prove too toxic to be useful in human patients. The discovery may, however, provide clues toward an understanding of the nature of the anti-tumor activity.

The John L. Smith Memorial for Cancer Research, where Dr. Rao's work was done, is a major research arm of the Pfizer company, a leading producer of antibiotics. The Smith Memorial will expend more than \$2 million this year in finding and screening anti-tumor compounds. Somewhat over \$1 million of this sum comes from the United States government through a contract with the Cancer Chemotherapy National Service Center of the U. S. Public Health Service—the largest such contract yet awarded—while the balance is contributed by Pfizer.

* * *

POWERFUL GROWTH-PROMOTING
SUBSTANCE FOUND IN TEST TUBE
PLANT TISSUES

NEW YORK—Powerful, growth-promoting substances, found in sunflowers, sweet clover and other backyard vegetation, can make plants grow faster and taller. They can even cause dwarf peas to grow to normal size.

Dr. Louis G. Nickell, a botanist at the Brooklyn phytochemistry laboratory of the Pfizer company, the international pharmaceutical firm, said his studies strongly suggest that this growth-promoting substance or substances are found in many plants and perhaps throughout the whole plant kingdom. His experiments are reported in a recent issue of the journal *Science*.

Unlike synthetic chemicals which are applied to plants to step up their growth, the substances now being studied occur naturally in plants and may play an important role in controlling growth, Dr. Nickell said. However, at the present time, their exact value to agriculture "still remains unanswered," he added.

Until recently, scientists believed that only gibberellin, a chemical product of a mold organism called *Gibberella fujikuroi*, could stimulate growth to the degree observed in Dr. Nickell's studies. However, Dr. Nickell's experiment suggests that gibberellin-like substances may be quite common to most, if not all, plants.

Gibberellin was first observed by Japanese researchers about 30 years ago when it caused unusual growth in rice shoots. Scientists in the United States have found that it causes increased seed production and faster rates of growth in certain plants and causes many flowers to bloom more quickly.

The plant extracts used in Dr. Nickell's experiments produced the same growth patterns in dwarf peas that gibberellin does: it made the dwarf peas grow into normal-size plants. Because of this, the botanist said there is strong reason to believe some similarity exists in the chemical structure of these two substances.

The substances used in Dr. Nickell's experiment were extracted from tissue cultures of sunflowers,

sweet clover, holly, pinto beans, century plants and periwinkle. These extracts were sprayed with an atomizer on dwarf pea plants. After three, five and seven days, these sprayed plants were compared with other dwarf peas—some of which had been sprayed with gibberellin and various other chemicals, and some that had been left untreated.

"Responses of the magnitude shown by the gibberellin standard solutions and by the plant extracts," Dr. Nickell said, "were not obtained with any other solutions of specific chemicals tested. Among the chemicals used were several common auxins (plant hormones), purines, numerous antibiotics, organic acids, amino acids, and various types of chelating agents (metal-binding chemicals)."

Dr. Nickell is conducting further experiments with the plant tissue extracts that produced the greatest growth.

SYNERMYCIN EFFECTIVE IN 95 PER CENT
OF PATIENTS STUDIED

According to a recent clinical evaluation of the effects of treatment with Synermycin, 94.7 per cent of 2,318 patients studied responded successfully.

This new round-up of clinical cases reported by independent investigators in 35 countries brings to 5050 the total number of reported cases in which the use of Synermycin has been described by physicians. Of this total, the new antibiotic proved effective in 95% of the patients.

Synermycin, the new "synergistic" antibiotic, joins oleandomycin and tetracycline in a combination highly potent against virtually all types of infections. It is a product of Pfizer, the international pharmaceutical firm.

Two important considerations in any new antibiotic are the absence of any significant side effects, and its ability to control organisms that have developed resistance to other commonly used antibiotics. On both these counts, Synermycin fared extremely well, the physicians reported.

"The fact that Synermycin was excellently tolerated in 98 per cent of patients is notable for a

broad-spectrum antibiotic preparations," the report said. "In only 0.3 per cent of patients was it necessary to discontinue therapy because of side effects. This result is most remarkable." In the remaining 1.7 per cent, side effects were mild enough to make discontinuance of therapy unnecessary.

While patients were able to tolerate the drug, bacteria definitely were not. In long-term therapy, one of the greatest hazards is that bacteria become resistant to antibiotics. Not so with Synermycin, stated the report. It continued: "Where Synermycin therapy has to be prolonged for more than the initial five to ten days, there appears to be no problem from superinfection due to newly resistant pathogens, or relapse due to the development of resistance by the original infecting strain."

Commenting on the report, Dr. George E. Peabody, Director of the Medical Department, Pfizer International, said: "The notable potency of Synermycin is perhaps nowhere more evident than in its singular effectiveness against difficult, usually refractory, mixed bacterial infections. On the other hand, Synermycin can be generally recommended for broad use even, if necessary, in the absence of an exact bacteriological diagnosis, or for specific therapy of acute or chronic infections, whether of a nature ordinarily susceptible to most antibiotics or of a variety generally refractory in short or long term therapy."

The patients, who spanned a wide age range from months to 90 years, exhibited an equally wide range of ailments. The types of infections, and the number of those treated successfully, follow:

Head and neck infections—274 of 287 successfully treated, for a successful response rate of 95.5%.

Respiratory tract infections—411 of 431 successfully treated, for a successful response rate of 95.4%.

	Total	Successfully Treated	Rate of Successful Response
Gastrointestinal infections	189	179	94.8%
Urogenital infections	363	339	93.4%
Skin and soft-tissue infections	539	524	97.1%

	Total	Successfully Treated	Rate of Successful Response
Bone and joint infections	111	99	89.2%
Gynecologic and obstetric infections	161	153	95.0%
Deep-seated and generalized infections	81	76	93.8%
Miscellaneous conditions	156	140	89.8%

Infections responding best to treatment with Synermycin were those of the skin and soft tissue. Of 539 patients so treated, 524 (97.1 per cent) responded satisfactorily. In many cases, Synermycin controlled the infection so well that surgical drainage, which ordinarily would be necessary, did not have to be done. In others, infection was so satisfactorily controlled that it was possible to postpone surgery until the patient's general condition improved. Vital surgical procedures could then be done, which previously had been impossible because of the debilitated condition of the patient.

New Product Introduction

DELTACORTRIL INTRAMUSCULAR

The first intramuscular form of Prednisolone—DELTACORTRIL INTRAMUSCULAR—has recently been introduced in the local market by Ravison Pharmaceuticals Private Ltd., sole distributors for Pfizer products in India.

Deltacortril, Pfizer brand of prednisolone, the most effective corticosteroid available, has been found to be five times more potent than cortisone or hydrocortisone with minimum effect on electrolyte and water metabolism. With Deltacortril now made available in intramuscular form, fast intensive corticoid control could now be attained in seriously ill or debilitated patients, in the presence of vomiting or coma and in patients undergoing surgery where oral corticosteroid therapy is impracticable. DELTACORTRIL INTRAMUSCULAR affords a convenient and precisely controlled dosage and is free of local irritation or pain. On mg. for mg. basis it is equipotent to oral Deltacortril therapy and is used in the treatment of acute and severe arthritis, asthma, allergy and inflammation.

DELTACORTIL INTRAMUSCULAR is an aqueous suspension of prednisolone, containing 20 mg. of prednisolone acetate per cc. of solution. It is supplied in 3 cc. rubber capped vials.

New Product Introduction

TERRAMYCIN PREMIXED PEDIATRIC DROPS

Ravison Pharmaceuticals Private Ltd., Bombay, sole distributors of Pfizer products in India, have recently introduced for pediatric practice new **TERRAMYCIN PREMIXED PEDIATRIC DROPS**. This ready-to-use delicious dosage form replaces the original Terramycin Pediatric Drops which was available in dry-powder form.

In **TERRAMYCIN PREMIXED PEDIATRIC DROPS**, Terramycin the best tested and best proved broad-spectrum antibiotic has been made available in the best tasting vehicle. It is wild-cherry flavoured and leaves no aftertaste. No reconstitution, as with the dry powder form, is necessary and the preparation is stable at room temperature for two years even after the vial is opened. It is a completely homogenous preparation with viscosity and dispersion rigidly controlled, with the result that every drop delivers the same high potency and accurate dosage is assured.

TERRAMYCIN PREMIXED PEDIATRIC DROPS is made available in 10 cc. vial, each cc. providing 100 mg. of Terramycin, with specially calibrated dropper.

SURGEON'S-EYE-VIEW OF OPERATIONS

Shadowless Lightfitting With Camera Attachment

An unexpected feature of particular interest at the first International Hospital Equipment and Medical Services Exhibition, held in London recently, was the new Kelvin Hughes Shadowless Lightfitting, Model 36, with a small camera attachment. This camera unit, mounted into the centre of the lightfitting, enables colour photographs to be taken, to give a surgeon's-eye-view of an operation.

The exhibiting of this special operating theatre equipment was unexpected as Kelvin and Hughes

(Industrial) Ltd., of London, had not anticipated the complete fitting would be ready in time. Working against the exhibition opening deadline Kelvin Hughes engineers had the lamp and camera operating only an hour before the opening.

Using 35 mm. film it will take 200 pictures size 24×24 mm. This synchronised shutter and 200 joules built in flash is triggered from a push button operated by one of the theatre staff. The push button can either be fitted in the operating theatre wall or on a cable hanging from the lightfitting counter-weight arm. In the lightfitting, at opposite sides, are two ranging lights projecting two triangular patches of light which when matched ensure correct focusing.

Prototypes of the camera unit were given intensive trials at St. Mary Abbott's Hospital in London, and Glasgow, Scotland, Infirmary before the model shown in London was completed.

MEETS EXACTING REQUIREMENTS

A good light which enables him to see without effort and without strain, light which permits him to concentrate and use the combined skill of eye and hand without distraction. These are the primary requirements of the surgeon. Using experience gained in the manufacture of operating theatre lights for over a quarter of a century, Kelvin Hughes met the surgeon's exacting requirements. Model 36 is a streamlined shadowless operating theatre lightfitting which has five large reflectors totally enclosed in a metal housing. The reflectors are made from the purest aluminium, electrolytically polished and anodised to give a hard, non-tarnishing and scratched resistant surface. The lightfitting is designed for easy servicing and the glass windows are made from non-splintering glass sealed with rubber to prevent entry of dust or fumes.

Five-fold infra red filtering is used to absorb the radiant heat without obstructing the light. By using 24 volts, via a mains transformer, the fitting conforms to Britain's Ministry of Health recommendations. In addition the light field and intensity do not change when the fitting is switched to the emergency supply.

Theatre sisters will readily appreciate the attractive clean lines of the Model. There are no external cables, on unhygienic overhead runway, no risk of dust particles settling on a sterile area.

Suitable for every kind of surgery, Model 36 with its friction damped, counterbalanced suspension enables the light beam to be positioned positively on any area of the operating table at the touch of a finger. A simple external remote control enables theatre staffs, during operations, to focus quickly and accurately the reflector unit for variations in distance.

Space between the reflectors is sufficient to enable specialised equipment to be added, for example, cameras to take colour transparencies, television and cinematograph pictures. The ultimate result achieved by Model 36 is a colour corrected, truly cool light of optimum intensity, the manufacturers claim.

"ELECTRIC" SLEEP AND ANÆSTHESIA

Sleep is a very great aid to medicine. Many mental diseases, such as schizopheenia, cyclophrenia, epilepay and psychoneurosis are treated by sleep. Hypertension, sequelæ of contusions and chronic headaches are also treated by means of sleep. It also aids in the treatment of peptic ulcer which is far from being a neuro-psychic disease.



Vyacheslav Dubkov, technician at the electric medical equipment factory in Moscow, checking a single-channel "Elektroson" (electric dream) apparatus, for treating patients suffering from nervous disorders and hypertension.

The scope of treatment by sleep has considerably broadened since electric apparatuses enabled physi-

cians to control sleep. Many people know how distressing insomnia can be. The long hours of the night drag slowly, the slightest sound irritates the patient: the ticking of the clock, the noise of the passing vehicle and even the rhythmical breathing of people sleeping nearby. In the morning he wakes up, jaded, with a headache. The usual sleep-inducing drugs no longer give any relief and only increase his weariness and fatigue.

Use of Electric Current to Induce Sleep

About a century ago, scientists noted that animals acted upon by direct current passed into a state of stupor and fell asleep. Further development of electro-technology, especially electronics allowed a sleep-inducing apparatus to be designed. In the Soviet Union a group of workers of the Scientific-Research Institute of Experimental and Surgical Apparatuses and Instruments has designed an apparatus for inducing deep sleep. This apparatus is in the form of a small box, its anterior wall being a control board on which different knobs and an oscillograph tube are located. With this apparatus it is possible to regulate the frequency of the electrical impulses and their intensity. The duration of impulses is from 0.0004 to 0.001 seconds. The potential equals 8 to 12 volts, with current intensity from 0.2 to 0.8 milliampere. A number of safety appliances are provided in this apparatus which immediately switch it off in case of disorder. This fully guarantees the safety of health and life of the patient during its employment.

How does electric current induce sleep in a person?

Electric impulses of definite frequency and intensity act on the patient's skin. They cause stimulation of cutaneous nerve endings. From here the nerve impulses are transmitted to the central nervous system. This causes inhibition in the cortex of cerebral hemispheres similar to that which takes place in usual sleep. The patient falls asleep. Depending on the condition of his health, the nervous system and other individual causes, sleep is induced in 8 to 12 minutes after switching on the current. Therefore, the doses of electrosleep should be strictly regulated on an individual basis.

Until recently sleep was induced by the administration of potent sedative and somniferous drugs which

at times were harmful to the patient, causing attacks of nausea or depression. There are no such side-effects in the employment of electrosleep.

How is artificial electrosleep induced?

We enter the ward. An apparatus is standing on a table in the middle of the room. Wires connect it to rubber bands placed on the patient's head. Metal contacts are enclosed in the rubber bands. These contacts are linked with cotton wicks moistened with a current-conducting liquid.

The apparatus is switched on and the patient begins to feel a slight pricking in the eyelids. This sensation soon passes and the doctor slightly increases the current. The pricking reappears, and the patient falls asleep.

Use of Electric Current as Anaesthetic

Sleep caused by electric impulses can be so deep that it can even be used as an anaesthesia in prolonged

and serious operations. At present the development of a new apparatus "Electroanaesthesia" is being completed at the Institute. Electric impulses are, as yet, employed in conjunction with local anaesthesia. But only half of the usual amount of anaesthetic is required in this condition. Experimental surgical operations are being carried out on animals at the Institute under electroanaesthesia. It appears that additional local anaesthesia is unnecessary here. Extensive work is being conducted at the Institute on the employment of electroanaesthesia in surgical operations on animals without additional anaesthetics. More than 150 successful operations have already been performed in these conditions. After the removal of electrodes the "patients" felt excellent and had a good appetite. The post-operative course was uneventful.

A positive feature of electroanaesthesia consists in the fact that the duration of sleep depends on the period of action of the apparatus. The new effective method greatly facilitates the treatment of diseases in which the use of usual narcotics is contraindicated.

Investigation of Pleural Lymphatic Circulation with the Aid of Isotopes

The impulse to the experiments was given by the observation that transudations of cardiac origin presenting in the pleural cavity appear on the right side, while those of renal or hypoproteinaemic nature favour the left. The authors supposed that the difference between the two sides may be due to the difference in lymphatic circulation. Absorption by the lymph of the thoracic duct from the pleural cavity was studied on healthy dogs and on those with artificial hypoproteinaemia. Bismuth lactate isotope was used for the experiments. Absorption was found to be much more rapid from the right than from the left. The absorbed isotope was eliminated mostly through the thoracic duct.

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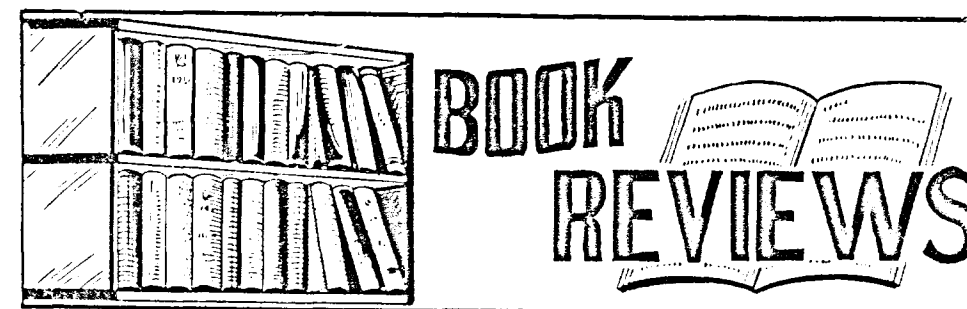
THE EFFECT OF ACTH ON INTRAOCULAR PRESSURE

In his experiments on four rabbits, the author recorded the fluctuations in the ocular tension of the animals over a period of one week. The following week

the animals were given daily 3 U. of intramuscular cortrophin per kg. body weight. A slight elevation of ocular tension took place. After an interval of one week a marked and constant rise in tension was noted upon daily doses of 6 U. per kg. body weight. Increased ocular pressure was observed in conjunction with ACTH treatment in a case of Bæck's sarcoid. Attention is drawn to the special importance of the regular checking of ocular tension during ACTH treatment of patients with a tendency to glaucoma.

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When Dr. N. Howard Hyman goes to a game, he likes company. For the past 15 years, his usual guests at outdoor sports here have been several hundred disabled veterans, most of them in wheelchairs. The New York dentist's work with the handicapped has just won him the first annual Hand-in-Hand Award, presented to a volunteer who has done an outstanding service to the community. Dr. Hyman was nominated for the award by the Eastern Paralyzed Veterans Association.



EYE SURGERY—

By H. B. STALLARD, M.B.E., M.A., M.D.(Cantab),
F.R.C.S.(Eng.) HON.LI.D. ST. ANDREWS.
Third Edition, Revised with 671 Illustrations,
John Wright & Sons, Ltd., Bristol, 1958

The purpose of this book is to give an account of surgical operations on the eye which have an accepted place in current practice.

The book is divided into 12 chapters. The first chapter is an introductory one and gives an account of the principles of ocular surgery. There are innumerable illustrations. The coloured picture of the set for 'cataract' is remarkable for its clarity. Chapter 2 deals with Anaesthesia and Akinesia for eye operations. This chapter has been re-written and includes accounts of the use of Basal Narcotics, Relaxants and Hypotensive drugs. Chapter 3 deals with the eyelids and reconstructive (plastic) surgery. Modern plastic procedures are incorporated. Chapter 4 concerns the Lachrymal apparatus. Chapter 5 is about the extra-ocular muscles: Strabismus and Heterophoria. Chapter 6 is on the Conjunctiva, Cornea and Anterior chamber, and Sclera. There is a modern and authoritative account of the Corneal transplant operation. Chapter 7 concerns Iris and the Ciliary body. Chapter 8 deals with the surgery of the Lens. This chapter includes a detailed account of the operations for Cataract. There is an account also of the intra-ocular insertion of acrylic lens after extraction. Chapter 9 is about Glaucoma. Chapter 10 deals with the surgery of the Retina, Choroid and

Vitreous. Chapter 11 is on traumatic surgery, civil and military. This section includes information on the management of conjunctival corneal burns. Adequate coverage has been given to the methods of dealing with foreign bodies in the eye. Chapter 12, the final chapter deals with the Orbit. It includes the management of fractures, operations of Orbitotomy, decompression of the Orbit and exenteration.

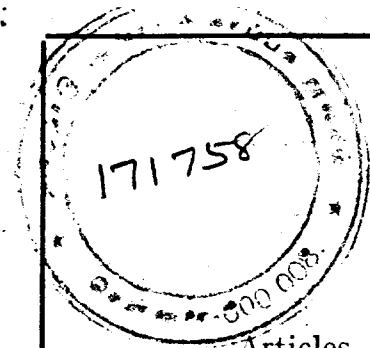
Many of the photographs have been taken with the cooperation of Dr. Peter Hansell of the Department of Medical Photography at the Institute of Ophthalmology. Almost all the chapters are preceded by an account of the anatomy of the structures of the eye. Stallard of Barts is more than a mere ophthalmic surgeon. His vast erudition is demonstrated by the choice quotations from the literature which precedes some of his chapters. He is to be warmly congratulated on using his artistic abilities to illustrate his book on operations on the eye. He states modestly in his preface: "I have done all the drawings. Some of these lack artistic finish, but I hope they will serve their purpose. My excuse for not employing a professional artist is that I enjoy the work and believe it to be good training for surgical hands." There is hardly any for such modesty because the primary object of medical illustrations is to be instructive rather than to be decorative. Stallard's views are fully endorsed by reviewer, who, although not an ophthalmologist has had the privilege and pleasure of seeing Stallard at work.

A medical library without Stallard's book on "Eye Surgery" cannot but be considered incomplete. The book is a 'must' for all eye surgeons.

The Use of Chlorpromazine in the Differential Diagnosis of Patients with Increased Basal Metabolism

With neurotic patients increased basal metabolism was normalized in one hour after the intramuscular administration of 25 mg. of Largactil, while in the case of hyperthyroid patients the drug exerted no influence on the rate of basal metabolism. The values obtained

after the injection of Largactil correspond to those recorded during investigation of the same patients under anaesthesia. The authors consider this method suitable for the solution of problems presented by differential diagnosis.



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Manuscripts should be submitted to us duly typed in double space with wide margin on one side of the paper in duplicate. Footnotes and bibliographic references should be on the lines of the Quarterly Cumulative Index Medicus of the American Medical Association, in the following order:-

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