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SURGICAL

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MEDICAL

NEWS

Vol. 7

1960
October

No. 1.



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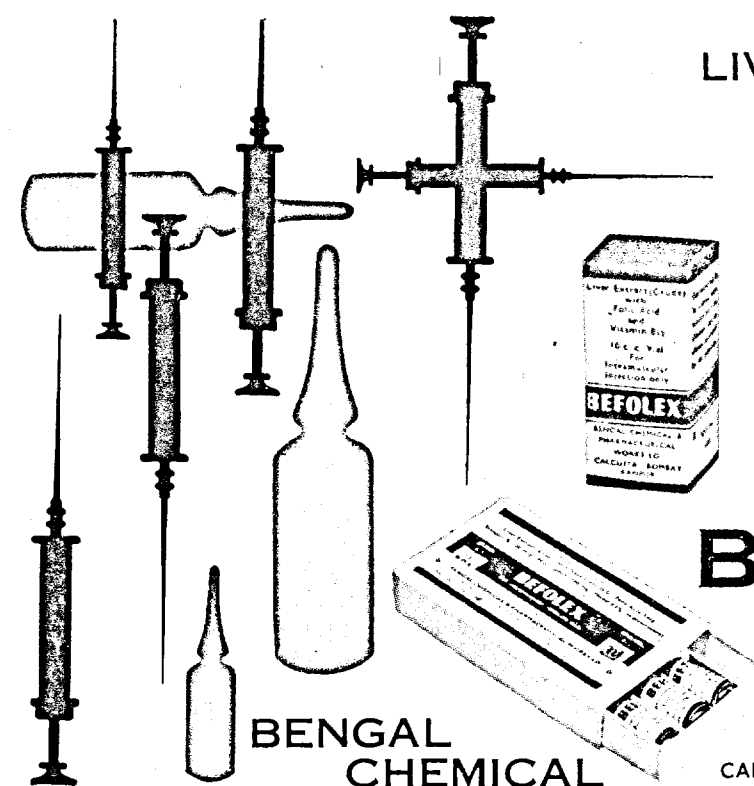
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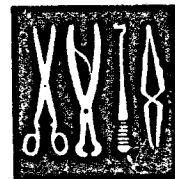
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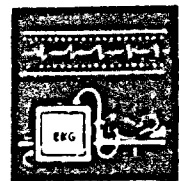
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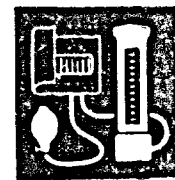
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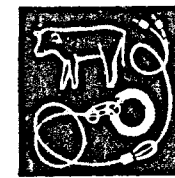
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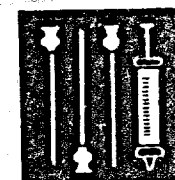
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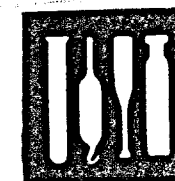
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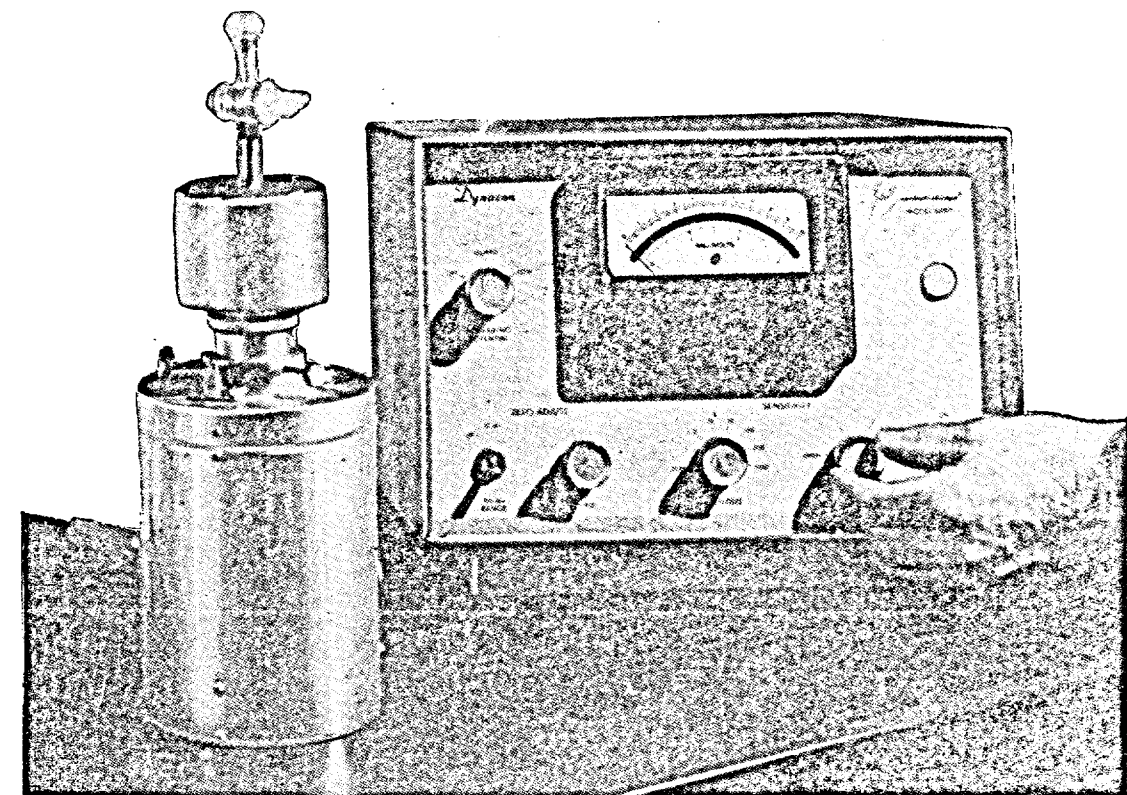
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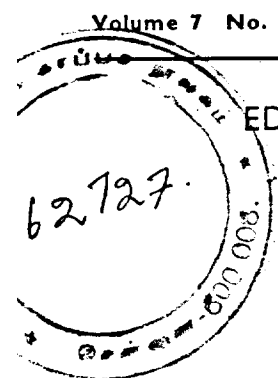
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SURGICAL & MEDICAL NEWS

OCTOBER 1960

SCIENTIFIC PURSUIT AGAINST ESTABLISHED AUTHORITY

- "1. A reappraisal of basic educational issues and evolution of a closely integrated programme covering all stages of scientific education, from the school to the post-graduate level.
2. Closer coordination between all agencies concerned with scientific and technological research, and the setting up of a suitable machinery for the purpose.
3. Measures for the rapid utilization of research processes and techniques.
4. An organisation for designing and developing research equipment, including precision instruments and pilot plant and
5. A central institute or clearing house for scientific and technical information."

These were five suggestions made by The Director General of the Council of Scientific and Industrial Research for the rapid development of Science and Technology in India. The report goes on to amplify that "Progress demands the services of a continuously increasing number of technologists with ever rising standard of training and specialization. This means that the Nations research effort should be stepped up on a progressively expanding basis with the accent on quality.

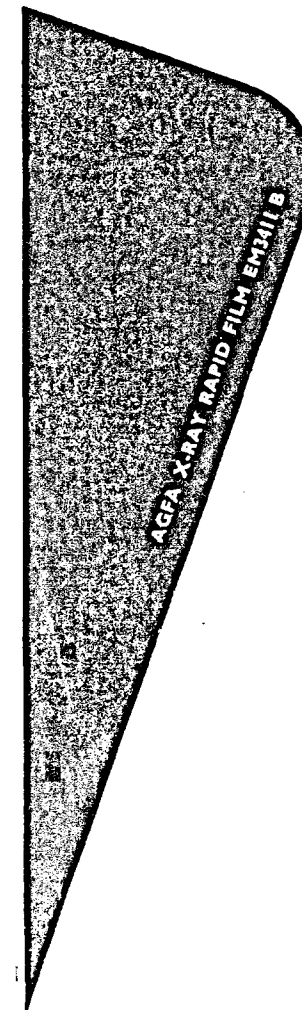
A coherent and integrated National educational policy must be formulated. There must be an improvement in the quality, the status and living standard of the teacher. There should be proper canalizing of the talents of students. Selection of students for admission to higher institutions of learning should be governed by merit, ability and aptitude, and liberal stipends should be provided for those who lack the means but possess the merit. Awards should also be given to provide incentives for further achievements and distinctions."

We must confess that all this sounds very nice but much of it is difficult to put into practice. I think all will agree that we must enhance the reputation of Indian science abroad. Undoubtedly our countrymen have made important and valuable contributions to scientific knowledge but these have been few and far between. To improve this state of affairs we need to encourage younger talent but that is the crux of the problem because initiative and enthusiasm are things which do not thrive in our climate of science. Vested interests and senior folk have entrenched themselves at the top and any younger scientist who does work does so at his own peril. The pursuit of knowledge by junior people has become a dangerous adventure which may be undertaken only at considerable personal risk and few will be willing to take this risk as their whole future will be marred. Let us take some instances.

Youthful X is engaged on a meagre research stipend on a research programme. His business is to perform detailed haematological studies on a large series of patients as part of the research work which has been allotted to him by his professor. If he mechanically does haematological studies and puts it up well tabulated before his boss, all is well. Supposing by his preliminary training he begins to draw conclusions from what he has observed he becomes a menace. His boss will look upon him with suspicion. If he comes to valuable conclusions which are supported and accepted by other research workers in other parts of the world, the professor considers it a top priority business to get rid of him and preferably in such a way that he will never again get into the research business either under him or any one else. So the idea has become established that a sincere research worker must be a technician to do work mechanically and put it before his superiors for their use in whatever way they think best. If their minds are rigid and not agile enough to perceive the importance of the conclusions, it should not be the concern of the junior worker. One of the best methods of preventing a junior from using his intelligence is to apportion to him only such a fraction of the overall work that the full facts will not be available to any one except the professor.

Take the case of another young research worker Y. He is not a research worker at all but an employee who does routine clinical work in a hospital but who is deeply interested in certain aspects of his work. He records on paper whatever he sees and in due course of time he comes to conclusions about what he saw and communicates it to those who are interested in this particular field of work in other parts of the world. He spends his own money on documenting scientific information which no one else appears to be interested in documenting. His work is of such a nature that learned men in other universities in other countries appreciate its value and quote it in their journals and their books. Y is not in charge of a research programme and he is not paid for doing what he does but in the long run his work brings honour to his country. What happens to Y? His seniors are out for his blood and to discredit him at every turn. They are anxious to liquidate him from the institution if not from its precincts. How right was the Goodenough report when it included the statement "No certain reward stimulates the young physician to engage in original work. His cue is faithful routine. In consequence his preliminary scientific training goes largely to waste".

An impression has gained ground that research may be done only by those interested and that without the approval of research grant committees, work should not be done. The persons furthermore have to be selected for research and this selection depends a great deal on the professor who is unlikely to want any one with any independent views or individuality. In this environment it is refreshing to read what more enlightened people write. Louis N. Katz writes in the Journal of the American Medical Association (March 31, 1956, 1137.) "Research is not done only in the laboratory. It may be conducted at the bedside, in the operating room, and in the field of public health and epidemiology. It is not the place that counts. It is the perspective. It is the original mind asking a question and designing an experiment to find the answer. It should not be pebble picking—it should be the building of magnificent castles. I have no sympathy for the view that any kind of



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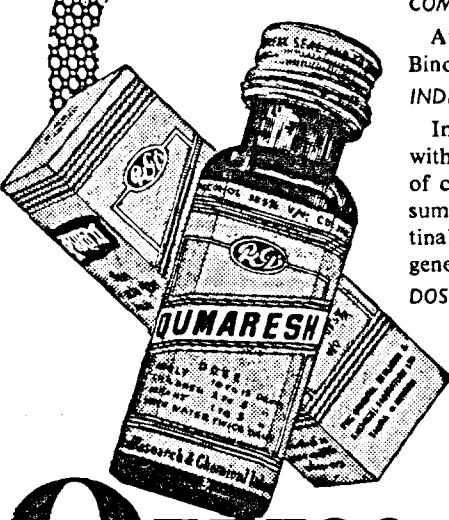
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research is good. Research should advance a fundamental concept or it should have an obvious practical value and early application. Research is not gadgeteering. It is the pursuit of ideas. With the development of elaborate tools, like flame photometers, ultracentrifuges, angiocardographs, electron microscopes, electrophoresis, and isotopes, there has developed a small group who play their instruments for all they are worth. Having acquired the equipment, the buildings, the technicians, and the project grants, they go madly searching for ideas. They scrutinize grant applications if they are on research allocation committees, they scan published reports, they rush to meetings, they write to their friends, and they ask visiting colleagues for ideas. This is obviously all wrong. Research should start from ideas, and then tools should be obtained, not vice versa."

I do believe it is imperative that there should be more academic freedom; research grants should go not to those whose professors decide they are good or not, but to those who can show by their work impartial scientific men elsewhere in the country and abroad that their work merits support. It is not enough to have a generous grants but they must go to the right people. You cannot have a safe investment in research but must make available funds for persons who are interested and not let their initiative and individuality be suppressed and destroyed by those who by virtue of their age and seniority have got to the top.



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PRESENT-DAY TREATMENT OF CANCER

By DR. B. MILONOV

Moscow City Oncological Hospital

FOR generations, scientists of the world were racking their brain for working out a solution for the problem of cancer. In the Soviet Union too doctors, biologists, chemists, physiologists and physicists are working hard in this field. Their work has enriched Soviet science and has shown that prophylaxis of certain forms of cancer is possible and that cancer can be successfully combated and vanquished. Scientists have in numerous cases demonstrated the effective treatment of cancer (of the skin, lip, tongue, womb, rectum, thyroid gland, the large intestine, etc.), especially in its earlier stages.

It should be noted that there is no single cause for the origin of malignant tumours of various types.

A state network of anti-cancer institutions has been set up in the USSR which conducts the necessary measures. Regional and city oncological dispensaries as well as oncological divisions at the out-patient departments of hospitals have been set up in addition to scientific research institutes and clinics.

Mass prophylactic oncological examinations of the population over the age of 35 is of great importance for the early diagnosis of cancer which is the basis for successful treatment. Prophylactic measures have resulted in a continuous drop in recent years in the number of patients in the Soviet Union, especially, in large cities, with neglected forms of cancer of the womb, the mammary gland, tongue, lip, skin, rectum. This has led to better results in treatment.

A thorough study has been made in the country in recent years of the possibility of diagnosing cancer by studying the cellular composition of secretions, especially phlegm, smears from cancer sores, etc. There has been a considerable improvement in the X-ray diagnosis of cancer of the stomach and lungs with new contrast matter appearing (diodrast, etc.).

The researches conducted by Academician L. A. Zilber have shown complex albumen of a virus origin in human and animal tumours which could be used for both diagnosing cancer and deciding the question of immunity.

Soviet scientists have improved methods for the surgical treatment of lung cancer, and cancer of the gullet and cardia. A great deal is being done to study

and radically improve combined methods for treating cancer of diverse organs.

A number of improved methods of ray treatment of cancer tumours have been elaborated, such as super-volt Roentgen therapy, rotary (cancer of the gullet), pendulum (according to the tomographic principle), multi-field Roentgen therapy of tumours, telegamma-therapy with radio active cobalt and the introduction of radium needles. All this has resulted in a considerable increase in the therapeutic opportunities when conducting independent ray treatment or in combination with the surgical treatment of cancer of the lung, the gullet, the rectum, the mammary gland and tumours in other parts of the body.

The great efforts exerted by scientists in combating cancer are clearly seen from the treatment of cancer of the mammary and prostate glands with certain hormone preparations (testosterone-propionate, sinestrol, cortison, etc.), as well as a number of chemical therapeutic preparations which are being studied by Prof. L. F. Larionov's school. It should only be borne in mind that every new means is not a universal cure for every form of cancer and is effective only within definite limits. The progress of clinical oncology is obvious at present; five and ten-year treatment of such frequent forms of cancer as that of the womb, of the mammary gland, the rectum and the lip produces from 40 to 50 per cent positive results.

The best results in treating the above-mentioned types of cancer are obtained during the first stage (60 to 70 per cent). Less favourable results in treating cancer of the internal organs, in particular that of the stomach, are explained by the early formation of metastases. Some 30 per cent of stomach cancer patients remained alive five years after being operated. Although this percentage is not very large in itself, it should be taken into account that in the past it did not exceed 10 per cent.

The USSR has attained concrete achievements in combating cancer.

It can be confidently said that the joint efforts of numerous scientists, prophylaxis and timely diagnosis, will result in a reduction in cancer and will considerably increase the stability of the results attained in treating patients.

PRIMARY PELLAGRA & ITS MANAGEMENT

By DR. A. P. S. RAGHUVANSHI, M.B.,B.S. (LUCKNOW)
Medical Officer, General Hospital, Udaipur

THE 3-D disorder — pellagra is not always three dimensional. Gastro-intestinal tract, skin and nervous system all are simultaneously affected only in more advanced cases. Early cases manifest only gastro-intestinal symptoms, moderate cases in addition the skin symptoms and advanced cases show the nervous symptoms also in addition to previous ones.

Secondary pellagra (Sporadic) is less common and is due to:—(a) gastrointestinal disorders—chronic dysentery, sprue, cirrhosis liver, gastric carcinoma, chronic gastritis (b) Thyrotoxicosis (c) Alcoholism (d) pregnancy (e) After Operations on gastro-intestinal tract and (f) during prolonged INH treatment etc.

Primary pellagra (endemic) is more common and is due to diet deficient in Tryptophane and/or Nicotinamide (Nicotinic Acid or Vitamin B7). Usually the average case of Primary Pellagra as seen in Pratapgarh (Rajasthan) has also other deficiency disorders simultaneously, eg. iron deficiency anaemia, Hypoproteinemia and deficiency states due to other vitamins specially Vitamin B, (Thiamine), B2 (Riboflavin), B6 (Pyridoxine) and Vitamin C (Ascorbic acid). Pellagra is more common in this part of the country due to the single fact that maize is the main food of local inhabitants.

I. MAIZE AND PELLAGRA

One ounce of maize has 101 calories, 2.6 gm. protein 0.4 gm. Fat, 21.6 gm. carbohydrate, 6 mg. Calcium, 0.5 mg. iron and 90 mg. phosphorus. According to Isselbacher and Dawson nicotinic acid is an essential vitamin, daily requirement being 12—18 mg. per day for men and 10—15 mg. per day for women and constitutes an integral part of two coenzymes DPN and TPN. Nicotinic acid is present in nature as Nicotinamide. Though essential for body nicotinic acid or nicotinamide need not be present in diet, as nicotinic acid can be formed in the body and prevent pellagra. Thus it is clear that nicotinic acid deficiency will be aggravated by a relative or absolute tryptophane deficiency. Maize protein is very low in trypto-

phane, so not only intake of nicotinic acid in maize diet is low but the biosynthesis of nicotinic acid in the body from tryptophane is also low due to its low content. Now the view that maize contains pellagra producing toxine is not accepted.

II. NICOTINIC ACID

It is present in nature as nicotinamide in yeast, marmite, wheat germ, lean meat, milk, fish, fresh vegetables and fruits. It is heatstable so not lost during cooking. Its absorption from the gut is rapid. Nicotinic acid has vasodilator action lasting for few hours, so flushing is noticed when it is taken. Therefore in treatment nicotinamide is preferred, because it has no vasodilatory action, so no flushing.

III. CLINICAL TYPES OF PELLAGRA

1. Primary pellagra.
2. Secondary pellagra.
3. Infantile pellagra—when the disorder is in infants. In these cases transient oedema of limbs and face may be present.
4. Pellagra sine pellagra—condition when skin lesions are absent and gastrointestinal and mental symptoms are present.
5. Pellagra typhus—when the condition is very acute and associated with marked constitutional symptoms like pyrexia, prostration along with delirium, convulsions etc. This type is very serious, three dimensional in true sense and may end fatally.

IV. DIAGNOSIS OF PELLAGRA

1. Clinical history—
 - (a) Monotonous diet deficient in Nicotinic acid eg. Maize diet.
 - (b) Seasonal incidence — occurring in spring and summer.

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(c) Similar episode in previous years.

(d) Environment—conditions of living and work giving more mechanical irritation or sunlight to exposed parts of the body.

(2) Clinical findings—

Specific findings according to the stage and type of disorder giving specific idea of nicotinic acid deficiency.

(3) Laboratory findings—

No definite and decisive laboratory tests for pellagra are yet known.

(a) Blood—Any type of anaemia may be present but usually one finds microcytic hypochromic anaemia. Serum protein values usually remain unaltered. Coenzyme I & II in blood are decreased

(b) Urine—Decreased coenzyme I & II is also noticed in urine but their actual value in diagnosis is doubtful. Abnormal urinary pigments are said to be present. Urinary output to the standardised test dose of nicotinamide is said to be decreased in either 24 hour urine specimen or in timed urine specimen. The nicotinic acid in the body after metabolism turns into NI. methyl-nicotinamide, which may be rendered fluorescent and so can be measured. But its actual value in diagnosis is doubtful.

(4) Response to specific treatment.

There is distinct and marked improvement to nicotinamide administration to such cases but its evaluation is to be utilized also in preventing the relapse of symptoms, which will occur if deficiency of nicotinic acid takes place again.

IV. SYMPTOMS AND SIGNS OF PELLAGRA

These differ according to the stage of primary pellagra.

(A) Very Early Stage

So vague and variable are the signs and symptoms at this stage that diagnosis purely on clinical basis is too difficult if not impossible. Anorexia, Dyspepsia, lassitude, loss of weight, altered bowel habits, forgetfulness, insomnia, palpitation, headache, irritability, burning sensation in extremities, burning pain in tongue, pharynx, Oesophagus & stomach aggravated by spices, hot foods and acidic foods, mental depression and confusion are the main prodromal symptoms. Whether blood and urine tests will be helpful in this stage is doubtful.

(B) Early Stage

1. Gastro-intestinal symptoms and signs—these include abdominal distention and pain, diarrhoea, achylia gastrica, nausea, vomiting, glossitis and stomatitis, burning pain in pharynx and oesophagus and stomach along with other symptoms of prodromal stage.
2. Skin Lesions—These lesions start appearing in the exposed parts of the body. They occur as erythematous areas which become dark brown and then desquamate. Skin becomes thickened and pigmented. There is burning and itching in these lesions which at times vesiculate. They are on the parts exposed to mechanical irritation and sunlight and are bilaterally symmetrical. At this stage diagnosis is possible on the basis of clinical history and findings.

(C) Average Established Case—

1. Gastro-intestinal Symptomatology—Glossitis, Stomatitis—"Beet tongue", Achlorhydria in 60%, pain in abdomen, diarrhoea and fatty infiltration of liver is present.
2. Skin and mucosal lesions—Skin lesions are bilaterally symmetrical and are present on the exposed parts of the body like dorsum of hands, wrists, elbows and forehead, Cheeks, angles of mouth, neck (castles necklace), knees, feet, perineum and under breasts in females. These lesions may be erythematous or exfoliative and are always in a state of flux. These lesions are distinct from the surrounding normal skin by "Hyperkeratotic border of Merck". At still later stages they resemble exfoliative dermatitis.

They usually follow GIT Symptoms.

Mucosal lesions include vaginitis, proctitis and urethritis besides stomatitis and glossitis and ulcers in jejunum, colon and rectum.

3. Nervous systems, Signs and Symptoms—These are diminished memory, depression, irritability, altered reflexes (First exaggerated and then diminished or absent). Burning sensation in limbs, tremors and atheroid movements, spasticity and loss of sphincteric control, altered gait, insomnia etc.

(D) Advanced Case

1. G. I. T. Symptomatology—All the lesions of an average case are present and are more pronounced. Beet tongue, achlorhydria, fatty infiltration of liver, ulcers in mucosa of gastro-intestinal tract being the main signs and symptoms.
2. Skin Lesions—Resemble exfoliative dermatitis, skin vessels dilate, corium rarifies, epithelial changes include hyperkeratosis, parakeratosis or acanthosis. Sebaceous glands atrophy—these are in same areas as in an average case.
3. Nervous system lesions—these include atoxic or spastic gait, diminished or absent reflexes, numbness and Paralysis of extremities, posterior-lateral degeneration of spinal cord, pellagrous encephalopathy, subacute combined degeneration, meningeal thickening, cerebral atrophy, hydrops of ventricles or subarachnoid space and insanity. Cerebro-spinal fluid remains normal throughout. Such cases do not survive long.
4. Cardiovascular system findings—Blood pressure is low and collapse occurs in very advanced cases. Heart undergoes atrophy.
5. Haemopoietic system findings—Blood vessels dilate. All types of anaemia can be met with but hypochromic microcytic anaemia more common. Count and morphology of leucocytes do not show any change; serum proteins also remain normal.
6. Genitourinary system findings—Vaginitis and

hypomenorrhoea in females and urethritis and diminished sexual desire in both sexes.

7. Respiratory system findings—Pharyngitis and laryngitis may occur. Lungs remain unaffected till, due to some intercurrent infection or exposure to cold, they are involved.

VI. TREATMENT OF AN AVERAGE ESTABLISHED CASE

It is evident from the above description that in the management of an average case of pellagra one has to deal with not only one but several problems eg. Deficiencies (of vitamins predominantly of Nicotinic Acid, of minerals mainly of iron, of fluids due to dehydration resulting from diarrhoea, and nutritional) and various signs and symptoms of gastro-intestinal tract, skin and nervous system and intercurrent infections if present. Therefore, it is of utmost significance that the patient should be treated as a whole keeping all the factors fully in view and not merely by replacing the main deficiency of nicotinic acid, which no doubt has to be administered adequately. The following plan of treatment is useful in an average established case:—

(A) REST

Strict bed rest till diarrhoea stops and mental symptoms show improvement. Later adequate rest should be given till skin lesions disappear and the patient shows around progress. Relaxation should be gradual.

(B) DIET

This is the most important factor to be kept constantly in view. A proper diet is required not only during the treatment but its continuation later in the same manner is also very important to avoid the relapse. Aim should be to give a well balanced diet of high caloric value (at least 200 gms per day and preferably of high class) high vitamin content (especially B Complex group and Vitamin C), high mineral contents (especially iron), high fat content (preferably of animal origin) and low carbohydrate content. Diet must include the articles which are good sources of nicotinamide—yeast, marmite, wheat germ, meat, milk, fish, eggs, liver, whole wheat flour and fresh green vegetables and fruits.

Till diarrhoea is present, give the following diet:—Khichri, curd, daliya, fruit juices, skimmed milk tea, coffee and plenty of water. Fruits having constipative effect should be given—Banna and “Bael” fall in this group. Sugar cane juice is very good for such cases. Green leafy vegetables should also be given. Later a liberal diet should be given keeping in view their nicotinamide content. Spices should be avoided.

(C) Control of Diarrhoea

If severity is less than Mist Bismuth kaolin and sulphamide with plenty of fluids orally suffice. If severity is more than streptomycin tablets or chlorostrep Kapseals should be given orally along with intravenous drip of glucose saline in adequate amount. Dehydration must be fully combated.

(D) Control of Anæmia

Crude liver extract should be given by intramuscular route daily in proper dosage till blood picture improves satisfactorily. When patient is having diarrhoea but shows no reaction, if intravenous iron is administered then it should be given till hæmoglobin percentages improves. Later iron should be given orally so that gastro-intestinal upset is minimum or absent. Vitamin B12 should also be given for first few days in every case and more in those in whom it is required more.

(E) Care of Skin Lesions

Protect the skin lesions from mechanical irritation and sunlight. Avoid stronger lotions and ointments unless absolutely necessary. Zinc calamine lotion applied locally suffices in most cases.

(F) Vitamin Replacement

As already mentioned, vitamin deficiency is multiple, so replacement should be of all which are lacking. Nicotinamide should be given intramuscularly for at least two weeks and then orally. Daily quantity of nicotinamide should range between 250 mg to 500 mg. per day in divided dosage according to the severity of the case. So far pellagra is concerned nicotinamide should be preferably be given in higher dosage as there is no risk of hypervitaminosis. Riboflavin should be given orally (unless severe diarrhoea) in 30 mg. to 50 mg. dosage daily. Thiamine should be given by intra-

muscular route in 100 mg. doses daily till required. Pyridoxine should be given orally in 5 mg. to 10 mg. doses daily. Cyano cobalamium is to be given intramuscularly every day in doses ranging from 100 mg. to 1000 mg. according to the severity of the case for at least a week.

Ascorbic acid should also be given in the first fortnight orally in divided doses, daily amount being 300 mg. to 500 mg. Thus we find that B Complex group and vitamin C are to be administered in proper dosage for sufficient time in an average case of pellagra. When the condition has improved then the amount of various vitamins should be brought to maintenance level, but they must be given for a considerable period to avoid a recession of symptoms.

(G) Accessory Drugs

Administration of Dilute Hydrochloric acid orally in 30 minimum dose thrice daily is said to be helpful, as achlorhydria is present in such cases. Oral administration of gastric juice and various enzymes is also said to be beneficial.

(H) Symptomatic—Treatment

- (1) Itching of skin lesions—if severe then Sovental tablet is useful. Soothing lotion locally to be applied.
- (2) Nausea and vomiting—Salol menthol drops in less severe cases and largactil in severe cases suffices.
- (3) Insomnia — Mist chloral Bromide or Barbiturates according to requirement.
- (4) Excitement and irritability—if too much then paraldehyde should be given by intramuscular route.

(I) After Treatment

When patient is discharged from the hospital after around satisfactory improvement then he must be advised properly in simple words regarding the diet to be taken and also about the maintenance dose of nicotinamide 30 mg. to 50 mg. to be taken for sometime more. He should be told to take it also in the following spring and summer seasons.

VII. PROGNOSIS

Mortality in an average case of pellagra is nil. Poor prognosis is noticed at extremes of life in both sexes, in cases complicated with fever, in cases secondary to gastric cancer and when the symptoms pertaining to gastro-intestinal tract, skin and nervous symptoms are present simultaneously. The prognosis is good when the treatment is started in prodromal or early stage. Prognosis is good in uncomplicated cases. Disease usually runs a chronic course and seasonal fluctuations to occur. Death results in untreated advanced cases in three to fifteen years. Once dementia has set in, then full recovery is not possible and mental symptoms persist. In an average case complete recovery almost always takes place with proper and prolonged treatment.

VIII. CONCLUSIONS

Primary pellagra is common in Pratapgarh (Rajasthan). Average has had signs and symptoms pertaining to gastro-intestinal tract and skin predominantly and

to nervous system to a lesser extent. Such cases have no doubt the main deficiency of Nicotinic acid, but to some degree deficiency of Thiamine, Riboflavin, Pyridoxine, Gyanocobalamine, Ascorbic acid and iron are also present simultaneously. Patient should be treated as a whole, all deficiencies being replaced and symptomatic treatment provided. After treatment and diet must be cared for to avoid a relapse.

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Domiciliary Treatment of Pulmonary Tuberculosis

By DR. P. K. SEN

Chest Department, Medical College, Calcutta

THIS paper is based on part of the data and conclusions of an investigation made by the author and presented by him at the Domiciliary & Ambulatory Committee meeting of the International Union Against Tuberculosis at Paris in July, 1958. The report was submitted to the Tuberculosis Association of India soon thereafter.

The study attempted to answer broadly the comprehensive question: "Is home or domiciliary treatment good or beneficial enough to justify its acceptance in the control programme of pulmonary tuberculosis in a country"? A direct answer to this question can only be given if in a community two comparable groups are investigated over a long period one having this treatment and the other none. Such an experiment is hardly possible and is probably unethical in the light of established values of chemotherapy. As this is impracticable, the answer should be sought in an indirect manner accepting the result of hospital treatment as the standard of adequacy and comparing the result of chemotherapy at the home and hospital.

In addition, it will be reasonable to assess the effect of factors in which the home differs from the hospital. Provided chemotherapy is adequate or comparable, then, any difference in the result of treatment between these two will mainly be due to such factors. Important factors in this respect are (a) movement of the patient, (b) social status indicating nutrition and general environment, and (c) supervision. In all these respects the hospital is likely to be much superior to the home specially for the groups of patients included in this study. Besides a comparative study of the results of treatment at the home and the hospital, an evaluation of the effects of these factors were attempted by comparing the results of treatment in different groups of domiciliary treated cases with distinct differences in respect of these factors.

It may be well worth remembering that in assessing the justifiability mere finding of the comparative result with hospital treatment or evaluation of differing factors may not be quite adequate. Keeping patients at the homes may prove more dangerous for the contacts than isolating them at the hospitals. Regu-

lar self-administration of drugs may also be very much more difficult at the homes than in the hospitals. On the former issue the author has published a study on home contacts of the domiciliary cases in this journal in Vol. VI, No. 4 September, 1959. A comparative study of such contacts with contacts of hospital treated cases is necessary. This could not be made as he did not have sufficient material for the purpose. The author intends to present a study soon on the issue of the extent and nature of irregularities in self-administration of drugs at home.

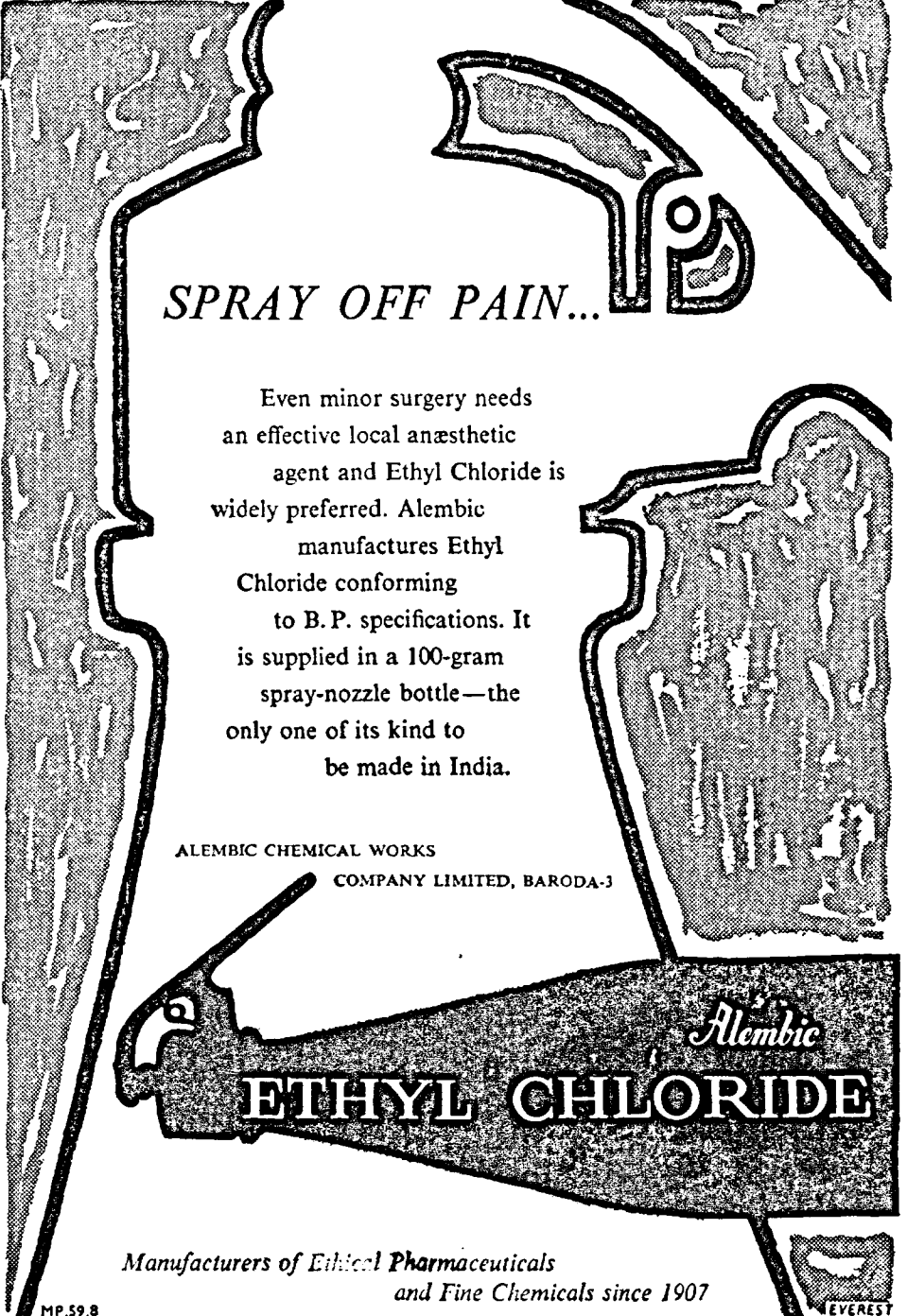
MATERIAL, METHOD AND RESULT

Domiciliary Group

Under the term "Domiciliary Treatment" were included those cases who had been treated at home and not known to have been hospitalised anytime. It also included cases who had different grades of ambulation from the very start of treatment, thus ambulatory cases as well as those who followed adequate rest regime had been included under the same heading: "domiciliary". In the vast majority of cases the treatment was meant chemotherapy by a combination of two drugs in which INH has always been used.

Random samples of 5,883 domiciliary treated cases from different clinics in Calcutta (Chest Department, Medical College, Tuberculosis Clinic, Urban Health Centre, All India Institute of Hygiene & Public Health; Corporation Clinic, Kidderpore; Chest Clinic, Islamia Hospital; Tuberculosis Relief Association Clinic and Niramoy Clinic), private cases of the author and one clinic from a small town (Chinsurah) were collected. No case was accepted who had less than three months treatment or had major irregularity in chemotherapy.

These cases were re-assessed by very experienced and competent workers of different clinics and by the author and his colleagues in his department under a common schedule with clearly defined terminologies prepared by the author. To reduce many elements of errors and biases that may enter into a retrospective study of this type two workers sat together to assess



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most of the cases with clear direction that in cases of doubt the lower category in terms of improvement should be accepted. Smear tests only for sputum were accepted.

Hospital Group

Similar procedures could not be adopted for the assessment of the hospital cases. Information gathered were under the terminologies used by individual hospitals (U. M. T. Sanatorium, Madanapalle, S. India; Lady Linlithgow Sanatorium, Kasauli; K. S. Ray T. B. Hospital and Bangur T. B. Hospital, West Bengal). They were neither alike for all hospitals nor the same as used for the clinic schedules. The author, therefore, took the liberty to rearrange the data from different hospitals in such a way that they may be roughly comparable to the clinic data. The author was aware that there might be some error in doing so but, at the same time, he felt that, by and large, the rearranged data were comparable. Information on 2,472 cases from different parts of India were collected in this respect.

COMPARATIVE RESULTS OF DOMICILIARY AND HOSPITAL TREATMENT

The results are summarised in tabular form with brief explanations whenever necessary.

Terminologies and definitions used to indicate the results of treatment were as follows :

1. Worse— Extension of infiltration, and/or enlargement of the cavity, and/or new cavitation, and/or appearance of new lesion, and/or sputum reversion.
2. Stationary— The lesion and the cavitation and the sputum status remain almost the same.
3. Improved— Retrogression of infiltration, and/or diminution in the size of the cavity, and/or sputum conversion.
5. Quiescent— (a) Lesion must be stable showing adequate fibrosis and retrogression, and must not show evidence of cavitation in the ordinary P. A. view of the chest. (b) Three consecutive sputum tests must be negative for AFB by direct smear examination. (c) No tuberculous toxæmia and exercise tolerance normal.

TABLE I

A comparative study on the result of domiciliary and hospital treatment in respect of X-ray findings.

Groups	Results—X-ray findings					Total
	Worse	Stationary	Improved	Quiescent	Dead	
Domiciliary—Ambulatory	257 4.4%	857 14.6%	3,431 58.3%	1,338 22.7%	—	5,883
Hospital-at discharge	45	157	1,140	1,023	107	2,472
U. M. T. & Lady Linlithgow Sanatorium	0.02%	6.35%	46.11%	41.38%	6.14%	

TABLE II

A comparative study on the result of domiciliary and hospital treatment in respect of sputum test findings.

Groups	Result—in relation to sputum test				
	Total	Total	Total	Total	Total
	2132	3306	3306		
	Con- verted +/-	Statio- nary +/+	Statio- nary -/-	Revert- ed -/+	Not known
Domiciliary— Ambulatory	1,618	514	3,203	103	445
Percent reverted or remained stationary	75.9%	24.1%	96.9%	3.1%	
Hospital (K. S. Ray and Ban- gur)	432	210	1,365	31	
Percent reverted or remained stationary.	67.3%	32.7%	97.8%	2.27%	

Accepting the categories of “improved and quiescent” together as hospital terminology for the “quiescence” seemed somewhat more lenient, the result seemed to be slightly superior for the hospitals but the sputum conversion rate was slightly better for the domiciliary group. The latter may be also due to better sputum examination in hospital group. Considering the results as a whole, it may justifiably be concluded that the result of treatment at home is slightly inferior to that in a hospital.

EFFECTS OF FACTORS IN WHICH HOME DIFFERS FROM HOSPITAL ON THE RESULT OF TREATMENT

SOCIAL STATUS AND SUPERVISION BY HOME VISITORS

It has been assumed that poorer classes of patients have poorer nutrition, inferior housing and environmental conditions. That this assumption is likely to be true will be evident to anybody who had visited the Calcutta Bustees where the majority of the poorer classes lives.

Supervision at home by the Health Visitors and Doctors is also not uniform for all clinics. There had

been regular home visitings for some of these cases, only casual visits for another section and none for the others.

To show the influence of these factors, the domiciliary treated patients have been grouped according to their social status and extent of home visiting in the following way and the results of treatment of each such group in relation to X-ray and sputum test findings are shown in Tables III and IV.

GROUPS

Group ‘A’— Upper and middle class. No home visits (City).

Group ‘B’— Poor class. Regular home visits. (City).

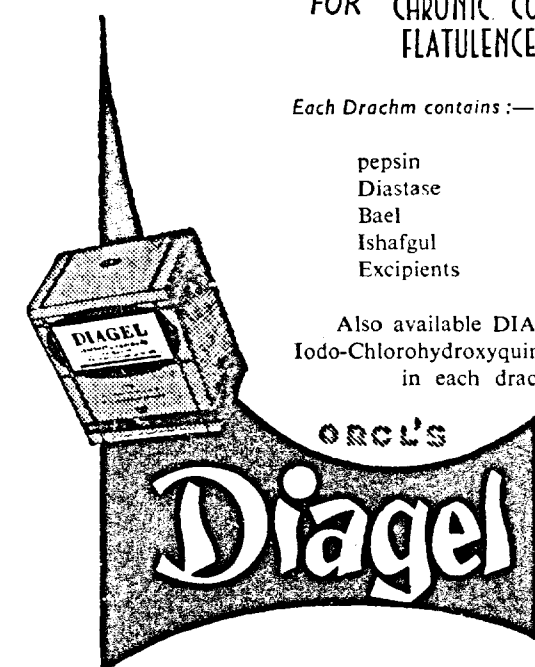
Group ‘C’— Poor class. No home visit for majority. Casual home visits for a few (City).

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Group 'D'— Lower middle class. No home visits (City).

Group 'E'— Poor and lower middle class. Casual or no home visit (small town: Chinsura.)

TABLE III

Result of treatment in relation to X-ray findings according to social status and home supervision.

Groups	X-ray				TOTAL
	Worse	Stationary	Improved	Quiescent	
A	2 0.39%	35 6.86%	351 68.82%	122 23.35%	510
B	42 4.80%	190 21.96%	544 63%	89 10.29%	865
C	136 4.4%	443 14.4%	1,663 54.2%	825 27%	3,067
D	51 6.21%	60 7.30%	576 70.15%	134 16.32%	821
E	26 4.2%	129 20.8%	297 47.9%	168 27.1%	620
TOTAL	257 4.4%	857 14.6%	3,431 58.3%	1,338 22.7%	5,883

TABLE IV

Result of treatment in relation to sputum test findings according to social status and home supervision.

Groups	Sputum					Total
	+/-	+/+	-/-	-/+	Not known	
A	192 80.0%	48 20.0%	248 100%	0	22 4.31%	510
B	292 72.5%	109 27.5%	424 96.3%	16 3.7%	24 2.8%	865
C	567 74.0%	199 26%	1,886 96.7%	61 3.3%	354 11.5%	3,067
D	334 86.4%	64 13.6%	386 96.2%	15 3.8%	22 2.9%	821
E	233 71.2%	94 28.8%	259 95.1%	11 4.9%	23 3.7%	620
Total	1,618 75.8%	514 24.2%	3,203 95.8%	103 3.2%	445 7.5%	5,883

No appreciable difference in the result of treatment is evident whatever might be the social status, that is, nutritional and environmental conditions, and also the nature of home supervision except in Group B. In order to ascertain the reason for this and for the presence of any other bias the groups were checked against the duration of chemotherapy, the nature of initial disease and sputum status on diagnosis. No significant difference in the duration of chemotherapy could be detected for any group. There was, however, appreciable differences in the nature of lesions in terms of presence or absence of cavitation and, to some extent, in sputum status. These differences are shown in Table V. The whole of group 'D' and part of group 'C' had been eliminated as these had miniature films only.

TABLE V

Distribution of Cavitary and Sputum Positive Cases.

Groups	Total	Cavity	Positive Sputum
Group A	510	253 49.6%	240 47.1%
Group B	865	576 66.5%	401 46.3%
Group C	1451	487 33.5%	387 24.3%
Group E	620	372 57.3%	341 53.8%

It may therefore be accepted that the nature of the lesions, specially cavitations had noteworthy influence on the result of treatment whereas special status, home environment and supervision did not show any appreciable effect on this result.

MOVEMENT AND WORK

Rest followed by graduated movement is still an accepted measure in the treatment of tuberculosis. In the hospital such a regime can be well controlled but not so at home. Home treatment will, therefore, generally differ from that of hospital in this regard. An attempt has, therefore, been made to evaluate the effect of movement and work on the result of treatment.

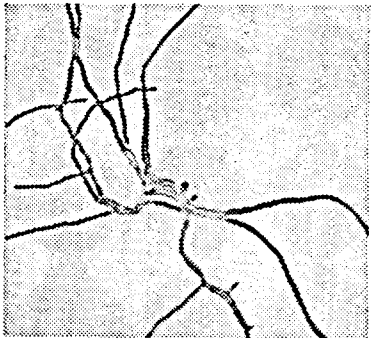
One thousand seventy-five patients were separately investigated in this regard. Each patient was closely interrogated in respect of their movement and work

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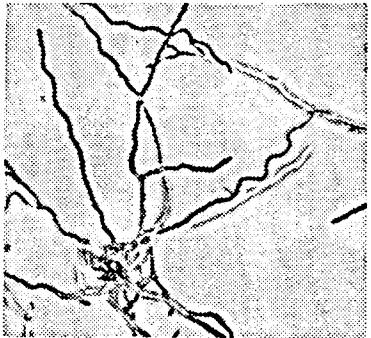


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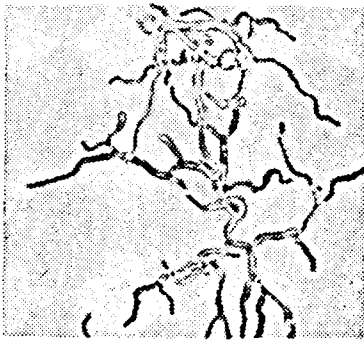
The effect of 'Fulcin' (griseofulvin) on the hyphae of a fungus growing in a nutrient.



Growth in nutrient with no griseofulvin present.

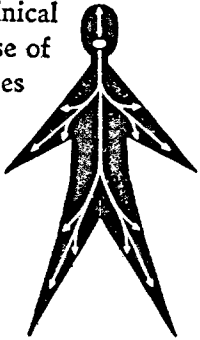


The effect on growth when 0.1 part per million griseofulvin is present.



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from the start of treatment. The patients were classified under the following heads according to this information.

W₁—Those who had generally followed the medical advice of initial rest and thereafter graduated movement.

W₂—Those who moved about somewhat against medical advice but did not do usual work.

W₃—Those who continued to do his usual work not involving manual labour against medical advice.

W₄—Those who continued to do work involving manual labour against medical advice.

Table VI shows the result of treatment in relation to such "movement and work".

TABLE VI

Work and Result of Treatment

Working status	Worse	Stationary	Improved	Quiescent	Total
W ₁ (Rest etc.)	14 6.78%	47 22.27%	123 49.42%	23 11.11%	207
W ₂ (Casual)	16 3.65%	102 23.29%	287 65.53%	33 7.53%	438
W ₃ (Light)	10 3.66%	62 22.71%	167 61.17%	34 12.46%	273
W ₄ (Heavy)	6 3.82%	38 24.2%	102 67.97%	11 7.00%	151
Total	46 4.27%	249 23.17%	679 63.17%	99 9.20%	1,075

It will be noted that there is no appreciable difference in the result of treatment between these groups.

Large random samples from each group were then tested with regard to the duration of chemotherapy, initial extent of the lesions and cavitations and sputum status in search of possible important biases. The following tables summarise the findings.

TABLE VII

Analysis of cases according to sputum status at the start of treatment

Working status	Total No.	Sputum Status Positive
W ₁ Rest etc.	118	40 33.9%
W ₂ Casual	301	143 47.5%
W ₃ Light	203	108 53.2%
W ₄ Heavy	114	61 53.5%

TABLE VIII

Analysis of cases according to the extent of the lesions and cavitations at the start of treatment

Working Status	Total No.	Nature of the lesions			Cavity Present
		I	II	III	
W ₁ Rest etc.	128	66 51.56%	18 14.06%	44 34.38%	65 50.78%
W ₂ Casual	317	76 23.97%	50 15.77%	191 60.26%	112 57.41%
W ₃ Light	214	35 16.35%	44 20.50%	135 36.91%	130 60.74%
W ₄ Heavy	130	36 27.69%	11 8.46%	83 63.85%	82 63.07%

CLASSIFICATION OF EXTENT OF LESIONS:

- I. When the total area involved is not more than the area of one zone roughly.
- II. When the total area involved is more than one, but not more than two zones.
- III. When the total area involved is more than two zones.

TABLE IX

Analysis of cases in relation to duration of treatment

Working status	Total	3-6 months	7-9 months	10-12 months	more than 12 months
W ₁ Rest etc.	128	36 28.12%	22 17.18%	15 11.71%	55 42.99%
W ₂ Casual	317	106 33.43%	81 25.55%	45 14.19%	85 26.83%
W ₃ Light	214	66 30.84%	38 17.75%	42 19.62%	68 31.79%
W ₄ Heavy	130	37 28.48%	30 23.07%	29 22.30%	34 26.15%

Study of these tables show that there is no appreciable bias in these important factors. So, it may be justifiable to conclude that "movement and work", even from the very start of treatment, did have no appreciable influence on the immediate result of the treatment.

COMMENTS

This study should be regarded as a preliminary and rough one. The author is aware that in a retrospective study of this type from clinic records there could be many deficiencies and results obtained may not be as reliable as in a well controlled study. Important deficiency in this study was in the hospital group where the duration of chemotherapy could not be ascertained. Advantages are, however, its inexpensiveness and assessment of the result of a service under normal field conditions.

Another important deficiency in a study like this is uniform assessment of cases and proper recording. The author believes that both could be somewhat minimised, as in this case, by accepting a large number of patients and assessing them under a common schedule by many well qualified workers. By this process the biases, if any, may tend to be neutralised.

It may be noted that in some places differences in percentages seemed significant statistically but two good statisticians opined that, in a study like this, much differences may justifiably be noted as "no appreciable differences". So this notation had been recorded.

From experiences gained by this study, the author is convinced that there is a definite scope for co-operative studies on this subject which can be planned ahead and executed in a manner that most valuable light can be thrown on our field conditions and these, in their turn, may help greatly in the proper conduct of the domiciliary service.

SUMMARY AND CONCLUSIONS

Five thousand eight hundred eighty three cases were accepted for this study. Records were randomly collected from 8 clinics and were reassessed under a common schedule with defined terminologies. The clinic cases could be differentiated, on the basis of the population they serve, into different social groups and also according to the home visiting service available to them.

A group of 1,075 clinic cases, not necessarily included in the above group, were specially investigated in

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the light of "movement and work" they pursued from the start of treatment.

All cases known to have been hospitalised and/or had less than 3 months chemotherapy and/or had major irregularities in chemotherapy were excluded from the study.

Informations on 2,472 cases were collected from 4 good hospitals/sanatoria. The data were rearranged, as far as possible, for a comparative study with the clinic group of cases.

In comparative studies among the clinic groups some important factors through which biases and consequently errors might occur were checked.

The findings were summarised in tabular form and analysis seemed to show that:

1. The result of treatment at the hospital was only slightly superior to domiciliary treatment.
2. The differences in (a) social status (implying good to poor nutrition and environment) (b) extent of home visits (from no visits to good supervision) and (c) extent of movement and work from the start of treatment (from rest to manual work) had no appreciable influence on the result of treatment.
3. Character of the disease, specially presence of cavitation, seemed to have significant harmful effect on the result of treatment.

Reasonable deductions made from these findings were:—

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1. Like many other bacterial diseases, control of the bacillary population is of prime importance in tuberculous disease also. And further, the anti-tuberculous drugs seem to achieve this to such an extent that all other measures and conditions are relegated to an unimportant position in the cure of the disease.

2. Drug action and ultimate healing was in some-way related to structural changes.

3. If these preliminary findings are even roughly true, then, the question is not where we treat but when we diagnose and how best we treat (chemotherapy) barring a group needing additional care for major surgery and emergencies. Only in this context the question of home or hospital treatment arises. Conduct of proper chemotherapy should, therefore, be a must in domiciliary service and to this end our main efforts should be channelled.

4. Some of the findings of this investigation were, therefore, somewhat revolutionary and deserves to be further studied.

ACKNOWLEDGEMENT

I am very grateful to Drs. T. J. Joseph, J. Frimodt Moller, N. N. Sen, and S. K. Ganguli for kindly supplying me with the informations on hospital group and to Drs. B. Sarbadhikari, A. Sen, K. N. De, D. Banerjee, L. B. Banerjee, B. Manna, S. K. Nandy, B. Chatterjee and B. L. Mazumdar for their kind co-operation in collecting and assessing a part of the clinic cases. Without their help this study would never have been possible.

(Courtesy: The Tuberculosis Association of India).

The production of combined anti-tuberculous preparations—dihydrostreptomycinpascate and dihydrostreptomycinepantetonate—is being piloted commercially. Soviet dermatologists will receive in the near future epilene and arachidonic acid, preparations designed to combat skin diseases. Highly interesting to therapeutists is novocainamide, a preparation for the treatment of fibrillatory arhythmia—a grave disease of the cardiovascular system. The production of galantamine—an effective means for the treatment of the consequences of polio—will be increased.

ON THE VIRAL ORIGIN OF TUMOURS

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OWING to many failures, the search for neoplastic bacteria was relegated into the background around the turn of the century. However, this did not affect the infectious theory of tumour genesis; on the contrary, it was received in a new form, i.e. the virus theory, by the works of Borrel and Bosc. Even today the virus theory remains the most important, dominating concept within the framework of the theory based on the hypothesized infectious aetiology of tumours.

ROUS SARCOMA

Only a few years had elapsed after the publication of the virogenic theory when Rous (1910) found in hens a spindle-celled sarcoma which was transmissible also with the filtrate of the tumour. Since then, several dozens of tumours passable with the cell-free filtrate of the tumour have become known, and most of the transmissible tumours of animals are now believed to be of viral origin. It is therefore understandable that a group of research workers (Gye, Heidenhain, Daranyi, Haagen, Oberling, Rous) ascribe also human malignancy of viruses.

Of the cancers of animals, the adenocarcinoma of Ehrlich, as it occurs in mice, has proved to be eminently suitable for experimental study.

CANCER OF THE BREAST AND THE MILK FACTOR

As early as 1911, Murray pointed out that in a strain of mice susceptible to mammary cancer the incidence of breast cancer was three times higher when the strain originated from mothers and grand-mothers with breast cancer. By coupling tumorous individuals, stock was produced where 90 per cent of the females developed cancer by the age of 10 to 14 months. At the same time it became known that the tendency to cancer was transmitted by females, because the females of the highly susceptible strain showed no decrease in the incidence of cancer even after mating with males from a strain not inclined to cancer. On the other hand, males from the highly susceptible strain did

not increase the incidence of cancer when mated with females from a non-susceptible strain.

These genetic studies made it clear already in the early 'twenties that *in this case the Mendelian law had completely failed*. Then Little definitely stated that a factor other than the genetic material itself should be held responsible for the transmission of mouse cancer.

Finally, in 1936, Bittner proved that the carcinogenic factor is transmitted to offspring in the *maternal milk*. When the offspring of mothers with a tendency to cancer were breast-fed by mothers not susceptible to cancer, the incidence of cancer in the cancerous strain dropped from 97.4 per cent to 1.9 per cent in ten generations. In 1944, Andervont removed progeny by caesarean section before birth in the susceptible strain and let non-susceptible mothers raise them; These offspring remained absolutely free of cancer. The circle of proofs was completely closed when it was shown that the incidence of cancer among offspring from a non-susceptible strain rose to 70 per cent when they were raised by mothers inclined to cancer.

Recognition of the role of milk has, of course, intensified research to elucidate the nature and properties of the factor transmitting cancer. It became apparent that the milk factor of Bittner passed the Seitz and Berkefeld filters (Andervont and Bryan, 1945).

According to Bittner, the milk factor is carcinogenic only when in the genetically susceptible strain hormonal stimulation also prevails simultaneously. Thus three factors must interact to cause mouse cancer, but the weakness of one or two of the accessory factors may be partly balanced by the milk factor.

After recognition of the causes of mammary cancer, the question arose *whether similar causes may be responsible for mammary cancer of humans*. As an experiment, Gross and Hammett suspended breast-feeding by mothers in certain areas where a tendency to mammary cancer was noted. However, Bittner rejected

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this view, as he saw no proof of the milk factor playing a role in the genesis of human breast cancer. In their search for factors similar to the milk factor, Passey et al. claimed to have found similar conditions in man. But their results are far from being convincing, because even in the case of breast cancer of the mouse the milk factor is by no means the only responsible one.

According to Andrewes, the milk factor is an independent parasite like exogenous viruses. Magnus and Magnus have actually proved in mice that the virus of encephalomyelitis may be transmitted in milk, a fact that substantiates the view that the milk factor may exist as a similar independent virus.

Electronmicroscopy has supplied no unequivocal evidence as to the morphology of the milk factor. There are two principal views today, opposing each other. Graff et al. claim that the milk factor is a round body measuring 100 millimicrons, whereas according to Passey et al. the size of these bodies varies from 20 to 120 millimicrons, with the average size not exceeding 30 millimicrons. In 1948, Porter and Thompson succeeded in visualizing virus-like structures corresponding to the milk factor in adenocarcinoma of mice. As stated by Claude et al., the virus-like agent of Rous sarcoma can also be rendered visible by electronmicroscopy. However, this finding could not be fully confirmed by Oberling et al., and the problem remains open even though a number of reports discuss apparently confirming evidence.

DEMONSTRATION OF VIRUSES "LATENT" VIRUS FORMS

With the aid of electronmicroscopy, viruses have been demonstrated in human tumours recently by Gessler et al., Hellwig, Witt-Fox, Timofeyevski and Deriugin. The electronmicroscopic studies of Timofeyevski have shown that structures corresponding to elementary bodies may frequently be found in 5 to 10 days old cultures of tumorous human tissue. Of course, it needs proof that these are specific and responsible for the tumour.

Zilber maintains that no virus is found in most tumours, possibly because it may be present in some "latent" form, not demonstrable by present methods. However, in this case it should be detected by serologic methods as a foreign (heterologous) protein.

Earlier, Zilber actually demonstrated the presence of heterologous protein in tumours by precipitation and complement fixation techniques. In an attempt at confirming this by the anaphylactic test of Besredka, he has shown the anaphylactic reaction associated with desensitisation to be conclusive of the presence of the assumed second antigen in the tumour.

Nevertheless, Zilber regards the experimental results of Timofeyevski and Benevolenskaia as the most convincing evidence of the viral origin of tumours, since it is upon the addition of tumour filtrate, i. e., according to Zilber, of the virus itself that the intact cell in tissue cultures becomes tumorous.

Also Duran-Reynals ascribes tumours, or at least most of them, to virus action. Likewise, Andrewes and Rondoni have suggested that omnipresent virus produces tumour if and when the balance between the virus and the cell is upset by some tumorigenic influence.

According to one theory, transformation into cancerous cells takes place when the latent, probably ubiquitous cancerogenic virus penetrates the cell. It has therefore been investigated whether true, virogenic tumours could be produced by treatment with cancerogenic chemicals. In 1930, McIntosh injected tar into the pectoral muscle of hens. Four of the resulting tumours proved to be transmissible, in three cases even with the cell-free filtrate. Thus tar was proved to be capable of producing tumour transmissible with filtrate. The responsibility of some chemical tar derivatives could be ruled out with certainty, as the tumour could be passaged through several generations.

However, Peacock was unable to confirm the results of McIntosh in 1933-35. The tar-sarcomas that developed in hens were not transmissible. Moreover, Zilber's experiments in which he produced tumour with the filtrate of tumorous growths could not be reproduced either. By re-investigating the problem, Diadikova obtained negative results. Gye (1938) claimed that he had succeeded in transmitting transmissible mammalian tumours with cell-free material, after deepfreezing. It turned out, however, that viable cells still remain in such material, and so the evidence was not convincing. At present, it is generally believed to be impossible to transmit with cell-free material fowl sarcoma, or the tumours of mammals resulting from treatment with certain chemicals.

CHEMICAL CANCER (TAR, BENZPYRENE)

Kidd and Rous (1936) painted the ears of rabbits with tar and observed the development of the well-known tar-produced warts in two to three months. Then they inoculated the animals intravenously with the papilloma virus of Shope. Three weeks later rapidly growing cancers developed at the tar-painted sites, but nowhere else. At that time no cancer could be noted in the animals treated with tar alone. Completely similar results were obtained in the benzpyrene experiments of Lacassagne and Nyka (1937).

Rous and Friedewald approached the problem from the opposite angle (1941), treating with tar or methylcholanthrene rabbits previously infected with papilloma virus. Cancer never arose from the virus-caused papillomata or in the areas treated with the solvents of methylcholanthrene, whereas cancer grew as a rule at an unprecedented rate from the virus papillomata treated with methylcholanthrene. Thus, according to these workers, *cells infected with virus show a great tendency to chemical cancer*. Friedewald (1944) believes that in animals and man certain factors may occur which, like the Shope virus, will produce no pathological changes by themselves, but when pathological alterations arise in the tissues, the latent tendency to tumour may become manifest.

ENDOGENOUS VIRUS

During the past three decades, the classic view accepted since Pasteur that infectious agents may be exclusively *exogenous* has been losing credit as a result of research concerned with tumours, and now many authors claim that tumours may be due to *endogenous agents* produced by the affected cell itself. Already in the early 'thirties Loeb suggested that neoplastic proliferation originated in an intracellular accumulation of *autonomic duplicants*, or of compounds produced as a result of *autocatalysis*. The "ens malignitatis" hypothesized by Teutschlander (1928) is thought to be such an endogenous product.

Rous, Gye, Haagen, Purdy, and Andrewes believed the agent causing fowl tumour to be true exogenous virus. Doerr, Teutschlander, Pentimalli, A. Dietrich, Fischer-Wasels, Murphy and Rondoni, on the contrary, were of the opinion that the factor eliciting the Rous sarcoma of fowls was an agent produced and multiplying intracellularly

endogenously in response to a cancerogenic stimulus. According to Doerr no exogenous infection could be demonstrated in hen sarcoma transmissible with filtrate. It is also known that hen sarcoma transmissible with cell-free filtrate has been induced also with non-specific stimuli (Doerr). Carrel was the first to succeed in transmitting with filtrate hen sarcoma produced by treatment with tar, indole, and arsantrioxide. De Ligneris malignified normal hen-fibroblasts in vitro cultures by treatment with dibenzanthracene, then inoculated hens with filtrate. In a considerable percentage of the cases the tumour proved to be transmissible. Therefore Graff concluded that no substantial difference may be assumed to exist between chemically induced and filtrate-transmitted hen sarcomas.

The fact that the neoplastic action of the Rous or Fujinami agent may be neutralized in the presence of complement with serum from animals previously immunized with normal hen protein or with tumour extracts indicates that a serological relationship exists between the agent and normal fowl protein. According to Doerr, it is hardly conceivable to explain this in any other way but by assuming a genetical correlation. Amies has succeeded in bringing about neutralization with highly purified anti-Rous agent chick-serum even in the absence of complement, which again suggests that the agent is closely related to normal chick protein. Amies thinks this phenomenon unique. Anti-rabbit goat serum is known to have no effect on elementary vaccinia bodies produced in the rabbit, suggesting that the Rous agent belongs to a separate group. In Doerr's opinion another evidence against an exogenous organ is that the serological properties of the agent may be mistaken for those of the animal harbouring the tumour. Sarcomas have been induced both in chickens and ducks by treatment with the cell-free filtrate of Fujinami's duck sarcoma. On the other hand the agent isolated from chicken tumour could not be neutralized with anti-duck immune serum but only with anti-tumour or anti-chicken serum. Sarcoma that had developed in the duck could be neutralized exclusively with anti-duck or anti-tumour sera, anti-chicken serum being ineffective. These variations of antigenic properties are the more remarkable if we realize that for example chondro-osteosarcoma produces tumours of strictly identical structure in every passage.

The parallelism existing between the multiplication of the virus and of tissue cells is quoted by Doerr as further evidence indicative of the Rous-agent's endogenous nature. Still another confirmatory fact is that the Rous agent, like the organelle of cells, possesses high specificity.

It has also been suggested that the *endogenous virus* of tumours develops not in the usual form of an elementary body, but as part of the cell, distributed throughout the cell, linked to its structure. Moreover, the hypothesis has been put forward that the corpuscular elementary body-like variant of viruses might be the form of a stage in viral development.

In Rondoni's opinion, endogenous virus may arise from the nucleoproteins or liponucleoproteins of the cell and may multiply synchronously with the other constituents of the cell; *it may even become hereditary as a newly acquired property*. Potter thinks that *endogenous* enzymes controlling oxidoreductive processes may be responsible for the pathologic changes. Also Euler believes that *enzymoids* involved in protein

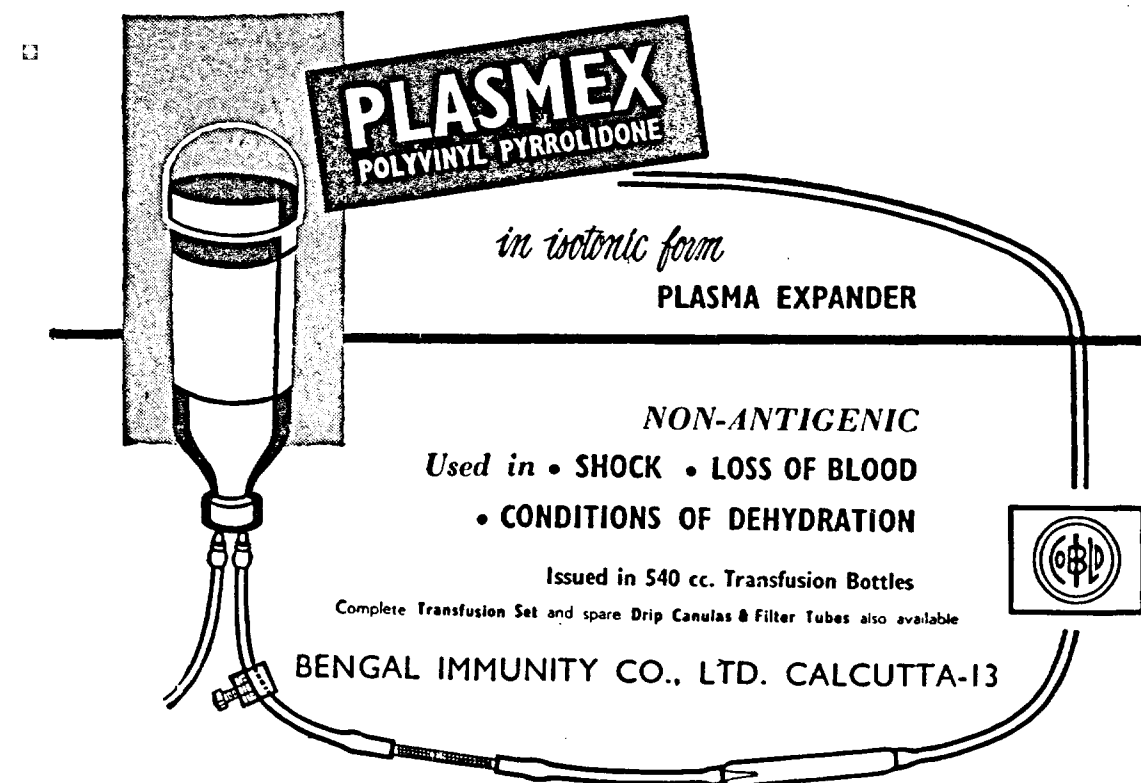
synthesis and capable of multiplication may be the cause of cancer.

AUTOCATALYSIS

Kidd has suggested that intracellular autocatalysis, by interfering with the normal synthesis of proteins and thereby giving rise to anaplasia and malignant transformation, may be responsible for cancer. This view is based on the presence of a protein of high molecular weight giving also the complement fixation reaction in the Brown-Pearce tumour. A similar protein has been found in the cancer designated V₂ that developed from Shope papilloma after several passages. According to Oberling and Guerin, we are only at the beginning of research in this field and a long time will have to pass until it becomes clear in what way the *nucleoprotein* may turn parasite, which may induce the development of tumour.

VIROIDS

As it can be seen, increased knowledge about the virus theory of tumours has raised many problems



that should be elucidated in order to gain insight into the tumours actually caused by virus. The first question to be answered ought to have been *whether the tumours* apparently caused by viruses *are in fact due to true viruses*. It has been claimed that the agents causing such *tumours are not completely identical with the viruses causing viral diseases*. Altenburg (1946) spoke about *viroids*, Darlington and Mather about *provirus*. Murphy, Haddow, Kidd, Rhoads are apparently convinced that the virus-like agents causing tumours can be differentiated from the common viruses on the basis of certain properties. One of the most important differences is supposed to be that the viruses causing tumours are less potent antigens than the common viruses and often occur in conjunction with intact animal proteins, in complex linkage. Oberling and Guerin admit that this may be so, but the same properties may be found in the viruses of common cold, influenza, and equine encephalitis.

The introduction of the above concepts and new terms only adds to our difficulties: how shall we then define the concept of filtrable viruses? According to the earlier definition, viruses are pathogenic agents of submicroscopic size, capable of division, reproduction, growing exclusively in living cells and causing antibody production.

CHANGES IN THE GENE PATTERN

Until recently, the site of formation of the virus causing tumorous proliferation was usually thought to be the nucleus and the evolution of the virus was believed to follow the rule of *somatic mutation* (de Vries, Hansemann, Boveri, Whitman, Schwartz, Strong, Bauer) that was supposed to alter the desoxyribonucleic acid material of the cell nucleus, changing the *pattern of genes*.

Butenandt and v. Euler think that in fact the genes of viruses and of the cell nucleus alike are *living macromolecules* composed of nucleoproteins of similar size and chemical structure. Both are capable of utilizing living cellular material for their own reproduction. According to v. Euler, the neoplastic virus is exogenous in the sense that it may enter the cell from without, but is endogenous because it uses the body, materials of the host cells to build up its offspring. He thinks that the endogenous virus that may become pathogenic is already present in the living cell in the form of an *inactive precursor* which

may develop into a pathogenic form as a result of mutation or other influences.

This view assuming the close relationship or identity of the genes of viruses and the cell nucleus has been radically revised recently. To-day, after Nothdurft and Darlington, we ascribe the site of formation of such gene-like autonomic particles to the cytoplasm rather than to the nucleus. Among the cell constituents involved in the transformation into endogenous virus, we think in the first place of the *mitochondria*, the *microsomes* of the cytoplasm, as well as of the hypothetical *plasmagenes*. As stated by Oberling and Guerin, at the level of present knowledge an identification of such *endogenously* formed substances with viruses is quite acceptable.

Graff has shown that carcinogenic hydrocarbons may cause irreversible changes in mitochondria, and their metabolism may become more or less independent from that of the cells. This may be so marked that the mitochondria may be completely separated from the life of the cell and from the influences that control it, and may thus become closely *similar to viruses*. Woods and Du Buy have arrived at a similar conclusion from entirely different evidence. They think that in certain plant diseases associated with changes in the colour of affected plants, the pathogenous *chloroplasts* of the cytoplasm appear in intact cells, may replace normal chloroplasts, thus spreading the disease. As these plastoids are formed in the cytoplasm and are produced by the cell, this example is excellently illustrative of how infective elements may develop from intact mitochondria and how they may become similar to viruses. *Nevertheless, the conversion of mitochondria into viruses is by no means a decided issue*. As early as 1914, Warburg suggested that the mitochondria of the cytoplasm, the "grana", are autonomic, because they show respiration inhibitable with narcotics, and according to his recent view (*omne granum e grano*), they are capable of reproduction.

At present, the properties of the Rous agent, this best-known factor causing animal tumours, are no less obscure to us than are those of other viruses. Whether the agent responsible for Rous sarcoma is exogenous or endogenous, continues to form the subject of endless debate.

Now it is known that in response to the Rous agent various kinds of tumour: fibrosarcoma, even

myoma, or osteoma may develop, but it is also known that the sarcoma itself contains at least *two different kinds of antigen*, from which several workers conclude that the agent is apparently a *plasma-organizer* responsible for neoplastic transformation (Gottschalk, Haddow, Darlington). Thus the Rous agent corresponds to a *mutated plasmagene*. According to Haddow, the cells incorporate the agent causing the Rous sarcoma as an acquired gene, which then leads to a continuous production of the pathogen and thereby to malignancy. Of the two kinds of antigen mentioned above, one corresponds to the *cellular gene*, the other to the *acquired gene*. According to Oberling and Guerin, the pathogenicity of the Rous virus for several species is another evidence pointing to the probability of its close relationship to or identity with, mitochondria.

The role of the fine plasm granules, *microsomes*, described by Claude, also requires elucidation. If we accept that they are identical with viruses, it remains to be explained how these elements of capable of multiplication.

In Darlington's view malignant tumours may be

caused by various factors: *plasmagenes, proviruses*, of true *viruses*. Most of the mammalian tumours transplantable with intact cells he believes to be of plasmogenic origin. The tumours of birds are assumed by Darlington to be due to proviruses, which are capable of reproducing themselves in plants and animals, and under normal conditions are passed on by heredity from generation to generation. However, they may also enter new cells in the same way as an infection.

Thus the *proviruses* of Darlington corresponds to a *kind of endogenous virus*, which develop by mutation from existent plasma granules capable of reproduction. The Rous sarcoma-like tumours of birds are the result of such a *plasmagenic mutation*. In contrast with this view, Andrewes, Duran-Reynals have shown that at an advanced age most normal hens contain antibodies which neutralize the agent causing Rous sarcoma. This suggests the possibility that *even tumour-free chickens harbour the virus in the form of occult infection*.

It has been known for a long time that viruses may be present for long periods *in latent forms*.

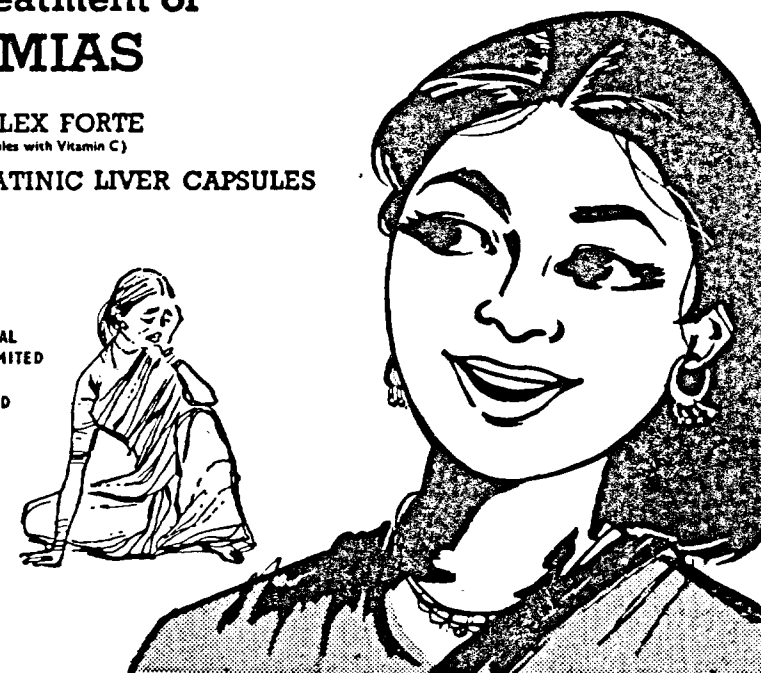
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Nevertheless, the successful artificial creation of an *endogenous virus* by Yamafuji et al. has aroused considerable interest. Yamafuji, Yamafuji, Fujii and Akita, Yamafuji and Yuki claim to have induced jaundice of silkworm (*Bombyx mori* L.), caused by the *Borrelina bombyx* described by Paillot, in worms clinically free of infection, by the use of nitrite, hydroxylamine, and oxim. In Vago's experiments apparently normal silkworms became ill also in response to fluoride, but unlike Yamafuji, Vago attributed this to an outbreak of a formerly latent disease. Kriegfeld silk worms under aseptic conditions on dried leaves of mulberry (*Morus alba*) soaked with the above-mentioned chemicals. The strain employed was free of polyader virus infection and did not develop the disease on this treatment.

TRANSDUCTION

The marked similarity between genes and viruses is illustrated by transduction which has been re-appraised recently. Lederberg values the discovery of the mechanism of viral infections. Transduction is understood to mean the acquisition of genetically new properties by the entrance of infective phages into cells, when the phage, incorporated into the cell like a gene, transmits to the new cell the hereditary properties of its former host.

It has been known for about a quarter of a century that individuals of *Escherichia coli* K₁₂ may contain phage. In a free state this phage, now termed lambda phage, occurs in cultures in very minute amounts. There is about one extracellular phage to 1,000,000 bacteria. However, lambda phages living latently in bacterial cells may be set free by inductors: ionizing radiation, nitrogen mustard, reducing substances, and then they may enter new bacteria, lysing them or being built into them in a latent form, transmitting to the new host the hereditary properties of their previous host.

Transduction may cause the formation of an enormous number of variants biologically. In a DNA chain containing 100 nucleotides the number of possible variants, according to Stanley, is 10⁸, and this alone is more than all the individuals of the various species living on earth combined. This explains why at present the nucleotides of the carcinomatous cell are in the focus of research. The principal aim, of course, is to find substances that

interfere with the metabolism of the nucleic acids of altered structure building up the cancer cells.

Furth has first of all suggested three explanations for the viral origin of leukemia. He thinks that the disease may be caused by specific or non-specific virus. But it is also possible, as has been suggested by Murphy, that the mutagenic virus latent in the organism causes irreversible changes in the cells under neoplastic conditions, and finally tumours may also develop through transduction.

In Seeger's view, inoculation of the organism with cancer-virus or microsomes, containing cancer-virus, takes place already through the placenta or during breast-feeding. The virus may remain latent in the cells as long as reactive oxygen is present to prevent it from becoming pathogenic. In old age, when the oxidative enzyme content decreases, the virus accumulates and malignancy becomes possible. A deficiency of catalase leads to intracellular accumulation of hydrogenperoxide, which may cause polymerisation or coagulation of nucleoproteins, and thereby production of virus.

EFFECT OF CARCINOGENIC AGENTS

Investigations by Bloch (1924), with reference to ionising irradiation, by Bryan and Shimkin (1941) to carcinogenic hydrocarbon, and by Druckrey (1949, 1954) to butter yellow have revealed that the various carcinogenic effects exert their action slowly, gradually, as *summation poisons*, and must reach a certain threshold to produce tumorous proliferation. Thus tumorous growth is the function of the duration of action and of the sum of actions. It starts when the total dose is reached, after a short time following stronger effects, and after proportionately longer time following prolonged exposure to minor effects. According to Druckrey, transformation into cancer takes place after more than two and usually after around 100 repeated exposures. The law of "all or nothing" does not apply to tumorous growth, and it is likely that because of the large number of "hits" required, cancer is *not due* to gene or chromosome mutation, but to changes in reproducible *duplicants* often present in the cells in larger numbers. This view is corroborated by Weiler's observation: under the influence of butter yellow, when hepatoma formation begins, the microsomes of

the liver cells have already changed their organ-specific nature, because they do not react any longer with anti-liverprotein immune serum.

According to the present view, an infection will become effective when sufficient virus has entered the organism, on the one hand, and when the organism is susceptible, on the other. Bryan considers the oxidative phospholipids of the body to be one of the important defences of the organism against viral infection. He thinks that just because they are dissolved in lipids, the carcinogenic agents antagonize the protective action of phospholipids, promoting thereby the development of viral proliferation. It is well-known that the pathogenic action of viruses depends on the age of the host. Duran-Reynals assumes that the intracellular mucopolysaccharides in the connective tissue of the skin usually act against infection. He has suggested that the age not only of the recipient, but also of the donor organism is of importance.

Classification and understanding of the neoplastic viruses is rendered difficult by the evidence that some of them are not specific. For example, the virus causing renal cancer in the leopard frog causes chondrosarcoma in the triton, according to Rose and Rose. Borges and Duran-Reynals have successfully transplanted Rous sarcoma into pigeons, and we know that the agent of Rous sarcoma may sometimes produce other connective tissue tumour. Olson and Cook found that the virus of papilloma of the bull produced sarcoid in the horse.

Also their transplantation properties may be different. Rous sarcoma has certainly been transplanted successfully with cell-free filtrate. But the virus of adenocarcinoma of the mouse can be transmitted with cell-free filtrate only exceptionally, in the case of extremely susceptible strains. Other kinds of mammalian tumours can be transplanted exclusively together with intact tumour cells.

SUMMARY

During the past two decades, feverish research work has been in progress all over the world to elucidate the origin of tumours. In spite of the doubtlessly enormous advance achieved in this field, all we may state today is that a virus-like agent may

in fact produce tumour in some animals, and the transplantable tumours (with cell or filtrate) of animals; the tumorous haematological diseases are probably of viral origin. Most of the transplantable tumours that can be passed from one animal into another will kill the animals within a few weeks or months, with a *short period of latency*, and this alone makes it difficult to compare these tumours with the spontaneous malignancies of man which may remain latent for as long as fifteen or twenty years. Another evidence against the infectious origin of spontaneous malignant tumours of man is that while the body produces specific *antibodies* to bacterial and virogenic infections, *in individuals with cancer no such antibodies could be detected so far*. According to Henschke (1942), it is even questionable whether antibodies are formed at all against transplantable animal tumours. Also statistical data *speak against* the infectious theory of tumour genesis. Since the turn of the century the incidence of tumorous diseases has been steadily increasing throughout the world, without showing changes, peaks, suggestive of a "genius epidemicus" of infectious diseases.

Although so far we have failed to demonstrate the presence of pathogenic, specific, exogenous or endogenous virus in malignant tumours of man, the question is far from being closed. Future research will have to supply the final answer to the question whether viruses do or do not play a role in the genesis of malignant tumours of man.

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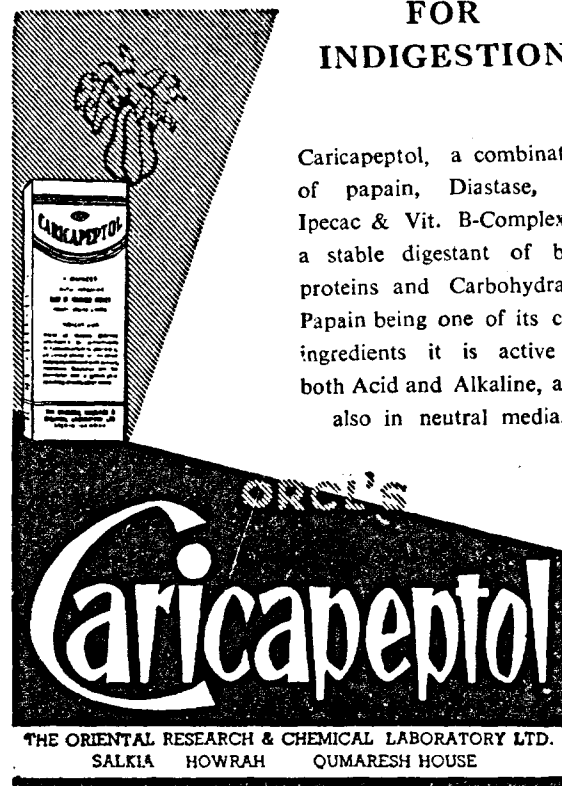
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FOR INDIGESTION

Caricaeptol, a combination of papain, Diastase, Tr. Ipecac & Vit. B-Complex, is a stable digestant of both proteins and Carbohydrates. Papain being one of its chief ingredients it is active in both Acid and Alkaline, and also in neutral media.



SOVIET DRUGS AND MEDICINAL PREPARATIONS

BY A SCIENTIFIC WRITER

SOVIET drugs are widely known in many countries of the world. Among countries purchasing Soviet drugs are Great Britain, France, the Federal German Republic, Switzerland, Greece, and the People's Democracies, as well as many countries of Asia, Africa and America. During the current year hundreds of Soviet drugs have been delivered to over sixty countries.

The interest displayed in Soviet drugs is quite understandable. Once a backward country, the population of which suffered from many epidemic and other diseases that carried away millions of human lives, the Soviet Union has been able within a relatively short period of time to advance to first place in the world in the speed at which the death rate is being lowered. The USSR has achieved a sharp increase in the average span of life and has practically eliminated such diseases as plague, cholera, smallpox, relapsing fever, itch, malaria, syphilis, and the like, which to this day are the scourge of many a country.

Unquestionably the decisive part in this advance has been played by the substantial improvement in the life of the population and by the new system under which the health services are organized, but great credit also goes to the Soviet pharmacists who have developed a large number of highly effective drugs.

SOME POPULAR SOVIET DRUGS

Here are some details about a few of the Soviet-made drugs which have become very popular abroad.

First of all we would call attention to *Shostakovsky Balsam*—an effective new remedy extensively used in treating ulcer of the stomach and the duodenum. It was developed by M. F. Shostakovsky, Professor of the Institute of Organic Chemistry, USSR Academy of Sciences, and his brother Dr. Z. F. Shostakovsky, a therapist.

Before giving a description of this new Soviet drug, an account of a case in which it was successfully used

and which has become known in many countries, would not be amiss.

A patient who was seriously ill was brought to a clinic in Greece, the diagnosis being "ulcer of the duodenum—acute stage". The patient's condition was hopeless. He could only be saved by an operation but this was out of the question because of his old age and weak heart. Treatment with the usual medicines was ineffective. There was no hope for his recovery.

The patient's son applied for *Shostakovsky Balsam* and the drug was immediately sent to the clinic by plane.

200 g. of the remedy was sufficient not only to save the patient's life but to have him discharged from hospital in excellent condition. This case is striking example of the new drug's wonder-working properties.

Shostakovsky Balsam is a light yellow, viscid liquid of specific odour; sparingly soluble in methyl, ethyl and propyl alcohol; insoluble in water. It can be mixed in all proportions with butyl and isoamyl alcohol, chloroform, sulphuric ether and acetone, as well as vegetable and mineral oils. It does not thicken or dry on exposure to air. Average molecular weight is about 2,000.

In surgery *Shostakovsky Balsam* is successfully used in treating wounds received on the battle-field and other fresh or old wounds, burns or frost-bite. It fosters the cleansing of wounds and facilitates granulation and epithelization during the period of regeneration.

In dermatology and venerology it is used in cases of suppurative processes of streptococcal or staphylococcal origin, and in treating acne vulgaris.

The Balsam gives excellent results in the treatment of such internal diseases as ulcer of the stomach and the duodenum, hemocolitis, gastritis and acute and chronic dysentery.

In X-ray therapy the Balsam is used to prevent damaging of the skin and mucous membrane.

Shostakovsky Balsam is used both in the pure form and combined with other vegetable or mineral oils.

The wide field in which this Balsam can be used, along with the fact that it is completely harmless, has made it very popular in many countries.

The Balsam is available in vials of 100 or 200 g, neatly packed in boxes, with labels and instructions for use in English.

A BOON FOR GLAUCOMA PATIENTS

Phosarbin is an effective Soviet drug for treating diseases of the eye; it has restored sight to many patients suffering from glaucoma.

Until recently an operation was the only way to cure this disease.

But no operation for glaucoma is radical and a cure is not guaranteed. Every eye-surgeon has observed this time and again. Academician Averbakh, the well-known Soviet surgeon, has pointed out that an operation for glaucoma does not always give good and permanent results: "...in the great majority of cases we insist on an operation, without putting it off, but this of course is an experiment. We may have a case that will hold out for a long time with conservative treatment but where no operation is possible. Without an operation the patient is sure to go blind, but he may also be blinded by an operation".

Academicians Arbusov, Sr. and Arbusov, Jr. have proposed a new myopic drug called *Phosarbin*, which gives excellent results in treating glaucoma, making an operation unnecessary.

Phosarbin is a colourless liquid of specific odour. It is used in the form of oil solutions in a concentration of 0.02 per cent.

The enthusiastic testimonials of many patients who have been cured by *Phosarbin* have promoted a great demand, and it is now being exported from the USSR in considerable quantities.

(Continued on page 35)

FOR TREATMENT OF TUBERCULOSIS

Para-Aminosalicylic Acid (PASC) is a drug that has in recent years come into increasing use in therapy. PASC is particularly effective in the treatment of tuberculosis. Its principal effect is in normalizing the patient's metabolism. PASC improves the functioning of liver, kidneys and other organs and has a general beneficial effect on the patient's organism. When a patient begins to take this drug his temperature falls during the first week. This naturally causes an improvement in his general condition: he has a better appetite and better digestion, and begins to add weight. There is less coughing and less phlegm; coughing is less painful and the phlegm is more easily expectorated.

PASC not only gives a symptomatic improvement in tuberculosis patients—it also brings about a diminishing of the pathomorphological changes in the patient's lungs.

PASC also has a favourable therapeutic effect in cases of lupus erythematosus, a disease that is very difficult to cure.

It is very important in surgical operations that the anaesthetics used should be effective, and especially that it should have no bad effects on the patient. One of the best anaesthetics is the Soviet *Scopolamine-Pantopone-Thiopental*. When it is administered the patient tranquilly falls asleep and the state of insensibility persists during the entire operation. He regains consciousness approximately four-and-half hours after the beginning of narcosis. This long sleep is an advantage of this anaesthetic, since in the overwhelming majority of cases this prevents the patient from experiencing the severe pain that follows operations. There is no vomiting while under the anaesthetic, something that is often observed when some other types of anaesthetics are used. There is likewise no post-operative excitement. Post-operative shock is entirely absent, as are complications of any kind.

ANTIBIOTICS

In recent years antibiotics have come to be used in many countries; they have been found to have wonder-working curative properties in the treatment of infectious diseases.

LEPROSY

BY DR. T. V. VENKATESAN, M.B.,B.S., F.C.CP.(USA), F.A.C.A., F.I.A.A., F.D.S.(Lond.),

Hony. Physician (Skin), Erskine Hospital and
Hony. Secretary, Hind Kusht Nivaran Sangh and
Medical Officer, Pudupatti Leprosorium, Madurai

RECENT observations show that among healthy contacts 10% have leprabacilli. Even in non-infective cases Leprabacilli can be shown. The infection is now. There is first invasion of superficial Nerve plexus. B. C. G. will convert a Negative Lepromin to a positive one. It is doubtful if B. C. G. gives—immunity. Lepromin Test possibly indicates tissue immunity.

CLASSIFICATION

- (1) Lepromatous Negative Lepromin reaction.
- (2) Tuberculoid Positive Lepromin
- (3) Dimorphic Weak Lepromin reaction.

CLINICAL

- (1) Macular.
- (2) Infiltrative.
- (3) Poly Neuritic.

MACULES : Three types of macules.

- (1) with vague edges. (2) with distinct edges.
- (3) Indistinct.

- (1) *The Lepromin Test is positive* in macules with distinct edges. The histopathological section will show involvement of small nerves in the corium with round cells and macrophages.

The Bacilli are few: No fish in stream appearance.

- (2) *In Lepromin Negative type* there are Round cells and histiocytes; there is perineural cuffing. Bacilli have *Fish in stream* appearance.

- (3) *Macules with slight positive lepromin reaction* There is tendency for focalisation. Bacilli are seen in moderate numbers. Perineural cuffing is present.

(Continued from page 34)

Soviet pharmaceutical industry, which is equipped in accordance with the last achievements in technology, is supplying a number of original antibiotics, among them *albomycin*, *colimycin* and *biomycin*.

Albomycin is a yellow or brownish powder. It is effective against penicillin-resistant strains of staphylococci and pneumococci. *Albomycin* is used in cases of pneumonia in adults and children; secondary pneumonia during measles, whooping-cough and dysentery; abscesses and sepsis; and infectious skin diseases. It is also beneficial in cases of relapsing tick-fever.

Colimycin is an antibiotic of the neomycin group and is obtained from the culture medium of an actinomycete mold. It is a white powder of faint, specific odour and a salty taste. It has an antibacterial action on staphylococci, streptococci and pneumococci.

Colimycin is used in treating piodermatitis, various skin diseases and suppurative processes in the abdominal region.

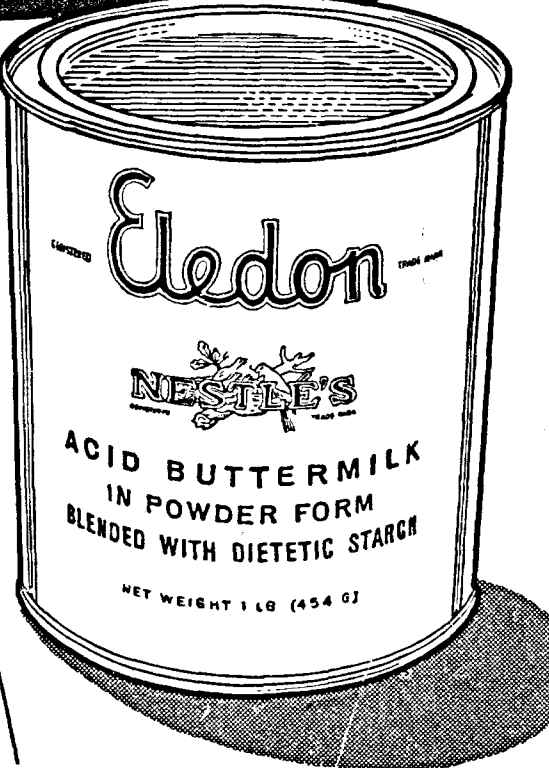
Biomycin is a golden yellow powder of bitter taste; it has a wide range of anti-bacterial use. It is effective against gram-positive and gram-negative microbes and rickettsia, as well as some viruses. It gives a good effect in infectious diseases resistant to streptomycin and penicillin. *Biomycin* is used in the treatment of pneumonia, dysentery, brucellosis, tularaemia, whooping-cough, typhus and amebic dysentery. It is also effective in trachoma and conjunctivitis.

In the last few years new vaccines against tularaemia, anthrax, intestinal infections and other diseases have appeared in the list of medicines exported from the USSR.

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Lepromin positive indicates hypersensitivity reaction.

Lepromin weakly positive indicates unstable equilibrium.

Lepromin negative indicates Densitivity reaction.

According to Dr. Khanolkhar, all leprosy is neural.

INFILTRATED LESIONS

I. *Lepromin Negative* : *Lepromatous type*

Free sub-epidermal zone. No focalisation Round cells. Macrophages showing vaculles. Nerves are not involved. Plenty of bacilli. "Fish in stream appearance" Previchow cells show definite vacuolisation.

II. *Lepromin Positive* : No free sub-epidermal zone.

Epitheloid cells	Focalisation.
Giant cells	
Bacilli Few	
Nerves are invaded. Bacilli are few in number.	

III. *Dimorphic* : Infiltration more diffuse.

Epitheloid cells, giant cells and Macrophages, Virchow cells. Free sub-epidermal zone, Bacilli are in moderate number.

Poly Neuritic lesions : Only polyneuritic changes.

No skin lesions. The bacilli are present producing Fish in stream appearance. Three main groups occur according to Lepromin.

CLINICAL TYPES

I. *Lepromin Positive*

- Maculo anæsthetic.
- Tuberculoid Macule.
- Infiltrative lesions.
- Polyneuritic tuberculoid.

II. *Lepromin Negative*

- Macular Leproma.
- Infiltrative Nodules : Diffuse lesions.
- Poly-Neuritic leproma.

III. *Dimorphic variety*

- Dimorphous macule.
- Infiltrative lesions.
- Dimorphous polyneuritic.

DIAGNOSIS

- Type of lesions.
- Sensation test for pain, Temperature and touch.
- Duration of lesions
- Thickening of the Nerves complications of Leprosy.

LEPROMATOUS

- Laryngeal
- Testes involvement.
- Corneal ulcer.
- Lepra reaction.
- Penumonia.
- Tuberculosis pulmonary.
- Nephrosis.
- Muscular atrophy.
- bone Necrosis.

Treatment : *Sulphones*

METHOD OF ADMINISTRATION AND DOSAGE

- D. D. S. Dapsone*—25 mgm twice weekly. Increase gradually till until 100 mgm twice weekly is reached. Then raise each month 100 mgm till 400 mgm twice weekly is reached.
- Sulphaterone* : $\frac{1}{2}$ cc I. M. twice weekly gradually increase to 3 c. c. I. M. twice weekly.
- Promin* : 2 gm. daily I. V. and gradually increase till 5 mgm daily is reached. Rest periods between doses.

Thiosemicarbazone : 25 mgm daily and gradually increase till 100 mgm daily. They are less efficient.

Streptomycin : Six weeks course of 1 gm. daily. Three months rest and repeat three such course.

I. N. H.

Results are disappointing. A combination of

sulphone and I. N. H. has been tried in some cases with good results.

RESULTS OF TREATMENT

- I. In tuberculoid leprosy there is good response; but hypopigmentation is left over, for which it is advisable to give local treatment with E. C. O.
- II. *Lepromatous*: Treatment for 5 years is sine qua non
- III. *Demorphous* cases: They show gross tissue destruction and damage to nerves.

ACTION OF SULPHONES

Lepromatous cases:— There is fragmentation of acid Fast bacilli.

Thus the sulphones act by preparing the bacilli for more adequate destruction and phagocytosis by macrophages cells.

Inadequate therapy will leave pockets of bacilli.

Tuberculoid Leprosy: In 8 months there is reasonable improvement. The sulphones stimulate bacilli producing favourable tissue response. The bacilli multiply and sets trigger mechanism.

REACTIONS IN LEPROSY

- (1) Violent local tissue response
- (2) Acutelepra reaction or Erythema Nodosum
- (3) Chronic lepra reaction.

Erythema Nodosum Leprosorum is a Jarish Herheimer reaction occurs in *Lepromatous* cases and respond to Corticosteroids.

When patients do not respond with sulphones, the drug used is Dephenyl thiourea (DPT) 2 gm daily commencing with 250 mgm daily.

Dr. Davey et al reported favourable results with Ditophol inunction externally and D. D. S. orally. According to Dr. Kupfer B. C. G. administration favours recovery.

THE RESPIRATORY SYSTEM IN OBSTETRICS AND GYNAECOLOGY

BY DR. VISHNU SARMA

M.A.(Cantab), M.D.(Cantab), B.Chir., M.R.C.S.(Eng.), L.R.C.P.(Lond.), D.G.O.(Madras)
Fellow, The Royal Society of Medicine, London.
From The Govt. Women and Children's Hospital, Egmore, Madras.

THE respiratory system, contrary to what might at first be supposed, has quite a lot to do with Obstetrics and Gynaecology.

Obstetrics and Gynaecology is not an isolated speciality. Although it deals primarily with problems pertaining to childbirth and the normal working of the female reproductive mechanism, it cannot ignore other parts of the human body.

Procreation is an important function of the life process. General ill health can seriously thwart or even make impossible the creation of new life. Disease of the female genital tract may not, sometimes be apparent. It may present with symptoms and signs in some distant part of the body. The real diagnosis can never be reached by a gynaecologist who lacks sound training in general medicine and surgery.

The specialist in Obstetrics and Gynaecology must be his own physician. That is not to say that he should not seek the aid of specialists in other branches of medicine when he is in doubt. At times he can profitably consult a cardiologist, a neurologist, a gastro-enterologist, an urologist, an abdominal surgeon or a chest physician.

One of my teachers in gynaecology (Howkins 1952) would advise those of his students who were interested in the subject to learn as much general medicine and general surgery as could possibly be learnt, because, in his own words "there is no more pathetic figure than the untrained gynaecologist".

The lungs are of course the organs by which blood is oxygenated. Respiratory disease may devitalize a patient, whether she be a wailing parturient in the labour ward or one about to undergo a gynaecological operation. The great strain of difficult labour or the

shock which goes with a surgical operation may aggravate the respiratory lesion. It may even prove fatal if it does not make a chronic invalid of the patient.

Certain diseases of the female reproductive tract involve the lungs and present with pulmonary symptoms and signs. The gynaecological nature of the disease may seem insignificant. Before considering these diseases a brief outline of the method of eliciting an adequate history and making a thorough physical examination may not be out of place. The following is reproduced from the author's private case-record and is a guide to record relevant facts obtained by examination of the respiratory system.*

During puberty nasal epistaxis is not uncommon. Epistaxis may be precipitated by sexual excitement during coitus. Olfactory senses play an important sexual role. The nose may be the seat for secondaries from genital cancer. In a case report entitled "Widespread skin secondaries in a case of chorion-epithelioma". Marikar and Chandravada (1959) report a patient whose nose was deformed by chorion-epitheliomatous skin deposits.

Infected accessory air sinuses may act as a distant source of sepsis in pelvic inflammatory disease. Infected sinuses need attention in any patient who is to undergo a gynaecological operation.

Laryngeal congestion may occur during menstruation that some singers cancel their vocal appointments at this time. In genital tuberculosis examination of the larynx is a part of routine examination, but a tuberculous laryngitis may be aggravated by menstruation. The prognosis of laryngeal tuberculosis in a pregnant woman is very poor.

The other structures of the respiratory tract and

Sedonal

ORAL AMINOPHYLLINE
with PARENTERAL EFFECT

in
the management
of
HYPERTENSION

Vitazyme

insures

- * DIGESTION
- * ABSORPTION
- * ASSIMILATION



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Examination of the Respiratory System*

Respiratory System :

- | | | |
|----------------------|----------------------------|----------------|
| 1. Nose | 4. Trachea | 7. Pleura |
| 2. Accessory sinuses | 5. Bronchi and bronchioles | 8. Diaphragm |
| 3. Larynx | 6. Lung | 9. Mediastinum |

Loss of smell / sinus pain / nasal discharge / epistaxis / nasal voice / hoarseness / stridor / stertorous respiration / Cheyne Stokes / retrosternal pain / pleuritic pain / other / dyspnoea / orthopnoea / slow respiration / paroxysmal, nocturnal / wheeziness / Cough, onset, character, duration, productive, paroxysmal, Sputum, quantity, nature, consistency, mucoid, mucopurulent, offensive, odourless, bloodstained, hæmoptysis / other

Inspection: Form of the chest: normal, abnormal / postural and developmental defects / evidence of disease, past or present

Movements of the chest, normal, decreased, increased, excursion,

Normal rhythm and rate of respiration, thoracic, abdominal

Palpation: Form and movement of the thorax,

Position of the apex beat

Position of the trachea

Vibrations, tremor, friction, rhonchi, tenderness

Tactile vocal fremitus, normal, increased, decreased

Percussion: Sound, character, quality, resonant, dull, crackpot, amphoric, myotatic irritability.

Auscultation: Character of breath sounds: vesicular, puerile, prolonged and harsh, cavernous, amphoric, jerking, irregular, weak, absent

Adventitious sounds, bronchial breathing, low pitched, high, medium

Rales, dry sounds, rhonchi, sibili, sonorous, moist crepitations

Friction sounds, succussion sounds,

Characters of vocal resonance, bronchophony, whispering pectiloquy, other

Special Investigations

Examination of the Sputum Quantity / Consistency / Homogenous or in layers / colour and transparency / mucus / mucopus / serous / purulent / bloody / other
Microscopic / Pus cells / epithelial cells / red blood cells / eosinophils / pathogenic organisms / malignant cells / other

Plain X-ray of the Chest

The bony skeleton

The position of the patient

The position of the trachea

The outline of the heart and mediastinum

The diaphragm

The lung fields

Antero-posterior view / Lateral view

(Photographs of radiographs may be affixed here)

Screening

Tomogram/Bronchogram/Other

(Reproduced from the author's private case record for personal use)

the way in which they are affected by pregnancy or gynaecological ailments are considered. A diaphragmatic hernia may sometimes complicate pregnancy.

Whether menstruation has any effect on the respiratory system is uncertain. The premenstrual stage seems to have a deleterious effect on the progress of pulmonary tuberculosis. During this period hæmoptysis is more frequent.

There appears to be some relationship between the premenstrual phase and attacks of bronchial asthma (Figure 1).

When the patient becomes pregnant the growing uterus does distort and disturb the normal anatomy of the respiratory organs, if it does not actually interfere with aeration in the last weeks of pregnancy. In the last months of pregnancy the diaphragm is raised and there is restriction in the movement of the abdominal wall. Although abdominal breathing is restricted the vital capacity is increased due to a rise in oxygen demand. During labour the type, rate and intensity of breathing are influenced by the pains and in the second stage of labour there is the additional stress of expulsion of the baby. The intensive straining may cause small extravasations of blood to appear in the upper part of the body notably in the skin and conjunctiva, and swelling of the thyroid gland. Sometimes pulmonary alveoli rupture and result in emphysema of the mediastinum and the neck (Figure 2). The emphysema disappears within the first few days of the puerperium.

Of greater importance than the physiologic changes of pregnancy are diseases such as eclampsia, which make the patient unconscious. Because respiration is shallow, aeration incomplete, and protective reflexes diminished, if not altogether absent, mucous secretions of the respiratory tract may accumulate and cause atelectasis and infection of lung tissue (Figure 3). Sometimes vomitus is inhaled and this causes aspiration pneumonia if the patient does not die immediately of anoxia. Acidosis is a common feature of eclampsia and this may stimulate the respiratory centre and make for rapid breathing.

The premenstrual period, it has been said, has an unfavourable effect on pulmonary tuberculosis. When a patient suffering from active lung tuberculosis conceives she offers a problem of considerable

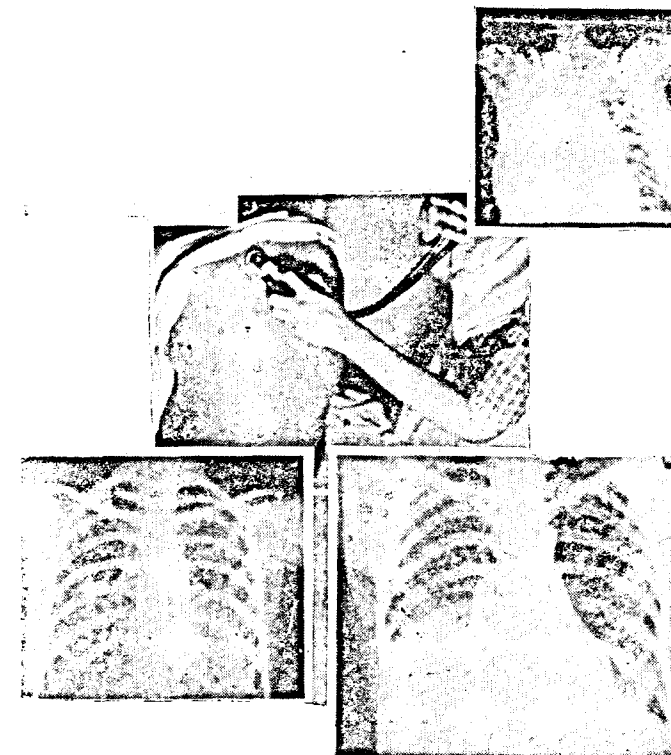


Fig. 1

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

A 55 year old woman with an extensive epidermoid carcinoma of the vulva (top left) was submitted to a radical vulvectomy and bilateral ilio-femoral lymphadenectomy. A chest x-ray was not taken as part of the routine preoperative evaluation. On the 9th postoperative day she became dyspnoeic and showed lung signs. Subsequently she developed a massive effusion on the right side. The x-ray (top right) was taken before her death on the 11th day. Was death due to pulmonary embolism? Was latent pulmonary tuberculosis activated by the formidable operation to which she was subjected? No definite conclusion was reached although everything was in favour of pulmonary embolism as a cause. The case demonstrates the very great importance of pre-operative chest x-rays in the evaluation of genital tract malignancy and in pre-operative assessment. The x-ray (bottom left) is that of a 22 year old woman who was thin and anaemic. She was suspected to have tuberculous endometritis and was subjected to a curettage under inhalational anaesthesia. Although an x-ray of the chest had been taken it was not available for study and the general anaesthetic could not have done her much good, as she had extensive bilateral pulmonary tuberculosis. This emphasizes the value of examining the lungs before an anaesthetic is administered and that too in a case where genital tuberculosis is suspected. The x-ray (bottom right) comes from a 26 year old multipara who reported with hæmoptysis at the 20th week of her fifth pregnancy. She had a right basal pneumonitis associated with amoebic hepatitis. Respiratory infections may complicate pregnancy and demand detailed evaluation of the respiratory tract in the management of pregnancy.

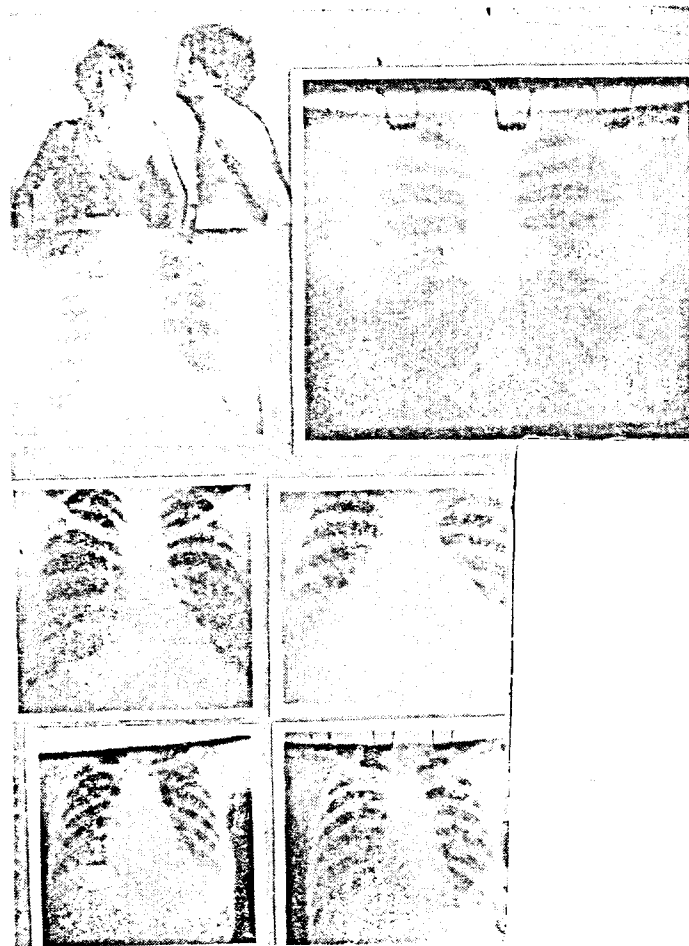


Fig. 2

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

The figure (top left) is of a patient who sustained an injury to the chest and consequently developed sub-cutaneous emphysema. The fullness of the supra-clavicular hollows particularly on the left side can be clearly seen. Crepitations could readily be elicited by palpating the skin. The x-ray shows clearly the accumulation of the air in the sub-cutaneous tissues. The figure (top right) is from a patient who had tropical pulmonary eosinophilia. This condition may complicate pregnancy. Sometimes it has to be ruled out before performing a gynaecological operation on a patient who has clinical evidence of pulmonary disease. The figure (centre left) is from a 26 year old patient whose pregnancy was complicated by asthma. She was about 5 months advanced in pregnancy and had severe asthmatic attacks. Bronchial asthma is sometimes better with pregnancy and at other times worse. It may appear for the first time in pregnancy or the puerperium. The picture (centre right) is an x-ray from a patient whose pregnancy was complicated by mitral heart disease. Slight enlargement of the left atrium is seen and there is some degree of pulmonary congestion. The picture (bottom left) is from a patient whose pregnancy was complicated by what was at first diagnosed as bronchiectasis. X-ray studies however showed the diagnosis to be cystic disease of the lung. With appropriate management she had a normal delivery at term.



Fig. 3

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

In comatose states as in eclampsia, pulmonary infection readily occurs. In the management of eclampsia the care of the air way and the prevention of respiratory complications contributes towards recovery and makes for a better prognosis.

importance in the management of her pregnancy. Correct decisions require great clinical skill and judgement to arrive at. To decide whether a pregnancy may be permitted to continue or whether it should be terminated (if so, when) in the best interests of the patient require from the obstetrician much more than a superficial knowledge of chest disease. Pulmonary tuberculosis frequently causes menstrual disturbances. Amenorrhœa may be the first presenting symptom of pulmonary tuberculosis. Often the menarche may be delayed. It is said that tuberculous patients have an increased libido.

The last picture (bottom right) is of a patient whose pregnancy was complicated by pulmonary tuberculosis. The prompt recognition of pulmonary tuberculosis in the ante-natal department depends on how skilfully case histories are elicited and that what thoroughness patients are examined. In many modern antenatal units routine screening of the chest has become an established procedure.

There is a clinical impression that babies born to tuberculous mothers are often larger and heavier than normal. As with all diseases in an advanced stage, the toxæmia of extensive tuberculosis may precipitate spontaneous abortions in the early months. The disease can infect the placenta sometimes. When the placenta is diseased the organisms of tuberculosis can cross the placental barrier and give rise to congenital tuberculosis. However this is extremely rare.

Pulmonary tuberculosis does not have any direct effect on labour; the second stage of labour should be shortened. Over-sedation with morphia may diminish the cough reflex and is best avoided. Experience is necessary both in the choice of the type of anaesthesia (general, spinal or local) and of the reagents to be employed.

An x-ray of the chest is essential to discover the primary lesion in genital tuberculosis. In some cases an active pulmonary lesion may be demonstrated (Figure 4). The principles of good treatment is based first and foremost on the general management of the patient and only next on local gynaecological therapy.

No patient should be submitted to any obstetric or gynaecological operation without adequate evaluation of her chest lesion. This applies to tuberculosis. Equally well it applies to all other diseases. The wisdom of examining the chest as a preoperative precaution is firmly established (Figure 1). To proceed with operation without examining the chest is tantamount to criminal clinical negligence (Figure 1).

Even where an emergency operation is necessary, the findings on chest examination may govern the type of anaesthesia to be given and the quantities of drugs to be administered. Where operation is not urgent, postponement until the chest disease has been cured, if not greatly improved, may be to the patients best advantage and safety.

Two thirds of anaesthetic deaths in obstetrics are due to inhalation of vomit causing gross bronchial spasm and pulmonary oedema or overwhelming bronchial obstruction and pneumonic consolidation. Gastric atonia is common in labour and a large quantity of partially digested food and fluid may be present. The administration of general anaesthesia in these circumstances is hazardous.

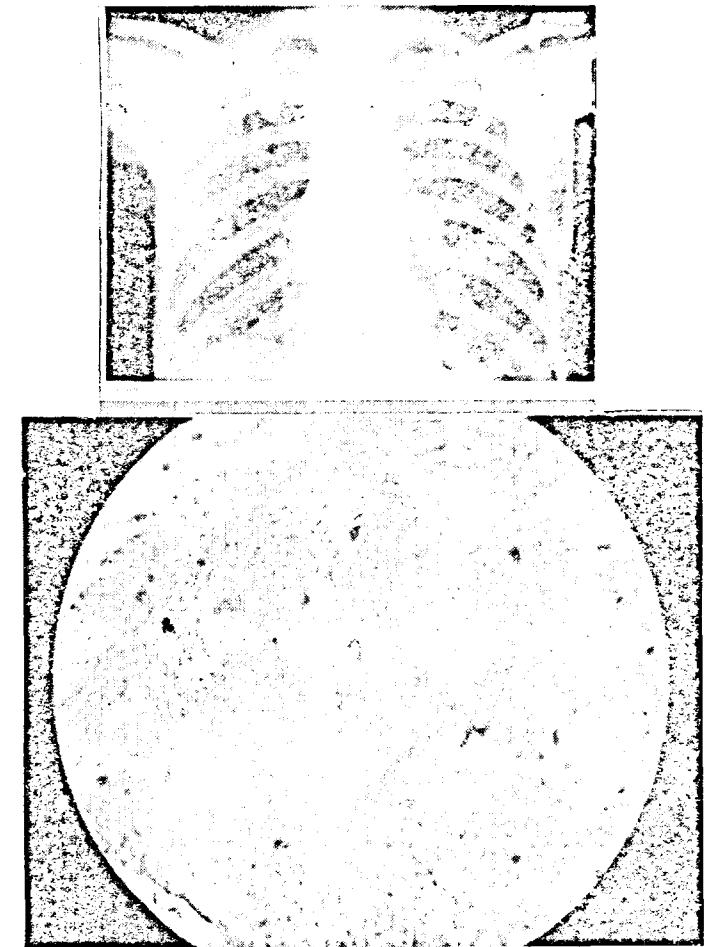


Fig. 4

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

A 47 year old patient was picked up on routine gynaecological examination as having a bulky unhealthy cervix and a palpable mass in the right iliac fossa. The cervix was ulcerated but the necrotic tissue did not bleed readily on touch. A cervical biopsy study showed the condition to be tuberculous cervicitis. A chest x-ray was taken and this showed bilateral pulmonary tuberculosis to be present. When genital tract tuberculosis is suspected a chest x-ray should invariably be taken. Genital tuberculosis is almost always secondary to a tuberculous lesion elsewhere in the body, usually the lung, and one might expect to find a history of pulmonary lesions; but pulmonary lesions are demonstrable only in about one third of patients who have genital tuberculosis (Schæfer 1953).

The aspiration of stomach contents into the lungs is preventable, and the following brief report demonstrates a typical case in which such a disaster could easily have been avoided by skilled anaesthesia.

"A 22 year old patient pregnant for the second time was admitted in labour at full term. Her first

child had been delivered by Cæsarean section 3½ years ago and was alive and well. The indication for abdominal delivery had evidently been an unengaged head. The present labour did not proceed satisfactorily and the head did not engage and during the course of observation the patient developed distension of the bowel and other evidence of prolonged labour. A lower segment Cæsarean section and sterilisation was performed under general anaesthesia. During anaesthesia the patient vomited a large quantity of undigested rice and coffee and inhaled quite a lot of it. In spite of an endo-tracheal tube having been put in brownish fluid was flowing out through the tube. The operation itself was successfully performed and a live female child weighing 5½ lbs. was delivered. The patient had a stormy post-operative course and kept pouring out blood-stained discharge through the nose. Both lungs were full of moist sounds. Respiration was laboured. The pulse became rapid and its volume and tension were very poor. Within 3 hours of operation the patient died and blood-stained thick dark fluid was escaping from the air ways."

In obstetrics the service of a skilled anaesthetist is a necessity.

Bronchial asthma is sometimes better with pregnancy and at other times worse. Asthma may appear for the first time in pregnancy (Figure 2) or the puerperium. Cystic disease of the lung (Figure 2), bronchiectasis and pneumonia may all complicate pregnancy. Another interesting condition is pulmonary complications associated with amebic hepatitis which sometimes complicates pregnancy in tropical countries (Figure 1). Pneumonia has become much less formidable a complication of pregnancy than in the past thanks to powerful antibiotics. If inadequately treated, pneumonia may be responsible for an increase in maternal and foetal mortality. Inadequate oxygenation of the foetal blood and profound toxæmia are two factors which contribute to premature labour and abortion in this disease. Rarely there is transplacental infection of the foetus by pneumococci leading to its death and premature expulsion. Changes in intrathoracic pressure during the second stage of labour may unduly strain maternal respiration. In addition the decrease in intra-abdominal pressure following delivery increases the excursion of the diaphragm. This in turn increases the activity of the lower lobes of the lungs and causes aspiration of inflammatory exudates from

affected portions of the lungs, thereby extending the pneumonia. Another danger is the infection of the puerperal uterus by blood borne pneumococci to lead to a fatal pneumococcal fibrinous peritonitis. The second stage of labour may usefully be cut short by a low forceps under pudendal block anaesthesia in the patient with pneumonia.

Amniotic fluid embolism is a rare but interesting complication in obstetrics. Embolic debris from the amniotic fluid become disseminated and get to the pulmonary arterial circulation and cause occlusion. The anaphylactoid shock associated with this is thought to be responsible for shock.

Air embolism is also a rare complication which can occur during Cæsarean section when the large venous sinuses which are severed are not clamped speedily.

LUNG LESIONS IN DISEASES WHICH ARE PRIMARILY OF GYNÆCOLOGICAL ORIGIN

Pelvic sepsis may go on to a pyæmia and give rise to multiple lung abscesses but this is very rare. A pelvic



Fig. 5

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

Extravasation of dye into the venous system following hysterosalpingography is beautifully demonstrated by this picture. The ovarian veins on either side are clearly outlined. Pulmonary fat embolism is a hazard of oily contrast media and in modern practice water soluble media are favoured.

infection may track up towards the diaphragm and give rise to a subphrenic abscess. Such an abscess can involve the base of the right lung by extension.

An exceedingly rare but interesting lesion of the lung is endometriosis. Lattes et al (1956) report its occurrence in a 34 year old woman who for about 3 years had episodes of hemoptyses associated with the menses. These hemoptyses started following Cæsarean section and an endometrial curettage for menorrhagia, and continued irregularly in spite of various hormonal treatments, until she again became pregnant. At about this time x-ray studies of the chest, which had previously been negative, showed a discrete coin lesion in the right middle lobe. Exploratory thoracotomy followed by segmental resection showed that the pulmonary mass consisted of endometrium with marked decidual reaction of the stroma. It was this decidual reaction which caused the previously present and functioning endometrial implant to enlarge and become detectable roentgenologically. The patient had since been delivered at term by Cæsarean section, and to the date of this writing further hemoptyses had not occurred.

Two gynæcological lesions should be mentioned which usually cause hæmoperitoneum. They are the ruptured ovarian follicle or the chocolate cyst (endometriosis) and tubal abortion or tubal rupture. Other lesions may exist as well. The blood collects beneath the diaphragm and breathing may be painful.

Pulmonary embolism may occur under certain circumstances. Vaginal insufflation with chemicals in the treatment of vaginal discharge especially during pregnancy may cause fatal air embolism. When a patient is being investigated for sterility, tubal insufflation should invariably be carried out using carbon dioxide. Fatal cases of embolism when air has been used for this purpose have been described. Fatal air embolism has followed intrauterine injections in attempts to procure criminal abortion. In late pregnancy certain procedures like amniography are not without danger.

Oil embolism used to complicate the performance of hysterosalpingography with oily media but this danger has been minimised by the introduction of water soluble contrast media (Figure 5).

Pulmonary embolism from a detached clot lodged

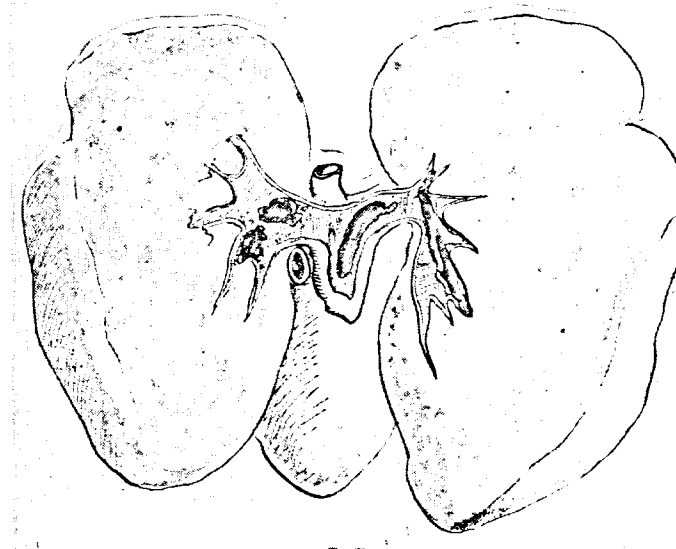


Fig. 6

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

One of the most dangerous and frequent complications of genital disease and operation is pulmonary embolism. It originates from thrombophlebitis or phlebothrombosis of the pelvis or the lower extremities. Massive pulmonary embolism is dramatic in its onset. The patient sits up on the tenth day, asks for a bed pan, suffers from a sudden bout of hæmoptysis and falls back dead. So dramatic is it that we are apt to forget that lesser forms occur which may go unrecognized until some complication results, such as chest-pain, pleurisy, an abscess or a segmental pneumonia.

in the pulmonary artery (Figure 6) is a well-known postoperative complication in surgery. The thrombus may come from veins of the calf muscle or the deep pelvic veins.

Malignancy in any part of the female genital tract can in theory produce lung metastases but such lesions are rare. In carcinoma of the cervix, among the viscera the lungs are one of the commonest sites (Figure 7) for secondary metastasis (Alvarez 1954). The frequency of pulmonary involvement is confirmed by Holzæpfel and Ezell (1955) who found a high incidence of pulmonary involvement in uterine cancer. Involvement of the pleura and lungs was present in 12.5% of treated cases and 23.2% of untreated cases in their autopsy studies. In advanced ovarian malignancy secondary deposits usually manifest themselves as pleural effusions (Figure 8). The fluid is often blood stained and malignant cells may be found when cell cytological studies are made. Sarcoma of the uterus sometimes gives rise to multiple deposits in the lungs. There are however two



Fig. 7

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

In genital cancer as with malignancies anywhere in the body the lungs may be the seat of secondary deposits. In the follow up of patients with genital tract malignancy, either by irradiation, surgery or a combination of both, the lungs should be examined. Secondary deposits in the lungs from cancer of the cervix is not common but may occur as evidenced by the picture above. In pre-operative care in surgery for pelvic cancer the importance of radiological examination of the lung fields to exclude secondary deposits is too self-evident to require emphasis (Scheffey and Lang 1954).

extraordinarily interesting conditions of the genital tract with close pulmonary associations. One is a benign tumour (fibroma) of the ovary which produces a pleural effusion in addition to ascites (Meigs' syndrome). The effusion and ascites disappear when the tumour is removed by operation. The other is the fascinating but sinister lesion—the dreaded chorionepithelioma.

FIBROMA OF THE OVARY

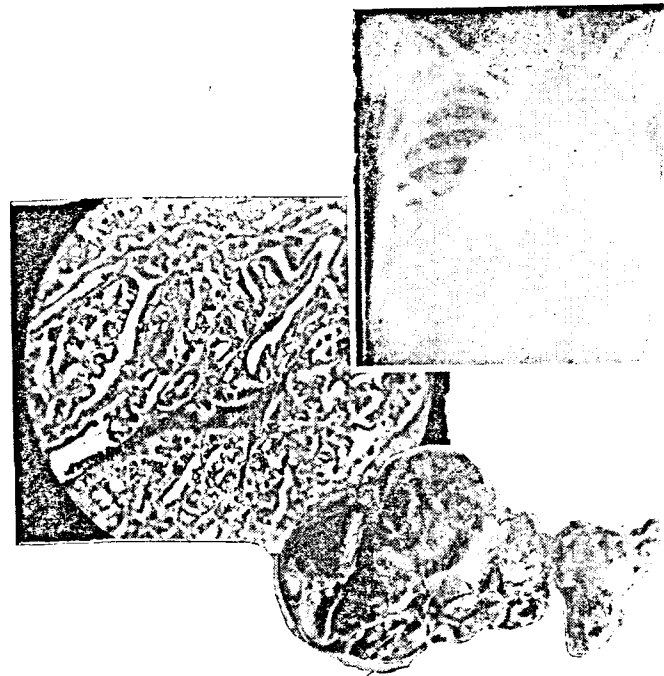
In January 1890, Lawson Tait (who at that time was Professor of Obstetrics and Gynaecology at Queens College, Birmingham, England) encountered at his clinic a 36 year old patient. She complained of

cough and dyspnoea and her abdomen was enlarged. Lawson Tait found on examining her that her abdomen was greatly distended, the superficial veins were enlarged and the umbilicus was everted. There were all the signs of ascitic fluid free in the peritoneal cavity. In addition deep pressure through the fluid revealed the presence of a large rounded solid tumour apparently moored in the pelvis and floating freely in the ascitic fluid. There was fluid present in the left pleural cavity which seemed to be the cause for dyspnoea. To relieve this he aspirated 95 ounces of serum. It was blood stained. A few days later fluid collected in the right pleural cavity and this was similarly aspirated. He made the diagnosis of malignant disease of the peritoneum with secondary involvement of the pleural surfaces. He declined to operate on the abdominal tumour and the patient returned home to die.

Fig. 8

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

In ovarian malignancy the lungs may be the seat of secondaries. Involvement of the respiratory tract by ovarian malignancy usually takes the form of a blood stained pleural effusion. Sometimes cytological study of the fluid obtained by thoracentesis may show malignant cells to be present. An x-ray of the chest should invariably be taken as a preoperative measure before operating for ovarian malignancy. The x-ray above is that of a 25 year old patient who had a malignant ovarian tumour with ascites.



However she returned some weeks later and Lawson Tait aspirated pale yellow fluid from the left pleural cavity. The pleural effusion did not subsequently recur. During the next twelve months the abdomen was tapped of its ascitic fluid more than thirty times and each time about 8-14 quarts of thin clear yellowish fluid was obtained. Except for transitory oedema of her lower extremities her general condition, contrary to all expectations remained satisfactory. The patient's persistent refusal to die was finally rewarded when in March 1891 Lawson Tait performed a laparotomy. He removed a large fibroma of the ovary. The patient was cured and he concluded "I think it is perfectly certain from the result that the disease was not cancerous and an operation has resulted in a cure absolute and I trust, permanent".

Lawson Tait was responsible for advocating exploration of the abdomen in patients with pelvic tumours who had in addition fluid in their abdominal and pleural cavities. He considered that such a combination did not always mean malignant disease.

In 1937 Joe Vincent Meigs and Cass in a paper from the Massachusetts General Hospital revived interest in the subject. They described the association of hydrothorax and ascites with ovarian fibromas (Meigs' syndrome).

If cardiac, renal, or liver disease is absent a pleural effusion and ascites in a patient is usually the result of tuberculosis or carcinomatosis.

Meig's syndrome should however be borne in mind. It is uncommon but when present the patient can be cured. The ovarian tumour is always benign. The amount of fluid in the abdomen and pleural cavities bears no relation to the size of the tumour. The fluid is serous and sterile but in exceptional cases it may be blood stained. Unless infection is introduced in the tapping there is no fever. After thoracentesis the fluid re-accumulates rapidly. When the tumour is removed by operation the fluid both in the abdomen and chest disappears and does not recur. The fluid is found more often in the right pleural cavity than the left. In some cases it is bilateral. The cause for the accumulation of fluid in the chest is thought to be due to some form of trans-diaphragmatic lymphatic transport, but this is quite conjectural (Figure 9).

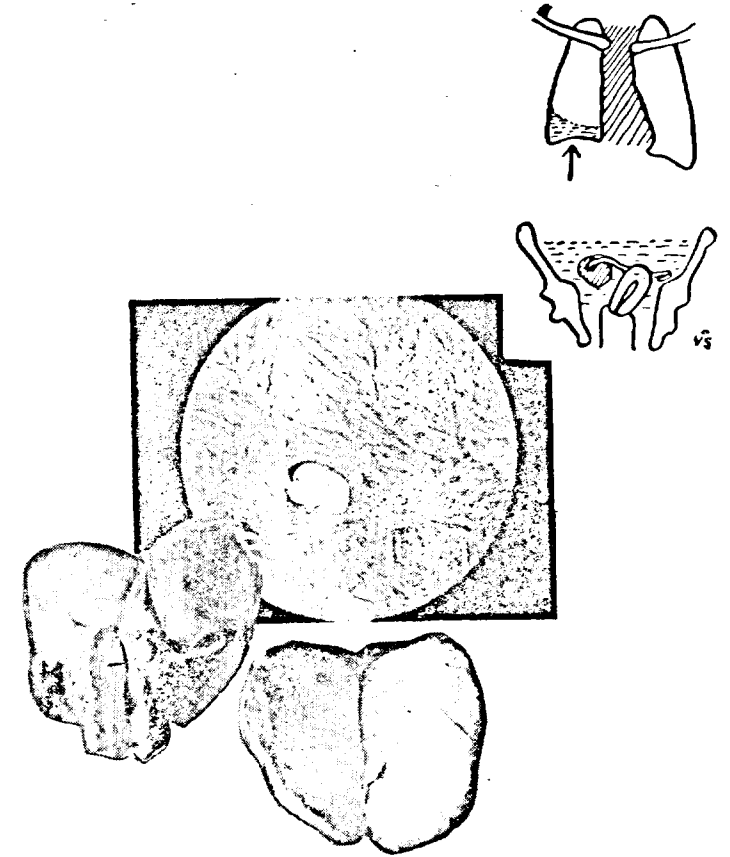


Fig. 9

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

A 38 year old patient presented herself with an irregular hard hypogastric swelling reaching almost to the umbilicus. A clinical diagnosis of fibroid uterus was made and laparotomy undertaken. A solid tumour of the left ovary was found and so a total hysterectomy and bilateral salphingo-oophorectomy was carried out. Subsequent pathological studies showed the tumour to be only a benign fibroma of the ovary. The association of ascites and hydrothorax with benign fibroma of the ovary goes by the name of Demon-Meigs-Cass syndrome. In all solid hard mobile slow-growing tumours of the ovary the chest should be examined for evidence of a pleural effusion.

Certain benign ovarian cysts and sometimes fibroids of the uterus also, are associated with small quantities of serous fluid within the peritoneal cavity. The fluid disappears when the cyst or fibroid is removed. Except in Meig's syndrome fluid in the pleural cavity is never found.

Malignant ovarian tumours produce blood stained fluid in the peritoneal cavity. Pleural effusion when it occurs is often blood stained and indicates the presence of a generalized carcinomatosis with lung involvement (Figure 8).

CHORIONEPITHELIOMA

This is a parasitic tumour which arises from foetal trophoblast (chorionepithelioma). In 50% of cases it follows vesicular degeneration (Hydatidiform mole). Sometimes it follows miscarriage. Pathologists have not yet been able to correlate pathological appearances with the clinical behaviour of these tumours but it would appear that all grades exist ranging from the locally destructive choriadenoma destruens to the terribly malignant moles which metastasize widely and prove rapidly fatal.



Fig. 10

(Courtesy: The Govt. Women and Children's Hospital, Egmore, Madras)
Multiple generalized spherical discrete opacities are seen in chest x-rays when genital chorionepithelioma has metastasized to the lungs. This chest x-ray is of a young patient 19 years of age whose presenting symptoms were hæmoptysis, vaginal bleeding following a normal delivery and symptoms of severe anæmia. It shows massive lung secondaries. A diagnosis of chorionepithelioma was made and after blood transfusions and improvement of the general condition a total hysterectomy and bilateral salpingo-oophorectomy was performed. The cavity of the uterus was filled by a vascular necrotic mass of tumour tissue and the ovaries were the seat of multiple lutein cysts. The diagnosis of chorionepithelioma was confirmed by histopathologic studies. When genital chorionepithelioma is suspected clinically, a chest x-ray must be obtained.

Although a characteristic history which includes intermittent hæmorrhage may be obtained from a patient with this condition, the symptoms and signs produced by metastatic deposits may be the most prominent and presenting feature. The lungs are a favourite site for secondaries which show up on the x-ray as discrete spherical opacities — "cannon ball appearance" (Figure 10). The patient may complain of respiratory symptoms such as cough, hæmoptysis, blood stained sputum, dyspnœa, cyanosis and chest pain. Loss of weight and anæmia may also occur. The primary uterine trouble may be overlooked.

CONCLUSION

This article has been a general survey of the inter-relationship which exists between the female genitalia and the respiratory system. It is by no means comprehensive but it is very important to appreciate that the specialist in Obstetrics and Gynæcology must possess a sound knowledge of general medicine. Specialization is necessary because medical knowledge is too vast for one person to master. To develop efficiency, the field in which one practises must be circumscribed.

Yet to be ignorant of how certain systemic maladies both psychological and somatic manifest themselves by altering the anatomy and disturbing the function of the reproductive organs, is to be an imperfect physician. A good gynæcologist is first and foremost a sound physician and an able surgeon.

If he confines his interest to the pelvis alone and remains ignorant of how disease in this area may spread to involve other parts of the body and even affect the psyche, he is a mere charlatan, a "peddler in the pelvis".

The late John Ryle was one of the most distinguished physicians of Britain. For a time he was Regius Professor of Physic at Cambridge University and before his death he occupied the newly founded Chair of Social Medicine at Oxford. He would urge everyone to try and become "a good naturalist"; and this should be the constant endeavour of all of us.

ACKNOWLEDGMENT

I wish to acknowledge my gratitude to Dr. Mrs. S. Abraham, M. D., Professor of Obstetrics and

Gynæcology, 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.

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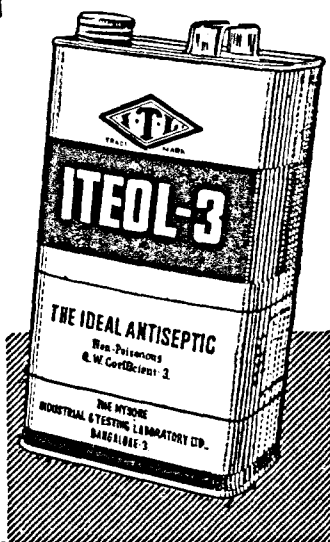
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Antibiotic therapy of bacterial endocarditis: IV. Successful short-term (two weeks) combined penicillin-dihydrostreptomycin therapy in subacute bacterial endocarditis caused by penicillin-sensitive streptococci. Geraci, J. E. and Martin, W. J., *Circulation*, U.S.A., 8 : 494-510, October, 1953; through : *Journal of the American Medical Association*, 153 : 1577, December 26, 1953.

Short-term combined treatment with penicillin and dihydrostreptomycin for two weeks was given to 16 men and 7 women with subacute bacterial endocarditis caused by penicillin-sensitive streptococci. A low-grade fever, malaise, anorexia, tiredness, and weakness characterized the illness of most. The presence of a heart murmur was the clue to the source of the patient's difficulty. Rheumatic heart disease was present in 18 patients, degenerative or "arteriosclerotic" heart disease in 3, and syphilitic heart disease with syphilitic aortic insufficiency in one. In one patient, it was not possible to state whether any pre-existing heart disease was present. Anemia, noted in 15 of the 23 patients, was mild in 12 and moderate in 3. The values for hemoglobin ranged as low as

6.2 gm. per 100 cc. of blood and averaged 10.3 gm. Leukocyte and differential counts were abnormal in only a few patients. Eighteen patients (78%) remained well during follow-up periods of from 3 to 24 months. No therapeutic failures or relapses occurred in the living patients. Five patients (22%) died. Four of the deaths were due to complications of the endocarditis and the underlying heart disease, namely, congestive heart failure and cerebral embolism, while the fifth was due to coronary occlusion with myocardial infarction. One million units of aqueous procaine penicillin G and 1 gm. of dihydrostreptomycin sulfate given intramuscularly every 12 hours for two weeks represent adequate and curative treatment for subacute bacterial endocarditis caused by penicillin-sensitive streptococci.

THE DEAD CAN HELP THE LIVING

BY DR. VLADIMIR DEMIKHOV

Dr. Demikhov is one of the most famous Soviet surgeons who leads the work on transplantation of vital parts of the body at the First Moscow Medical Institute. He has devoted himself for a long time to the problem of transplanting healthy organs to replace badly injured ones.

EVEN temporary connection of a revived heart, lung or other organ from a dead body will be able to save the lives of those whose own organs have been badly damaged.

SUCCESSFUL TRANSPLANTS

A number of human tissues have already been successfully transplanted. Transfusion of blood—"Liquid tissues"—has, for example, saved millions of lives. Thousands of people have had their eyesight restored by the transplantation of cornea by Professor Filatov's method. Transplantation of the skin in cases of large burns is currently practised.

Even when the skin takes root only temporarily, these transplants save the lives of people who would otherwise be doomed. It may incidentally be mentioned that it was a Soviet scientist, Professor Shamov, who first proved that blood could be transfused to living men from corpses.

The first attempt at transplanting a kidney from a corpse to a living man was also made by a Soviet scientist, Professor Voronov. As a result of this daring operation he was able to observe, for a period of seven days, the revival of the transplanted kidney and its functioning.

TEMPORARY HELP

It must be noted that, in many cases, when the patient's condition is dangerous, a vitally important organ can help his recovery, even if it functions only temporarily after transplantation.

But the time is not far off when the transplanted organs will function permanently, not temporarily.

Together with my colleagues of the laboratory of organ transplantation, I have, for many years, experi-

mented on transplantations of the heart, lungs and other organs.

From a surgical and physiological point of view our experiments show the possibility of transplanting any vital organ, even the heart and the brain.

Although the animals operated on lived for a few days or weeks only, and in rare cases over a month, we believe that it is possible to apply the positive results of our experiments in the hospitals or clinics.

Of course, we do not intend to experiment on men or risk human lives. But, even in the first stage we shall be able to save many lives by temporary and safe connection of a revived heart, lung or other organ from outside the patient's body.

Artificial lungs and hearts have been developed of course, and they are undoubtedly of immense value during operations. But natural organs are much more perfect. When natural revived organs are connected with another organism, they are capable of functioning for days and weeks instead of hours.

If a revived heart or lung is connected with the patient's body (externally at first—for safety) and blood from the same organism transfused to the patient, we may expect the organ thus temporarily connected to be able to function for a long time, perhaps permanently.

In that case the organ connected externally can be transplanted internally, into its natural place.

The transplantation of a very great quantity of tissue is accompanied by a phenomenon called "immunological paralysis"—a state in which the organism stops resisting the implantation of a great quantity of tissue or a whole organ.

The Soviet scientist, Zotikov, for instance, has

established that small pieces of skin, transplanted within the limits of different organisms, do not take root, while large pieces of skin transplanted under the same conditions, take root well.

Other Soviet scientists, including myself, have observed that the skin and muscles of whole organisms join well (within the limits of one biological species).

In our experiments with the transplantation of whole organs, when the animals we experimented on lived over ten days after the operation, we observed that the transplanted organ took root and functioned very well.

The complications which prevented the experimental animals from living longer have been studied and can soon be eradicated.

PREMATURE DEATH

At present most people die prematurely from diseases, without reaching natural old age. Transplantation will enable the doctor to reconstruct the patient's whole organism and even postpone the advance of old age, besides saving him from premature death.

Weaker metabolism is a characteristic symptom of approaching old age. Some of the endocrine glands stop functioning, the heart and lungs work more slowly, man gets short of breath, gets easily tired, etc.

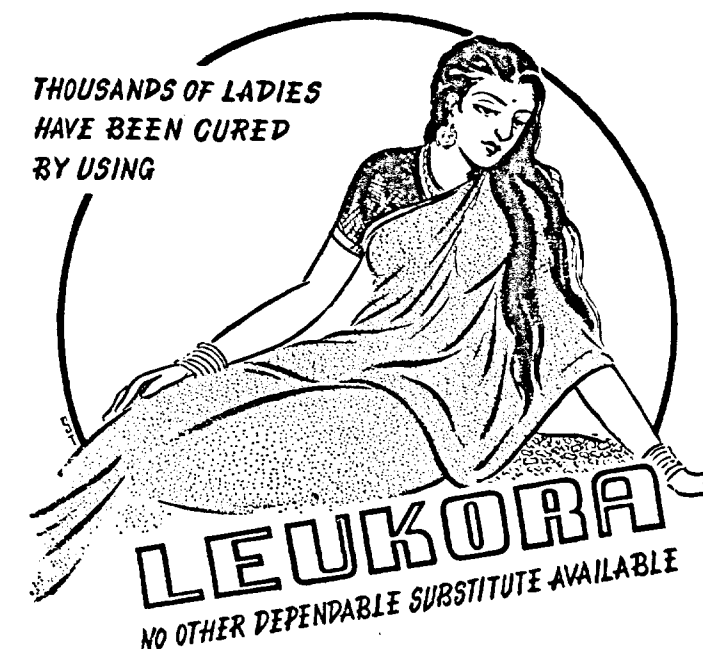
If the endocrine glands, heart and lungs of a young organism be transplanted to an old person, a considerable degree of rejuvenation could safely be predicted.

The Soviet scientist, Andreyev, succeeded in reviving the heart 112 hours after a man's death. But nobody has so far succeeded in reviving the brain more than ten minutes after death.

It is my belief that in the near future, dying men's lives may be saved quicker and more effectively owing to new achievements in medical science.

The important thing is to keep the brain functioning and then replace the irretrievably injured organ with a healthy one.

While trying for the present to make use of healthy organs, taken from men who have died as a result of accidents, scientists are seeking for other sources of organs and tissues for transplantation. But this still requires a great deal of research.



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"LOCAL HORMONES"

BY DR. R. K. SANYAL, M.D.(Pat.), Ph.D. (Lond.)

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DURING the past two or three centuries occasional scientists have toyed with the idea that cellular activity may be controlled or mediated by chemical substances. Chemical substances certainly can alter a number of body responses, but it was not certain as to whether such functions were regulated by chemical mediators. The first conclusive evidence of release of active chemical substances during activity was produced by Læwi (1921) who showed that a substance (Vagus toff) was released in frog's heart during stimulation of vagus which caused a slowing of the heart beat when injected in a second frog. The phenomenon is now so well-known, that it may come as a surprise to many, that the theory was not accepted by a majority of scientists and Læwi had to defend his theory of chemical mediation against overwhelming odds. With the discovery of Minz (1932) that esserinized leech muscle is very sensitive and can quantitatively detect extremely small amounts of acetylcholine, (1 part in 1000 million parts of solution, 10^{-9}) it was conclusively demonstrated that Læwi's vagus toff was identical with acetylcholine. Evidence soon piled up to show that acetylcholine, is also liberated in mammalian heart during stimulation of vagus (Feldberg & Kraye, 1933), at the motor nerve endings (Dale, Feldberg & Vogt, 1936) in the autonomic ganglia (Feldberg & Gaddum, 1934) and in the central nervous system (Bulbring & Burn, 1941). After the breaking of the first hurdles by acetylcholine, it was easy for adrenaline to be recognized as the mediator at sympathetic post-ganglionic nerve endings.

The physiological role attributed to these chemical substances is based on the fact that injection of these substances closely reproduce the effects of physiological stimulation of the organs, and that they are released during such activity. However the action is evanescent, the active substances being quickly disintegrated by enzyme action in the body. Following nerve injury, there is disappearance of such enzymes, and consequently, the tissues become hypersensitive to the action of injected mediators. The role of acetylcholine, adrenaline and nor-adrenaline as mediators in the autonomic nervous system is quite well established. In recent years some

evidence has been produced that in addition to acetylcholine, both adrenaline and noradrenaline may have a role in physiological functions of the brain cells, and a number of diseases and drug actions can be explained on the basis of such an action.

However, the physiological status of histamine, and its young follower, 5-Hydroxytryptamine (5-HT) is not so certain. It has now been conclusively demonstrated that these substances are involved in a number of physiological and physio-pathological processes (Feldberg, 1954; Erspamer, 1954; Page, 1954; Parratt & West, 1957; Sanyal & West, 1958; Mishra & Sanyal, 1958; Sanyal, 1959 a), but their significance cannot yet be firmly stated in clear terms.

The discovery of these mediators has clarified the mechanism of actions of a number of drugs, and it is not an overstatement to say that a considerable portion of modern pharmacology deals with drugs which mimic or antagonize such actions. With the development of ideas about specific cell receptors and structure-action relationship, new vistas have opened up for producing drugs, which will have some predictable action. An example of such an action is the four esters of choline. The chief ester of choline is acetylcholine. The structurally related acetyl-B-methyl choline possesses muscarinic actions of acetylcholine whereas succinylcholine antagonizes acetylcholine action at skeletal motor nerve endings, and benzyl choline has atropine like action.

In addition to those enumerated above, in recent years, a large number of substances have been detected in tissue extracts, which have powerful pharmacologic actions. The simple presence of an active substance in tissue extracts does not of necessity, imply a physiological function. Drastic extraction procedures are capable of converting an inert substance to a pharmacologically active one. However, there is good reason to believe that some of these newly discovered substances may, in years to come, assume important physiological roles.

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'Local Hormones' and are distinct from general hormones which are formed, stored and liberated by the endocrine glands in the blood stream and cause general effects. The term 'Local Hormones' was first employed in 1950 to describe a number of active substances in tissue extracts under discussion, at a symposium of the Royal Society. These substances must at least possess the following characteristics. (i) They are not produced in any specialized organ, the function of which is concerned only with the production of these substances but are constituents of a wide variety of tissues. (ii) They are not secreted in the blood stream in order to be carried to distant organs, but are released in close contact with the tissue cell on which they exert their action.

At least one of the local hormones 'adrenaline' is not only formed in tissue spaces but also is stored in the adrenal medulla, to be discharged in the blood stream in order to produce generalised actions. The distinction between general and local hormones is not absolute but a matter of convenience. The conflicting literature on the definition of local hormones has been reviewed by Feldberg (1955).

Some of these hormones like acetylcholine, adrenaline and noradrenaline have established their roles, whereas histamine and 5-Hydroxytryptamine have definite physiological functions, though their *locus standi* is not as definite.

A number of other substances have also been described in tissue extracts, like bradykinin, substance P, kallikrenin, darms toff, etc., the physiological significance of which have yet to be assessed. It is possible that in future more such substances will be discovered and some of them will be of momentous significance. The functions and the possible physiological significance of these can only be appreciated with a clear knowledge of the methods employed to isolate, identify and study them.

ISOLATION & PURIFICATION

The existence of an active substance in tissue extracts becomes more convincing when the substance can be isolated in pure state and identified chemically. This ideal state is seldom reached in actual practice, as the substances are present in infinite small amounts, rendering chemical identification and synthesis difficult. The active biological substances have been extracted from tissues by water, normal saline,

trichloroacetic acid, acetone, and mixtures of the same substances. When the substances can be extracted by simple procedures, they might be presumed to have been present in the tissue as such. 5-HT is extracted from the tissues by acetone, and is now universally accepted as a tissue constituent; on the other extreme is Ungar's splenin A & B, which though possessing undoubted Pharmacologic properties, require drastic unphysiological procedures for their extraction from the spleen which renders them unlikely candidate as physiological substances (Coburn, Moore, Wood & Roberts, 1955).

Once an activity has been demonstrated in the crude tissue extract, attempts are made to separate the active substance from other physiological substances by chromatography, electrophoresis or counter current distribution. Paper chromatography is the simplest of procedures, require minimal amount of apparatus and can be done in any laboratory; at the same time a properly conducted trial may be of immense value in identification of active substances in tissue extracts. Before proceeding further, it is desirable to eliminate the possibility that the active substance is not identical with any other known substances. This can be done by running spots of extracts and spots of all known substances simultaneously. The known substances are developed and corresponding spots eluted from the test run, and tested for biological activity. If the activity is contained in a spot not corresponding to any known substance, it is likely, though not certain that the substance may be a new one. If the active substance has the same Rf. value as a known substance in several solvent systems, then they are likely to be identical. Thus paper chromatography helps in both identification and separation of active substances.

PHARMACOLOGICAL ACTIONS

Pharmacologic procedures are employed to characterize and distinguish the active substances present in tissue extracts. The activity of the extract may be compared with those of known substances, on several pharmacological preparations—namely the blood pressure of cat or dog, action on various smooth muscles obtained from several species, the muscle nerve preparation etc. The fact that the activity is similar to that of a known compound does not signify identity as such, though the evidence may be considered suggestive. Further corroboration must be obtained, by quantitative methods and use of specific blockade. Parallel assays of the extract against the

known substance may be carried out on two or three preparations. If there is a matching of effects of the unknown and the standard and if similar matching be also noticed by proportionate changes in dose of both, it is very likely that the two substances are the same as this implies the tissue is equisensitive to both the unknown and the standard. There is hardly two substances which may have equal action on one preparation, but when the same answer is also obtained on another alternative biological preparation, there is hardly any room for doubt about the identity of the unknown substance.

Further confirmation is obtained by the use of specific blockade. There are number of antagonist drugs which block the action of one or more biological substances. If the actions of equiactive doses of both the unknown and standard are blocked by the same threshold dose of the antagonist, or reduced to the same extent by some subthreshold dose, and if the recovery of response occurs for both after one exhibition of such subthreshold dose, at the same rate, the substances are identical. In such cases the log-dose response curve of the unknown solution will be parallel to that of the known and both will exhibit same proportionate shift to the right when the curves are redetermined in low subthreshold doses of antagonists. The advantage of this method is that the same pharmacologic preparation may be used both for the assay and blockade test, and considerable amount of time is saved, and further such tests are fairly conclusive (Gaddum, 1955). The mathematical precision of such tests can be further augmented by determination of PAX value for both standard and unknown in several preparations. The PAX value represents the negative log-arithmetic of the concentration of the antagonist, in presence of which the effect of the agonist is reduced x times (Schild, 1949a). Identical values in several preparations will be obtained for both substances, only if they are identical. This again is a time consuming method.

It is an established fact that a biological substance administered at a high dose level blocks the action of the same drug in lower dose levels, as was demonstrated for histamine by Schild (1949b) and this is another principle which may be followed by research workers in identifying biological substances.

There are certain substances which exhibit tachyphylaxis on certain preparations, and even this property may be used in identifying unknown extracts. We

have employed this method for identification of 5-Hydroxytryptamine. This substance exhibits tachyphylaxis in an anaestrous rat uterus, and it was found that equiactive doses of standard and unknown when given alternatively produced a regularly diminishing response (Sanyal, 1958; unpublished data).

When it has been found that the unknown substance does not correspond to any one of the known substances in its properties, chemical, chromatographic and pharmacologic, it may be presumed to be a new one.

Using such yardsticks, the author was able to identify a new smooth muscle stimulating factor in mammalian intestines, extracted with 80% acetone (Sanyal, 1959).

A thorough knowledge of the pharmacological action of various biological substances thus becomes essential for identification of tissue extracts and some attempt has been made in the table to bring out the salient pharmacologic actions which may be of value in diagnosis.

The identification of these substances in biological fluids is not a matter of academic interest only. In a number of diseased states the blood level or excretion of one of the substances may be affected and may give diagnostic clues. The diagnostic value of such tests in pheochromocytoma or argentaffinoma may be cited as example. Such tests carried out off hand and without proper tests for identification of the active substance may easily lead to errors.

It has been mentioned before that mediators like acetylcholine, adrenaline, noradrenaline, histamine and even 5-hydroxytryptamine have now got general recognition. The others are not so well-known. It is likely that some of these may be found to be of importance in future and as such a brief description follows of some of the more promising of local hormones.

Substance P: Alcoholic extract of intestine and brain tissue were shown to contain an active substance contracting rabbit intestine, the action being atropine resistant, and not like any one of the known autopharmacologic substances (Euler & Gaddum, 1931; Gaddum & Schild, 1934). The methods of preparation of this substance and its assay has been described by Pernow (1953, 1955). The pharmacologic actions

TABLE 1

A summary of important actions of some local hormones. (†) indicates contraction

Local Hormones	Pharmacological Actions					Specific Antagonism	Activity after incubation with Chymotrypsin	Possible Physiological functions.
	Cat B. P.	Guinea pig Ileum	Rat Uterus	Rat Colon	Misc.			
Acetylcholine	fall	††	††	††	Active on leech muscle	Atropine 10 ⁻⁷	—	Transmitter at A. N. S. & C. N. S.
Histamine	fall	††	0	0	×	Mepyramine 10 ⁻⁷	Not affected	Involved in injury & allergy. Gastric Secretagogue
Adrenaline	rise	0	0	0	×	—	—	Transmitter in A. N. S.
5-HT	rise	†	††	††	—	BoL-148 10 ⁻⁷	Not affected	Involved in peristalsis & renal haemodynamics.
Bradykinin	fall	†	†	0	No action on hen caecum	—	Destroyed	Involved in inflam. & anaphylaxis
Substance-P	fall	†	†	††	Contracts hen caecum	—	Destroyed.	Activity in C.N.S. ().
Otin	—	†	0	†	—	—	Not affected	Indefinite
Irin	—	†	0	†	—	—	Not affected	Indefinite
Darmstoff	fall	†	†	†	Contracts frog rectum	—	Not affected	Involved in peristalsis
Kallikrenin	fall	0	0	0	—	—	Destroyed	Indefinite

of this substance is shown in the table. The distribution of this substance in tissues has been studied by Douglas, Feldberg, Paton & Schachter (1951), who found the substance to be present both in stomach and intestine. Substance P has also been detected in the brain, and the substances from both the sources are chemically and pharmacologically identical (Eliason, Lie & Pernow, 1956). It is too early to ascribe a physiological function, but it has been seen that the substances profoundly affect the activity of the central nervous system (Euler & Pernow, 1956).

Bradykinin : Like the previous substance, bradykinin is also a polypeptide and is released from the globulin fraction of the plasma by the action of proteolytic enzymes such as trypsin or certain snake venoms. Trypsin causes a release of bradykinin, but does not destroy it, while chymotrypsin fails to release it and destroys its activity. The pharmacological actions have been described by Rocha e Silva (1955) and Pernow & Rocha e Silva (1955). It has been postulated that bradykinin might be set free during inflammation or anaphylaxis and produce dilatation and

increase in capillary permeability (Rocha e Silva—loc. cit.).

Darmstoff : Darmstoff has been found in the intestinal tissues of all the species investigated. Unlike the previous substances darmstoff consists of several acidic phospholipids. The pharmacological properties and its chemical nature have been studied by Vogt (1955, 1957). It has been suggested that darmstoff may be responsible for physiological motor activity of the intestinal tract.

Apart from the above three, a number of such other substances have been described viz. kallikrenin, & Kallidin (Werle, 1955), Irin (Ambache, 1957), etc., but the knowledge concerning these substances is too fragmentary and their physiological role very doubtful.

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The mode of Action and Theory of Chlorpromazin Therapy

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CHLORPROMAZIN (N-[3'-dimethylamino-propyl]-3-chlorphenothiazin hydrochloride) was synthesized by P. Charpentier in 1950. Pharmacodynamic studies showed that the preparation had a broad-spectrum sedative effect (sympatholytic, vagolytic, sedative action and potentiation of action by nervous depressants) unattained by any of the previously known drugs. In 1952, the drug became available commercially under the name of Largactil and, it is now used extensively in every branch of clinical medicine. Since the first report on its use in psychiatry appeared (Delay, Deniker and Harl, June, 1952) it has come to be generally employed, and to-day it forms an almost indispensable part of therapy for psychiatric conditions. This will be easily understood, as each of the so-called active therapeutic methods in use since 1933 has numerous disadvantages or even serious hazards and, in addition, they have by no means been proved to be specific procedures likely to alter the final outcome of psychoses. It is therefore unquestionable that in the therapy of mental disease the advent of chlorpromazin represents an achievement at least as important as the introduction of the somatic methods. Apart from its high therapeutic value, chlorpromazin is of immeasurable theoretical significance; notably it has provided a possibility to employ purposeful, judicious pharmacological treatment which is not merely symptomatic and sedative, but also apt to alter the dynamism of symptoms.

The synthesis and therapeutic success of chlorpromazin started extensive psychopharmacological research. One of the trends in that work is to make planned modifications in the chlorpromazin molecule, in order to eliminate untoward side effects and to enhance favourable action on the symptoms of psychosis; the other is aimed at an exact determination of the cerebral sites of action of the various preparations and thereby to produce drugs whose activity is aimed at certain psychotic symptoms or syndromes, i. e. which are capable of stimulating or of inhibiting selectively and separately the activities of the various cortical spheres integrating complex psychic functions.

This clear-cut formulation of the problems involved

has been made possible by the fundamentally new angles of approach to the dynamics of cerebral function during the past twenty years. The facts disclosed by modern physiological research indicate that psychic functions are controlled and integrated in the reticular formation of the brain stem, whose part extending from the median thalamic centre to the mesencephalic tectum has been called by Penfield the centrencephalic system. This area is the starting point of various trunco-cortical dynamic spheres, whose charge to weaker or stronger potential, "tuning", connects the single factors of the starting position that furnish the basis of actual psychic activity, while the interaction of the single dynamic spheres determines the basic psychic state (wakefulness, sleep, grade of consciousness, emotion, drive, ego-relations, etc.). *It seems plausible to seek the basis of Pavlovian basic personality types and of endogenous reaction types in the relative stability and potential of the single trunco-cortical spheres, and it may be assumed that the essence of the schizophrenic pathological process is a congenital weakness and progressive degeneration of certain members of this system.* Studies by exact physiological methods on the action of various psychotropic drugs have shown that it is through this very reticular system that these drugs exert their specific activity, as opposed to the aliphatic depressors which act primarily on the cerebral cortex. *These facts will have to be considered in the future whenever we are faced with current diagnostic and therapeutic problems, and when we have to work out a therapeutic schedule, it must be done with due regard to the various pathological factors making up the clinical picture.*

During the past seven years, relatively exact evidence has been accumulating concerning the mode and site of action of chlorpromazin, well-known also in Hungarian psychiatric literature (Kardos and Pertorini, Boszormenyi, Gimes and Orthmayr, Magyar, as well as Angyal and Pertorini). On the basis of data in the literature and our own four years' experience, the essential features of the effect may be outlined as follows.

Courvoisier, and also Laborit and Delay believe

the activity of chlorpromazin to be essentially inhibitory, aimed at the peripheral synapses and at the diencephalic autonomic centres. At the same time the drug acts as a sympatholytic and vagolytic, but this lytic-depressor action is, strangely enough, only incomplete on either part of the autonomic system. Nevertheless, it has to be emphasized that the depressor-paralysing action on the sympathetic dominates the picture. Vegetative (autonomic) organs are under the dual influence of the sympathetic and parasympathetic nervous systems which, however, do not act against each other, but in many respects supplement each other's action. The organism, strained by the energy-mobilizing activity of the sympathetic nervous system is restrained, protected by the economizing forces of the parasympathetic. Thus in the background of apparently conflicting activities we may recognize a constructive trend, from which the functional optimum results. According to Binswanger, an essential feature of man is the experience of duality of instinct or drive, calling for control. If the antinomy of instincts and drives is too unexpected or sudden, the controlling instance of understanding (intellect) falls out and anxiety results. The reflex defensive response to this is inhibition and suppression which in the presence of a special constitutional susceptibility leads to a discontinuous mode of experience, a constant readiness to anxiety and to the experience of anxiety. The next step is autism, in which vital problems are overcome or experienced outside the sphere of reality, in the form of pathological phantasies. Each experience has its own correlate or synchronism in the cortex and diencephalon, as well as in other parts of the body (Schultz-Hencke). The experience striving for a change, with its correlates of synchronism, becomes manifest through the cortex and hypothalamus. *This complicated and continuously varying act, manifested in activity, speaking or thinking, according to the present view is under the control of the centrencephalon which acts through the harmonic interaction of its own trunco-cortical circuit systems.* An unexpected, intense, or lasting antinomy of instincts or drives may lead to disturbances in this regulation by disconnecting constitutionally weaker or less resistant and progressively weakening trunco-cortical circuit groups; this disorder in regulation gives rise subjectively to anxiety in the first place, and clinically to functional psychosis, exogenous reaction type or to endogenous psychotic episode, with the colourful symptomatology of mental diseases, and dissociation of the cortical, diencephalic and somatic correlates

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of synchronism belonging to the sphere of experiences and actions. In hyperacute cases the picture may reach the intensity of Cannon's alarm reaction and exhaustion may seriously endanger life (e. g. acute catatonia). *Chlorpromazin acts primarily on this centrencephalic control system; the essence of this primary action is the synaptic blocking of noxious, overstraining sympathetic and parasympathetic impulses, as well as the mobilization of the economizing, protective instances of the parasympathetic.* Thus chlorpromazin acts at a higher level of autonomic innervation which coordinates the cortical, diencephalic, and somatic correlates of synchronism of the act in progress according to physiological requirements. Only this angle of approach permits one to explain the complex response to chlorpromazin and to understand the various autonomic, somatic, and psychic effects well-known from the literature, such as partial adreno- and vagolytic action, hypothermia, diminution of muscle tone, hypotension, decrease in the O₂ demand of brain tissue (Siemons, Ganshirt), depression of general cell metabolism (Decourt), diminution of psychomotor drives, relief of emotional tension and anxiety, relaxation, indifference, withdrawal of psychotic contents from the "Ego" (only to mention the most outstanding features of the effect) *making up a uniform pharmacodynamic entity.* The EEG results obtained with chlorpromazin (Steinmann, Terzian, Heimann and Witt, Hiebel, Hippius, Shagass, Turner and Berard, Longo, v. Berger and Bovel), and even the results of the experiments with chlorpromazin labelled ³⁵S (Wase, Christensen and Polly) will be found to fit into this pattern. It should be borne in mind, of course, that the reticular formation is not a well-defined, uniform system either anatomically or physiologically, as stressed by Russel Brain. Moreover, Magoun has stated quite recently that the characteristic arousal reaction of EEG can be elicited by electrical stimulation not only of the reticular formation and tegmentum of the lower brain stem, but by that of the subthalamus, dorsal hypothalamus and ventromedial thalamic area as well. The activator reticular system of the brain stem has been pointed out as the principal site of chlorpromazin action by Lehmann, Hiebel, Bonvallet and Dell, and more recently by Whitelock, Kleh, Ehrmantraut and Fazekas, and they saw the essence of the effect in a selective inhibition of activation.

On the basis of these considerations it is easy to understand that *benefit from the use of chlorpromazin may be expected mainly when emotional or psychomotor*

excitation plays a decisive, or at least dominant, part in the development of the clinical picture, and why poor response is elicited in simple stupor, in cases of affectively burnt-out simplex or hebephrenic conditions, in chronic catatonic and paranoid pictures characterized by rigid motor and speech stereotypies, bizarreries, and long-fixed delusions, furthermore in depressions characterized by vital inhibitions.

★

Chlorpromazin has been employed at our department for several years and reports have been published on the favourable results obtained.

Plegomazin* has been used recently in 74 cases: The patients were naturally selected according to certain criteria, shaped by the experience gained with chlorpromazin during the past four years. In addition to patients suffering from psychoses of the exogenous reaction type, we gave Plegomazin also to patients with schizophrenia in whose condition affective tension, psychomotor excitation, or acute disintegration dominated the picture. Emotionally burnt-out, oligosymptomatic chronic cases of simple and catatonic hebephrenia, showing severe disturbances of personality and thinking, furthermore the chronic paranoid cases showing complete rigidity and fixed delusions were ruled out in the same way as we excluded from study the patients suffering from vital depression without anxiety. On the other hand, we employed Plegomazin therapy in several cases of defect paranoid mental disease developed in one or two decades and belonging to the various types described by Kleist and Leonhard, if a relative intactness of personality suggested that improvement may result. The well-known contraindications to the use of chlorpromazin were observed, i. e. we did not treat patients with severe liver or kidney disease, heart failure, or with infection, whether acute or chronic. During the course of Plegomazin, body temperature, the pulse-rate, and blood pressure were checked regularly. Tests for liver function and blood counts were done every week.

The diagnoses and the results are presented in two tables. With a view to the fact that in assessing the results of therapy in schizophrenia it is essential to know the data concerning the form, duration, and

*The oral and parenteral chlorpromazin preparation Plegomazin was made available to us through the courtesy of the Research Department in the United Works of Pharmaceutical and Dietetic Products, Budapest, for which we gladly express our thanks here.

type of the course of the disease, I endeavoured to include detailed evidence in table I which lists the 54 cases of schizophrenia. The cases treated with Plegomazin alone are separated from those in which Plegomazin was combined with electroshock therapy, and finally special care was devoted to show the grade of improvement as exactly as possible. All these details have undoubtedly made the table rather complicated, but they will disclose many essential data on the patient material and the results obtained, and may even facilitate the drawing of more general conclusions.

The most conspicuous feature in the table is the excellent response of acute and subchronic paranoid cases to treatment. The same applies to the paranoid cases where frequent acute episodes were separated by symptom-free intervals lasting months or even years. It is remarkable that in these cases psychosis became manifest over and over again with the same clinical symptoms and pathological experiences: anxiety, ideas of reference, dreamy state, hallucinations, and often the recurrence of earlier delusions. A total of 29 patients were in the three groups mentioned: of these, 12 recovered (A), or showed good

TABLE I — SCHIZOPHRENIAS

Diagnosis	Acute					Subchronic					Chronic					Chronic inter-mittent cases					Chronic defect cases					Total
	process																									
	0—6 months					7—24 months					2—10 years					2—25 years					over 10 years					
	A	B	C	D	E	A	B	C	D	E	A	B	C	D	E	A	B	C	D	E	A	B	C	D	E	
<i>1st category</i>																										
Paranoid schizophrenia	2	1				1		1				1	1	1	2	6	2				4	1	2			25
Catatonic schizophrenia																								1		1
Hebephrenic schizophrenia													1													1
<i>2nd category</i>																										
Paranoid schizophrenia	5					5						1			6						2	2				21
Catatonic schizophrenia	1					1									1*											3
Hebephrenic schizophrenia										1			1		1											3
Total																										
54																										

EXPLANATION

- 1st category. Cases treated with Plegomazin alone.

2nd category. Cases treated with a combination of Plegomazin and ES.

A. Symptom-free clinical recovery.

B. Good improvement, work resumed in former job, few residual symptoms.
- C. Social recovery with residual symptoms; unable to work but dischargeable.

D. Improvement in the institute.

E. Unchanged.

*Periodic catatonia.

improvement (B) in response to Plegomazin. In 16 cases Plegomazin had to be combined with ES treatment in order to achieve symptom-free clinical recovery. We had very few cases of catatonia and hebephrenia, as the therapeutic schedule was planned in every case with due regard to the structure and dynamics of the clinical picture and we strove to obtain rapid success. Thus therapy with Plegomazin is no longer in its experimental stage, on the contrary, we have already worked out clearly outlined therapeutic schedules for its use also as regards the single subgroups within the Kræpelinian forms. For example, in the cases of pure stupor characterized by a deficiency or lack of drive and by passive negativism, we do not expect benefit from chlorpromazin and therefore do not give it; in acute catatonic excitation ES will usually act more rapidly and reliably, whereas chlorpromazin and/or IC treatment play a prominent role only in the stabilization of the results obtained. The considerations outlined above determine at the same time whether in a given case Plegomazin should be employed alone or in combination with ES. As a result, we now have or resort to ES in a relatively small number of cases owing to failure of chlorpromazin, because most of such cases are treated by the combined method from the beginning. For example, if possible we give a combination of ES and Plegomazin in hyperacute cases associated with severe vegetative symptoms; three or four days later treatment is continued with large doses of Plegomazin alone. In rigid, but affectively lightly charged and consequently aggressive, destructive behaviour due to delusions in paranoid conditions, treatment is begun with massed ES series (with due regard, of course, to the reactions of the body as a whole). In such cases twelve to twenty ES treatments may be carried out in eight to twelve days, if the patient shows good tolerance. This is followed by massive Plegomazin treatment, first by injection then orally; of course, this schedule is not rigid and has to be often revised in the course of treatment, when the need arises. I have so far presented only two examples to illustrate the treatment of two clinical types; as a matter of fact, the therapeutic schedule has many variations and many fine detail-features which, however, cannot be dealt with here. In the following I shall give the summary of a few characteristic case histories.

CASE 1.—Mrs. Sz. F., aged 48, treated from August 23 till September 12, 1958. Two brothers alcoholics. She had been irritable, sensitive for

three or four years. About ten days before admission she became depressed, lachrymose, frightened of people, and had feelings of insecurity and guilt. On admission she was in an extreme state of anxiety, incapable of contact, and showed the picture of acute disintegration. Complete incoherence developed within a few hours. The administration of Plegomazin was begun without delay: she was given three times 50 mg. daily for three days, and three times 75 mg. daily for the next three days, by the intramuscular route. Owing to painful infiltrations, the course was continued orally. She was given three times 150 mg. daily for five days, three times 125 mg. for further four days, then three times 100 mg. daily for two days and three times 75 mg. for three days. Thereafter the course was continued with daily doses of three times 50 mg. The duration of the course was 21 days. Shortly after onset of treatment she developed a marked chlorpromazin syndrome: blood-pressure dropped from 145/80 to 85/65, the pulse-rate increased from 90 to 108 per minute, her face was pale, mimics was poor and she was somnolent. She became more and more quiet and after ten days she could be transferred to the quiet ward. A few days later she told us about a marital conflict that had caused long-lasting emotional tension and to which she ascribed her illness. She sought to explain her condition on reasonable grounds. After 21 days of treatment she was discharged completely cured, and was instructed to take three times 50 mg. of Plegomazin daily over a long period of time. Diagnosis: acute involutional schizophrenia.

CASE 2.—Mrs. K. B., aged 55. Duration of treatment: October 31 to December 23, 1958. Her daughter committed suicide at the age of 16. She had always been nervous and hypersensitive. She had been treated at a department for neurotics for two months and was then transferred to our department in 1953. On admission she was in an extatic mood, her face was flushed, she kept bowing as in prayer, exclaiming "Jesus of Nazareth, have mercy on us! I am a queen, I am Queen Elizabeth!" She was anticipating the proclamation of the Last Judgement, filled with fear, seeing ghosts in the corner, talking to her dead daughter. In response to ES treatment she had been free of

symptoms for five years and had been working normally, but in the summer of 1958 she had a recurrence with the same symptoms. This time the 5 ES treatments resulted in short improvement only; she was discharged, but had to be re-admitted a few weeks later because of the same symptoms. Plegomazin therapy was instituted; she was given three times 100 mg. daily intramuscularly for twelve days, then three times 200 mg. daily by mouth. By the end of the first week she had made excellent progress, yet the course was continued according to schedule. She was discharged completely cured, free of symptoms and complaints, and returned to work. Diagnosis: Chronic paranoid schizophrenia, with recurrent attacks.

The above two cases illustrate the course and effect of exclusive Plegomazin therapy. Let us now see examples of what combined ES and Plegomazin treatment can achieve.

CASE 3.—Mrs. Sch. A., aged 43, was under treatment from September 6 till September 16, 1958. Her brother a degenerate, stuttering, matrimonial swindler, is a morally debile person. The patient had been treated at our department in 1951, then in 1954 for hyperacute paranoid hallucinatory attacks, with extreme agitation, severe vegetative symptoms, and moderate disturbance of consciousness. Prior to the present admission she had developed carcinophobia in connection with the death of a friend, with anxiety and fear of dying. Then suddenly the psychotic picture turned into tenebrosity, with fragments of persecutory ideas and illusionistic misconception of events and persons in her environment. Because of the hyperacute condition, combined ES and Plegomazin treatment was begun. The dose of Plegomazin was raised to three times 100 mg. a day intramuscularly already on the fourth day. In four days she was given ten ES treatments. On the tenth day the daily 100 mg. Plegomazin injection was replaced by three times 200 mg. orally. The patient was practically symptom-free 24 hours after admission. On the eleventh day after admission she was discharged recovered, with precise instructions how she should take and reduce the dose of the drug at home.

Diagnosis. Paranoid-hallucinatory schizoph-

renia, with a course of episodes; third recurrence.

CASE 4.—Mrs. K. I., aged 42, treated from June 7 to October 17, 1958. Duration of illness about twelve years; she had been treated at closed wards seven times. Repeatedly employed various kinds of active therapy resulted merely in short episodes of social recovery. The principal symptoms were negativism, autism, visual hallucinations, primary ideas of reference, magic thinking, sexual delusions, ego-disturbances, regression of concepts. During the past few years bizarre bodily sensations developed: she had said that her internal organs were turned around, her abdomen was maltreated, her sight was being stolen; she heard voices from her sexual organs. In her speech schizophrenic elements, neologism, condensations were observable. On admission she was excited, aggressive; after 18 ES treatments she was still excited and aggressive, disoriented. On the 28th of July Plegomazin injections were started with three times 50 mg. daily. On the 6th of August she showed a marked chlorpromazin syndrome; she was somnolent, but could be aroused easily; she gave adequate replies to questions, did not mention her delusions, was quiet, calm, and friendly. Treatment was continued with three times 125 mg. daily by mouth. On the 13th of August, she continued to be calm, friendly, oriented; the dose was reduced first to three times 100, then, on the 21st of August to three times 50 mg. a day. She was discharged on the 17th of October, greatly improved, partially free from psychotic symptoms. She was instructed to take three times 50 mg. of Plegomazin daily for a long period of time.

Diagnosis: Chronic paranoid schizophrenia developing into a defect state, toward chronic somatopsychosis.

TABLE II—OTHER CASES

Diagnosis	A	B	C	Total	Average duration of treatment
1ST CATEGORY					
Reactive depression	7	2		9	18.1 days
Hysteric tenebrosity	3			3	10.3 days

Table II— (Continued)

Diagnosis	A	B	C	Total	Average duration of treatment
Epileptic tenebrosity	3			3	19.3 days
Porionic tenebrosity	1			1	
Subarachnoid hæmorrhage, disturbance of consciousness	1			1	18 days
2ND CATEGORY					
Epileptic psychosis, 6th admission			1	1	
Psychopathic hysteria					
Tenebrosity			1	1	
Reactive depression			1	1	
Total				20	

Explanation, see in Table I.

The above described four cases illustrate clearly the therapeutic schedule, which is planned individually with due regard to the dynamics of the clinical condition. As to the table, I should like to point out that the paranoid cases proceeding in episodes had to be isolated. In some of these cases the onset of disease dates back to two or three decades, yet they cannot be ranged with the group of defect paranoid conditions, as the single episodes passed away practically without leaving behind any defects and, which is even more important, the progression characteristic of process schizophrenia is absent. Such cases undoubtedly merit more detailed study in larger material, which would be likely to elucidate also their relation to schizophrenia.

Table II shows the diagnoses and therapeutic results of the remaining 20 cases.

As it can be seen, the results of Plegomazin therapy were excellent in these cases and combination with ES was necessary in three inveterate cases only. Of these, one was a case of recurrent epileptic psychosis with extremely severe changes in character, the other two

patients suffered from severe hysteric characteropathy, with diminished intellect, extreme liability of emotional and instinctive life, tenebrosity or hypochondriac-depressive states accompanied by symptoms of grave excitation which repeatedly developed in response to conflicts. In such cases treatment can, of course, relieve only the acute psychotic syndrome, but the difficult, conflicting life situation and the tendency to pathological reactions due to the morbid frame remain unchanged.

Plegomazin alone was employed when the predominance of exogenous factors in the genesis of the syndrome was obvious besides the pathological responsiveness and when the psychotic reactions were not yet fixed. In almost all of these cases the response to Plegomazin was excellent and rapid. The average duration of treatment does not imply the time required for achieving freedom from symptoms, because this usually resulted within one to four days, but includes also the duration of pharmacological stabilization and psychotherapy; the latter was extended in every case also to the personal conflicts and difficulties of the patient. In the following two case histories are presented.

CASE 5.—Miss Sz. B., aged 18 years. Duration of treatment: August 26 to September 16, 1958. Familial history non-contributory. Her mother died when she was one year old and she was brought up under difficult conditions. She had been treated at "functional" wards twice before, for tenebrosity and nervous breakdown. Prior to her present admission, she was forced to leave the room she was living in; her suitor had promised her a wedding ring for her birth day. When she did not get it, she became excited, then disoriented. On admission, she was tearful, tenebrosity, disoriented, and showed anxiety. Plegomazin, three times 50 mg. a day by injection, was started. In 24 hours she became absolutely quiet, stopped crying, was oriented, and could be transferred to the quiet ward. After three days injection treatment was replaced by tablets. She was discharged recovered after 21 days of treatment. She gained 3 kg. during treatment.

Diagnosis: functional tenebrosity.

CASE 6.—Mrs. B. L., aged 48. Duration of treatment: September 1 to September 12, 1958. Familial history non-contributory. She has been

epileptic since the age of 34. A few days before admission she had discontinued taking Diphedan. As a result massed epileptic attacks and disturbance of consciousness developed. On admission, tenebrosity, anxiety, fear, loud shrieking and disorientation were noted. Neurologically, no abnormality was found. EEG showed dysrhythmic electrical cortical activity. Analysis showed a focus near to the midline, deep in the left temporal lobe, with slow activity and bursts. Parenteral administration of Plegomazin (daily three times 50 mg.) was started. Seven days later treatment was continued with three times 50 mg. by mouth. Since the onset of treatment she had no epileptic seizures and she became completely oriented in three days. Then treatment was supplemented by the administration of Diphedan and Sevalal. She was discharged 11 days after admission, completely recovered.

Diagnosis: Epileptic tenebrosity.

★

The chlorpromazin syndrome, the side effects and complications caused by the drug are fairly well known; nevertheless, it is justified to ask how the Hungarian preparation, Plegomazin, compares in this respect with chlorpromazin of foreign make. In the following I shall try to answer this question, illustrating, at the same time the course of treatment.

In milder cases treatment is begun with three times 25 mg. a day intramuscularly. When the patient is extremely excited or shows psychomotor agitation, we give another 25 mg. dose an hour after the first, then treatment is continued with three times 50 mg. daily by the parenteral route. It seems that the 2 ml. ampoule (50 mg.) does not irritate tissues any more than the 5 ml. (25 mg.) ampoule and can be injected with reasonable safety deeply into the gluteal muscle. If so required, the dose may be increased to three times 75, three times 100, or even three times 150 mg. a day in three to five days. Of course, due attention should be devoted to the clinical picture and to the reactions of the patient. If complications (allergic dermatitis, jaundice, hæmatological changes) do not occur, the dose is increased until the characteristic chlorpromazin syndrome develops, which is essential for achieving therapeutic effect. The syndrome caused by Plegomazin does

not differ any way from that caused by foreign chlorpromazin preparations.

The vegetative changes include marked tachycardia, with a tendency to orthostatic collapse, a 20 to 40 mm. Hg drop in systolic blood pressure, a slight decrease in body temperature after transient subfebrility dryness of lips and mouth, weakness of accommodation; the face is greyish-pale, lightly swollen; mimic is poor. Appetite markedly improves and the patients usually gain weight by the end of the course.

The psychical effects are somnolence, from which the patient can be easily aroused, relief of anxiety and excitation, clearing-up of consciousness, withdrawal of pathological contents from the Ego, increased capacity for contact.

Parenteral administration is gradually discontinued after six to twelve days and medication is carried on with the double dose orally. By that time the vegetative symptoms are usually beginning to subside. It is emphasized that *psychotherapy should be started as early as possible, not only in functional, but also in schizophrenic conditions*, because most of the patients are in such a state that adequate approach and reasoning will lead to their recognition of the irreality of their distanced illusions, delusions, and pathological experiences having lost their affective content; thus they will come to see the above as symptoms of a disease and be inclined to subject them to criticism, to correct or reject. The variations in the course and duration of treatment have been described in connection with the case histories. It is of paramount importance not to discontinue treatment too early. There is no absolute rule as to how long treatment should last. In general, hospital treatment lasts ten to twenty days in neurotic cases and four to six weeks in schizophrenia. We always instruct discharged schizophrenics to continue taking the drug at home, three times 50 mg. daily for six weeks, then maintenance doses of 25, 25, 50 mg. daily for the next six weeks. If possible, the patients are to report several times for control examination during the period.

As shown by experience, complications and risks are slight.

The parkinsonoid syndrome, which often deve-

lops during treatment, is rarely severe. In such cases Artane will markedly relieve the symptoms in a few days without any need to reduce the dose of Plegomazin. Later, when doses are gradually decreased, the parkinsonoid syndrome disappears spontaneously in every case. Only one of our patients developed *jaundice*, after one month of treatment. Plegomazin was discontinued, Patek's diet, choline chloride and vitamin treatment were instituted. Jaundice improved rapidly and the patient was discharged practically cured, both medically and psychiatrically. When jaundice developed, urinary ubg was ++++, bilirubin ++, serum bilirubin 4.2 mg. per cent, direct +++, while the thymol test was merely 2 U; on discharge ubg in urine was normal, bilirubin negative, serum bilirubin 0.7 mg. per cent, direct negative, and the thymol test was 1 U. As mentioned before, the urine, liver function, and the blood count were controlled weekly during the courses, and except for the above mentioned case of jaundice, pathological changes did not occur. It is stressed emphatically that no hæmatological changes of any kind have been noted, though chlorpromazin therapy has been described to cause *agranulocytosis* as the most dangerous complication. In 1956 Schick and Virks reported on 21 cases of *agranulocytosis* collected from the literature, of which 8 were fatal. One of our patients developed *thrombophlebitis*, which was cured in the course of penicillin and Pelentan (an oxy-coumarin derivative) treatment. *Allergic toxic dermatitis* developed in a single case on the sixth day of parenteral treatment, with large spots of exanthema not protruding from the level of the skin, vivid red in colour; febrile reaction was absent. Plegomazin was discontinued and Suprastin (an antiallergic) was given, with excellent results. The rash soon faded and eight days later only pale pigmentation and fine desquamation were visible; even these disappeared in one week without leaving a trace.

I should like to deal briefly with the results of therapy. Plegomazin has excellent effects in functional depression and tenebrosity, also in epileptic tenebrosity, as can be seen in table II. On the basis of my experiences including more than 300 patients treated earlier with chlorpromazin, I may add that the drug is of almost sovereign effect against excitatory breaks (Pavlov), but good therapeutic results may be expected also in exogenous cases of inhibitory breaks, because

in these reactive depressive states the symptoms are usually on the productive level, the dynamics of experience being preserved (Gade) and the thymoplegic effect of the drug may be used to good advantage (Janzarik). Fink, Shaw, Gross, and Coleman, comparing the therapeutic results of insulin coma to those of chlorpromazin therapy in psychoses, state that both methods produce about the same grade of improvement and the same discharge rate from hospital, but treatment with chlorpromazin is easier to manage and, at the same time, less dangerous. I fully agree with this statement, but have to add that in certain cases a combination of chlorpromazin with ES is at present the method which produces the best clinical results (recovery and improvement) in schizophrenia. Angyal and Gyafas were the first to report on the combination of convulsive therapy with insulin coma, in 1936. In fresh and subacute schizophrenia convulsive therapy alone resulted in recovery and improvement in 44.4 per cent of the cases; combination with insulin coma increased this rate to 66.7 per cent. The present report deals with 35 cases of schizophrenia, acute, subacute, and intermittent. This number is too small to allow, the results to be expressed in percentages, but Largactil and Plegomazin being drugs of the same chemical composition, I may add to the discussed cases those I described together with Pertorini: 54 cases of acute and subacute schizophrenia. Thus in 89 cases of acute, subacute, and intermittent schizophrenia, chlorpromazin therapy alone or its combination with ES brought about clinical recovery in 55 per cent, good improvement with the return of earlier capacity to work in 38.2 per cent, in a total of 93.2 per cent.

Numerous problems relative to chlorpromazin therapy are still open. There are questions of the greatest practical consequence, namely the durability of the response, and whether the drug can ultimately alter the final outcome of schizophrenia. No reliable answer has been possible so far, since adequate information in this respect can be based only on long-lasting catamnestic studies on a large patient material.

SUMMARY

- (1) In the introduction the mode of action of Plegomazin therapy is discussed. The action of drug is believed by the author to be of a functional, localizing nature,

taking effect at a higher level of autonomic innervation which coordinates the cortical, diencephalic, and somatic synchronism-correlates of the action in progress. The primary effect is a coordination of disturbed function in the centrencephalic system; the essence of the effect is the synaptic inhibition or blocking of *noxious* sympathetic and parasympathetic impulses leading to overstrain, as well as the mobilization of the economizing, protective instances of the parasympathetic.

- (2) The author has carried out clinical assays with the Hungarian chlorpromazin preparation, Plegomazin, in 74 psychiatric patients, 54 of whom were schizophrenics, while 20 patients suffered from other mental diseases.
- (3) Plegomazin is equivalent to foreign preparations both as regards the vegetative and psychosyndrome it produces and the favourable action on psychotic conditions.
- (4) The 2 ml. ampoule containing 50 mg., originally intended for use as intravenous drip, can be given safely intramuscularly, deep into the gluteal muscle. It does not irritate tissues in a greater measure than the 5 ml. (25 mg.) injection.
- (5) Plegomazin has caused no allergic reactions in the personnel handling it.
- (6) As to the side effects, jaundice, thrombophlebitis, and allergic toxic dermatitis have occurred, in one case each. In all three cases the discomfort caused by the complication was slight and the untoward symptoms subsided within a short time after discontinuance of the drug.
- (7) In agreement with the experience obtained with other chlorpromazin preparations. Plegomazin alone proved to be highly effective against functional inhibitory and excitatory breaks, as well as in epileptic tenebrosity. In the cases of (acute, subacute, and intermittent) paranoid schizophrenia, clinical recovery and improvement ensued in 93.2 per cent.

It is to be noted, however, that in certain cases Plegomazin therapy should be combined from the beginning with ES treatment.

- (8) As regards the grade of improvement and rate of discharge from hospital, Plegomazin therapy is equivalent to insulin coma, but is more convenient and less dangerous.
- (9) Treatment with Plegomazin, combined, if so required, with ES therapy, is at present the method producing the highest percentage of clinical recovery and improvement in cases of schizophrenia.

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BRAIN DISEASES — NEW SOVIET METHOD OF TREATMENT

The Soviet Neuro-surgery Scientific Research Institute has reported a new method of surgical treatment for chronic diseases of the central nervous system such as Parkinson's disease.

This method, reported to the Presidium of the Academy of Medical Sciences of the USSR, is to introduce a thin pipe into deep-seated parts of the brain through which a small amount of alcohol is passed destroying the affected nervous cells.

Precise calculations using special apparatus are needed.

It is said more than 70 operations had been carried out under Dr. Boris Egogov, member of the Academy of Medical Sciences, and were highly effective.

It warned, however, that a complete cure could not always be expected, particularly in the later stages of the disease. (Tass Agency)

Respiratory Functions After Pneumectomy

By

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At present Pneumectomy is being widely used in the treatment of Pulmonary Tuberculosis where we come across a destroyed lung or where stenosis of the main bronchus is present and is considered a safe procedure both as far as the post-operative mortality and the ability of the patients to bear the strains of high degree of physical activity is concerned. Experimental studies on the physiological effects of removal of one of a pair of vitality important organ as the lung is have been studied by Bremer (1937) on cats and Longaere *et al* (1937) on dogs. The physiological studies in man will be of great practical value for assessing individual cases and chiefly in helping to decide which are the most favourable conditions for the maintenance of higher degree of functional efficiency in the remaining lung after pneumectomy. This has been attempted by few workers only.

Mc Ilroy & Bates (1956) reported that after Pneumectomy the Vital Capacity is reduced to half the normal predicted values. Hirdes & Bosch (1955) post-pneumectomy in 38 patients reported an increase in Vital Capacity & M. B. C. with the course of time. Cournand and Berry (1942) and Cournand & Austrian (1950) reported development of emphysema after pneumectomy. However, Hirdes & Bosch (1955) found a downward tendency in the values for Residual Volume, an observation which is in opposition to the widely held thought that after pneumectomy emphysema develops in the course of time. This shows that the ventilatory reserves become larger, a fact that is favourable for working conditions.

MATERIAL AND METHODS

The material for study was selected from cases admitted to K. T. B. Clinic & Hospital. A detailed examination of the Pulmonary Functions was done in each case considered suitable for Pneumectomy. The following tests were performed one week prior to the operation and repeated about two months after the operation when the patient had fully recovered :

1. Vital Capacity (V. C.)

2. Inspiratory Reserve Volume (I. R. V.)
3. Expiratory Reserve Volume (E. R. V.)
4. Residual Volume (R. V.)
5. Functional Residual Volume (F. R. V.)
6. Total Lung Capacity (T. L. C.)
7. Maximum Breathing Capacity (M. B. C.)
8. Breathing Reserve in Percentage of M. B. C. (B. R. %)
9. Exercise Tolerance Index. (E. T. I.)

All the patients were given respiratory exercises in the pre-operative as well as post-operative period. Before recording the values preoperatively the patients were already acquainted with the use of spirometer several times.

Some of the gradings and classifications used in the assessment of cases in the Pulmonary Function Test Laboratory are as follows :

1. GRADING OF DYSPNOEA

The patients are asked to step up and down a height of 20 cms, thirty times in one minute. The reaction of the patient is noted during the period of recovery limited to 5 minutes.

Less than 2 min. of recovery period...	No dyspnoea
Upto. 2 min.....	+ dyspnoea
From 2 — 5 min.....	++ dyspnoea
More than 5 min.....	+++ dyspnoea

2. GRADING OF RATIO R. V./T. L. C. X 100

Since the normal figures for this ratio in our Laboratory range from 25% to 35% we have found the following as a convenient classification.

Normal	.. 25—35%
Slight Emphysema	.. 36—40%
Moderate Emphysema	.. 41—50%
Advanced Emphysema	.. 51—60%
Far Advanced Emphysema	... Over 60%

3. UNILATERAL VOLUMETRIC MEASUREMENTS

The accepted normal values for the function contributed by the right lung are 55% and for the left 45% of the calculated normal value for both lungs. In the absence of facilities for unilateral volumetric measurements Hirdes & Bosch (1955) rated these values as 100% for the remaining lung and compared the changes in lung volume observed after pneumonectomy.

We have also followed this method with some modifications as in our laboratory; we have found lower values for the different lung volumes in normal healthy adults as compared with the European normal figures. Since the various prediction formulæ are based on European standards we did not think it proper to calculate the normal values from these formulæ. We therefore examined fifty healthy persons and calculated the average normal values for a healthy adult and then calculated the values for right lung (55%) and left lung (45%) separately. The values obtained for each were as follows:

Side	Vital Capacity in cc's	Residual Vol. in cc's	Functional R.V. in cc's	Total Lung capacity in cc's	Ratio R.V./T.L.C. × 100
Right Lung	2200	825	1375	3025	27%
Left Lung	1800	685	1135	2485	27%

4. RADIOLOGICAL CLASSIFICATION

The cases were classified according to the recommendations of Indian Tuberculosis Association (1940) into three stages depending on the extent of parenchymal involvement.

5. EXERCISE TOLERANCE INDEX

It was performed as described by Mütthuswami (1954).

A pneumonectomy was performed in the following group of cases:

1. Tuberculous cavitation (destroyed lung)... 6 cases (60%)

2. Unexpanded Lung after Tuberculous Emphysema... 2 cases (20%)

3. In the present series we were provided with an unusual opportunity to study two cases (20%) with Stage II disease in which originally a Lobectomy was planned but due to accidental nick in the pulmonary artery at the operation table a Pneumonectomy had to be performed.

Out of the ten cases studied, 6 cases (60%) were females and 4 cases (40%) were males. The female patients belonged to age group 20--28 years (mean 24 yrs.), and the male patient belonged to age group 25 years to 32 years (mean 28 yrs.). Two cases (20%) belonged to Stage II disease while the rest to Stage III disease (80%).

In six cases a left sided Pneumonectomy was performed and in the remaining four a right sided Pneumonectomy was performed.

RESULTS

This study comprises of ten cases in whom a Pneumonectomy was performed. In none of the cases supplementary collapse measures were undertaken for the reduction of dead space.

The data regarding functional changes noticed are given in accompanying table. An analysis of the data reveals the following results:

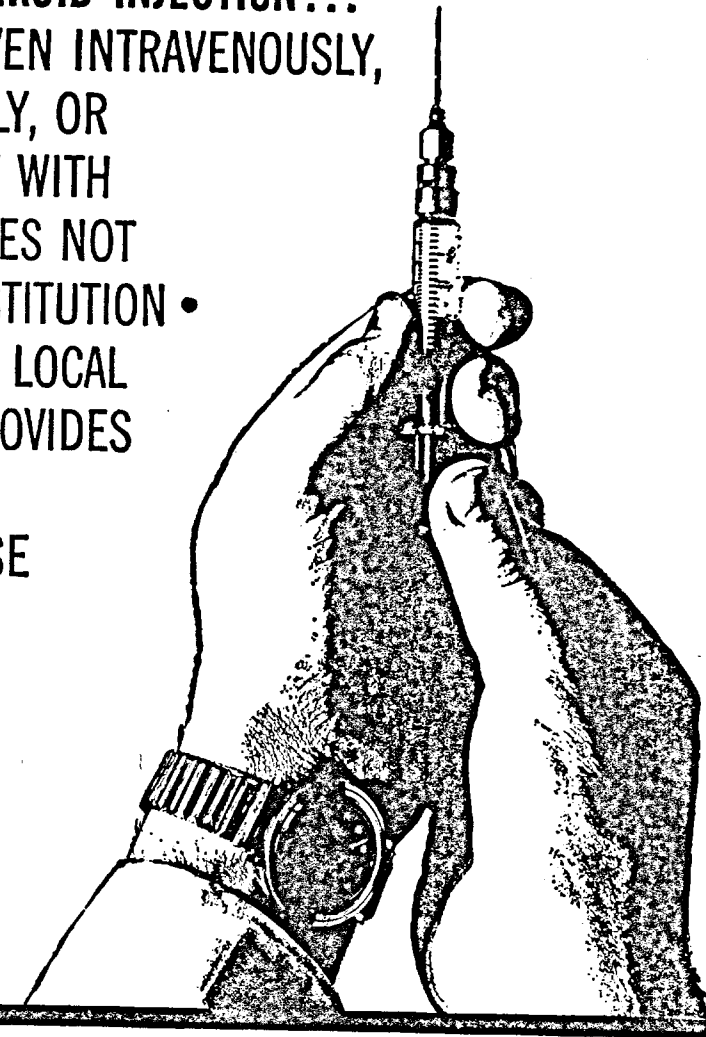
VITAL CAPACITY

It was reduced in all the cases. The maximum reduction noticed was 28% (range being from 3% to 28%) and the average reduction being 9.7%.

In two cases with Stage II disease in which originally a Lobectomy was planned but due to accidental nick in the Pulmonary Artery a Pneumonectomy had to be performed, demonstrated a reduction of 28% and 15% respectively.

In six cases with a destroyed lung the maximum postoperative reduction noticed was 12% (range being from 7% to 12%) and the average reduction being 8%.

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FUNCTIONAL CHANGES IN THE REMAINING LUNG AFTER PNEUMONECTOMY

Case No.	Name	Sex	Stage of Disease	Special remarks about Lung Lesion	Side of Pneumonec-tomy	VITAL CAPACITY		Preoperative		
						Change in terms of calculated average normal value for one lung (%)	Change in terms of pre-operative value (%)	I.R.V. in cc's	E.R.V. in cc's	Ratio
1	2	3	4	5	6	7	8	9	10	11
1	B.D.	F	III	Unexpanded left lung after empyema	Left	+ 6%	- 3%	1483	494	3
2	G.S.	M	III	Destroyed lung left side	Left	+ 2%	- 7%	1494	498	3
3	R.J.	F	III	Unexpanded left lung after empyema	Left	+ 4%	- 4%	1475	492	2.9
4	S.K.	F	II	Fibrocavernous lesion with in-filtration left upper zone	Left	+ 9%	-28%	1952	650	3
5	R.K.	M	III	Destroyed lung left side	Left	- 6%	-12%	1445	500	2.8
6	C.B.	F	II	Infiltration with a cavity left upper zone	Left	+17%	-15%	1947	649	3
7	C.K.	F	III	Destroyed lung right side	Right	- 8%	- 4%	1600	546	2.8
8	K.P.G.	M	III	Destroyed lung right side	Right	+ 2%	- 8%	1854	600	3
9	K.K.	F	III	Destroyed lung right side	Right	+ 4%	- 6%	1850	618	2.9
10	D.K.	M	III	Destroyed lung right side	Right	+ 2%	-10%	1870	630	2.9

In the remaining two cases with unexpanded lung postoperative reduction noticed was 3% and 4% respectively.

Analysis of the values found postoperatively in terms of the normal values for one lung the figures ranged between 92% to 117%.

MAXIMUM BREATHING CAPACITY

Out of the ten cases it was reduced in eight, while no change was observed in the remaining two cases. The maximum reduction noticed was 30% (ranged being from 7% to 30%) and the average reduction being 10%.

In two cases with Stage II disease the postoperative reduction noticed was maximum (being 30% and 25% respectively). While in the two cases with unexpandable lung, postoperatively no change in M. B. C. was noticed.

RESIDUAL VOLUME

It was reduced in all the cases studied. The maximum reduction noticed was 39% (range being from 25% to 39%) and the average reduction being 32%.

Analysis of the data found postoperatively in terms of the normal values for one lung, our cases demonstrated an increase of the Residual Volume in all the cases. The maximum increase was 33% (range being from 1.2% to 33%) and the average rise being 12.6%. The two cases with stage II disease had a rise of 1.2% and 2.5% respectively, which is small and negligible.

FUNCTIONAL RESIDUAL VOLUME

It was reduced in all cases studied. The maximum reduction noticed was 28% (range being from 18% to 28%) and the average reduction being 22%.

Analysis of the postoperative data in terms of the

TABLE—(Contd.)

Post Operative			Functional Residual Vol.		Residual Volume		Total Lung Capacity		R.V/T.L.C. ×100	
I.R.V. in cc's	E.R.V. cc's	Ratio	Change in terms of pre-operative value	Change in terms of calculated average normal values for one lung	Change in terms of pre-operative value	Change in terms of calculated average normal value for one lung	Change in terms of pre-operative value (%)	Change in terms of post-operative value (%)	Preoperative (%)	Post-operative (%)
12	13	14	15	16	17	18	19	20	21	22
1420	496	2.7	—21%	+11%	—30%	+12%	—15%	+ 8%	36	29
1344	500	2.6	—25%	+14%	—35%	+15%	—22%	+ 6%	38	30
1375	503	2.7	—20%	+ 8%	—30%	+ 6%	—16%	+ 5%	35	28
1480	493	3	—21%	+14%	—25%	+1.2%	—22%	+12%	28	29
1219	480	2.5	—28%	+15%	—37%	+22%	—30%	+ 2%	41	33
1580	527	3	—20%	+12%	—28%	+25%	—19%	+15%	27	27
1520	534	2.9	—20%	+18%	—37%	+33%	—24%	+ 4%	45	35
1665	579	2.8	—28%	+ 5%	—39%	+ 5%	—25%	+ 3%	37	28
1700	598	2.8	—22%	+11%	—30%	+13%	—18%	+ 7%	35	29
1600	644	2.4	—18%	+16%	—28%	+16%	—20%	+ 6%	35	30

normal values for one lung our cases demonstrated a rise in F. R. V. in all cases. The maximum rise was 18% (range being from 4% to 18%) and the average rise being 12%.

TOTAL LUNG CAPACITY

It was reduced in all the cases. The maximum reduction noticed was 30% (range being from 15% to 30%) and the average reduction being 21%.

Analysis of the data found postoperatively in terms of the calculated normal values for one lung, our cases demonstrated an increase in T. L. C. The maximum rise was 15% (range being from 2% to 15%) and the average rise being 6.8%. This much of rise in T. L. C. is of no significance.

RATIO R. V./T. L. C. X 100

Preoperatively a normal ratio was found in 5 cases, evidence of slight emphysema in 3 and moderate in 2

cases. None of the cases had evidence of severe Emphysema.

Postoperatively a normal ratio was found in all the cases. Thus evidence of Emphysema (as suggested by this ratio) was not found in any case postpneumonec-tomy, in the remaining lung.

RATIO I. R. V./E. R. V.

Mc Ilroy & Bates (1956) describe slight reduction in this ratio as representing Over inflation and from moderate to severe reduction as evidence of Emphy-sema. Analysing our preoperative data in these terms, a normal ratio was found in 8 cases, and evidence of over inflation in two cases only.

Postoperatively a normal ratio was found only in 3 cases while the remaining 7 cases showed a slight reduction. Thus postoperatively most of our cases had evidence of over inflation only but none of them showed evidence of Emphysema in the remaining lung, as judged by the standards of Mc Ilroy & Bates.

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Proteolysed Liver Extract from 100 G. Fresh Liver
Stomach Extract from 1 G. Fresh Stomach
Yeast Extract from 6 G. Dried Yeast B.P.C.
Folic Acid B. P. 10 mg.
Vitamin B₁₂ B. P. 40 mcg.
Vitamin B. B. P. 140 mg.
Riboflavin B. P. 10 mg.
Vitamin B₆ B. P. C. 7 mg.
Calcium Pantothenate U. S. P. 18 mg.
Nicotinic Acid amide B. P. 200 mg.
Choline Chloride N. N. R. 1 G.
Methionine N. F. 1 G.
PABA N. F. 35 mg.
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BREATHING RESERVE/M. B. C. X 100

Postoperatively a reduction in B. R. % was noticed in 8 cases. The maximum reduction noticed was 10.5% (range being from 0.9% to 10.5%) and the average reduction being 5.1%.

One case showed an increase of +2.4% and another did not show any change in B. R. %.

Preoperatively as well as postoperatively cases which had no dyspnœa on exercise the B. R. % was 79% or over. Below 79% dyspnœa was present on exercise. Between 73% to 79% '+dyspnœa' and below 73% '+ +dyspnœa' was noticed. In none of the cases '+ + +dyspnœa' on exercise was present in our cases either preoperatively or postoperatively.

EXERCISE TOLERANCE INDEX

Postoperatively 2 cases did not show any change and in three cases it increased, the values being +9, +2 and +1 respectively. In the remaining 5 cases it showed a reduction. The maximum reduction was -12 (range being from -3 to -12) and the average reduction being -6.4.

Preoperatively as well as post operatively no dyspnœa was noticed on exercise when the values were above 70, while dyspnœa was invariably present when figure was below 70.

CLINICAL AND RADIOLOGICAL FOLLOW UP

Postoperatively dyspnœa was seen on exercise in 6 cases. Out of these four cases had it already preoperatively. In case No. 2 '+ +dyspnœa' seen preoperatively lessened to '+' postoperatively. In cases No. 7 and 10 '+dyspnœa' seen preoperatively increased to '+ +' postoperatively. In case No. 7 postoperatively there was presence of Bronchitis while case No. 10 had a late postoperative recovery. He developed a huge serosanguinous effusion after Pneumonectomy which necessitated several aspirations. In the remaining cases No. 3, 5 & 9 only '+dyspnœa' was noticed postoperatively. The cases 3, 5 did not demonstrate any dyspnœa preoperatively. This can only be explained by assuming that in the remaining lung the ventilation for a given amount of exercise is doubled and the mean inspiratory resistance to the greater flow of air through the bronchial tree of the remaining lung is increased.

TABLE—(Contd.)

Change in Maximum breathing capacity in terms of Preoperative Value. (%)	Exercise tolerance index			Breathing Reserve %			Dyspnœa	
	Pre-operative	Post-operative	Change	Pre-operative	Post-operative	Change	Pre-operative	Post-operative
23	24	25	26	27	28	29	30	31
No Change	78	80	+ 2	79	79	—	Normal	Normal
—7.6%	60	69	+ 9	74.5	73.6	— 0.9	++	+
No Change	72	65	— 7	88.5	78.0	—10.5	Normal	+
—30%	98	98	0	88.6	82.5	— 6.1	Normal	Normal
—6.6%	80	68	—12	80.3	77.2	— 3.1	Normal	+
—25%	95	92	— 3	85.0	82.0	— 3	Normal	Normal
—7.6%	65	65	0	78.5	72.0	— 6.5	+	++
—10%	75	70	— 5	81.9	80.2	— 1.7	Normal	Normal
—10%	68	69	+ 1	72.6	75.0	+ 2.4	+	+
— 8%	55	50	— 5	74.1	65.2	— 8.9	+	++

None of the cases postoperatively developed any evidence of Bronchopleural Fistula.

Radiologically evidence of emphysema was found in case No. 4, 6 and 10. In others the remaining lung did not show any appreciable change as compared to the preoperative state.

DISCUSSION

I. VENTILATORY FUNCTIONS

There occurred a reduction in ventilatory functions in all cases postpneumonectomy. An average reduction of 9.7% in Vital Capacity and 10% in M. B. C. was observed. Such a small reduction in Ventilatory functions after Pneumonectomy suggests that most of the function was being contributed by the normal lung.

Two cases with Stage II disease demonstrated the maximum reduction in Ventilatory Functions—(V. C. —28% & —15%, M. B. C.—30% and —25%) while in other cases with Stage III disease the average reduction

noticed was only —7%. This clearly demonstrates that if a destroyed or completely unexpanded lung is going to be removed a minimal reduction in Ventilatory Functions should be anticipated.

II. DEVELOPMENT OF EMPHYSEMA AFTER PNEUMONECTOMY

When the preoperative values were compared with the calculated normal values for one lung, the cases demonstrated a raised residual volume without any change in the T. L. C. This shows the patient's inability to or unwillingness on his part to perform a deep expiration. This is supported by finding similar values of E. R. V. preoperatively as well as postoperatively which suggests breathing at a higher level postoperatively. A higher level of breathing without an increase in T. L. C. does not suggest emphysema.

Since we have been able to demonstrate an unwillingness on the part of the patient to perform deep expiration, it is expected that with the course of time this inhibition would disappear and the Ventilatory reserve would increase. Hirdes et al (1955) have

reported increase in ventilatory reserves with the course of time after following cases of Pneumonectomy for a period of two years.

The presence of raised Functional residual volume without any change in T. L. C. only suggests Overinflation of the remaining lung. This is further supported by the presence of only slight reduction in T. R. V./E. R. V. ratio.

III. ROLE OF THORACOPLASTY AFTER PNEUMONECTOMY

In follow up our cases did not demonstrate the development of Emphysema, bronchopleural fistula or any other complication which is supposed to be prevented by supplementary collapse measures after Pneumonectomy. Similar reports have come from Earland (1953), Nubær (1953) and Hirdes & Bosch (1950).

In none of the cases in present series a thoracoplasty was done so it is not possible to judge its value. But on one hand the report of Workers like Gaensler and Strieder (1951) and Mathey et al (1952) that thoracoplasty after Pneumonectomy accomplishes just opposite of the desired results, and on the other the finding in present series, that the patients are doing well without Thoracoplasty there is sufficient indirect evidence to conclude that the value of thoracoplasty is doubtful.

It is further supported by the fact that most of our cases had B. R. near about 80% of M. B. C. and Cournand & Berry (1948) have reported that when the B. R. is less than 85% of M. B. C. the possible advantages to be gained by Thoracoplasty must be weighed against the chances that a further reduction in Pulmonary Functions in the Post-operative period may reduce the patient to a permanently incapacitated individual, dyspnoëic on slightest exertion.

IV. INVALIDISM FOLLOWING PNEUMONECTOMY

Cournand & Berry (1942) reported that whatever dyspnoëa there was seemed to be most closely related to a diminution in B. R. We therefore made an attempt to correlate dyspnoëa with B.R.% and Exercise tolerance index.

We found a close association in between three :

B. R. between	80—85%	
E. T. I. above	70	+ Dyspnoëa not noticed.

(Continued on page 79)

B. R. between	80—85%	
E. T. I. below	70	Dyspnoëa present.
B. R. between	80%	
E. T. I. below	70	Dyspnoëa present.

Thus in marginal cases the dyspnoëa appears to be related to the data for E. T. I. If it was above 70 no dyspnoëa, while if it was below 70 dyspnoëa on exertion was noticed. Thus E. T. I. can be taken as a reliable test for determining the postoperative invalidism.

We have found an average reduction of 5% in B.R. and 6.4 in E. T. I. postpneumonectomy. In view of the findings if pneumonectomy is performed in a patient with preoperative B. R. of less than 85% of M. B. C. and E. T. I. of less than 77 there is danger of making the patient a respiratory cripple.

CONCLUSIONS

There occurs a reduction in Ventilatory functions after Pneumonectomy. The cases did not demonstrate any evidence of Emphysema two months after Pneumonectomy. Based on the indirect evidence the role of thoracoplasty after Pneumonectomy appears doubtful. The study suggests that if a Pneumonectomy is performed in patient with a preoperative B. R. of less than 85% of M. B. C. and E. T. I. less than 77 there is danger of making the patient a respiratory cripple.

SUMMARY

Ten cases have been studied to assess the effect of Pneumonectomy on Ventilatory Functions of the Lung, to assess the role of Thoracoplasty after Pneumonectomy. An attempt has been made to evaluate the minimal Ventilatory reserve when a pneumonectomy can be safely performed without making the patient a respiratory cripple. This is a preliminary report of the whole project in which the cases will be followed for a period of 5 years.

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Employees' State Insurance Scheme, West Bengal— Observations of one chest unit.

By

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AND

DR. (Miss) M. MITRA, M.B., B.S. (Cal.)

AND

DR. H. K. SAMANTA, M.B., B.S. (Cal.)

THIS unit was opened on the 22nd of August, 1955. The chest specialist is to work for 2 hours twice in a week with the help of one assistant. Due to tremendous rush in the department, a second chest unit was opened in this hospital in June 1957. The first unit is now catering areas Cal X, XI, XII and 24 Parganas XXI to XXXVIII. The statistical figures given are of chest unit No. 1.

TABLE 1.

The total number of new cases in 1955 was 466, old cases 932, total 1398, daily attendance 38, that means the time devoted was 3 minutes only to each patient for diagnosis and treatment including the filling-up of various "Forms" regarding investigations and treatment.

In 1956, total number of new cases was 1511, old cases 4407, total 5918, daily attendance 58.41, time devoted to each patient about 2 minutes.

In 1957, total number of new cases 1186, old cases 4493, total 5679, daily average attendance 58.83, time devoted for each patient was about 2 minutes.

In 1958, number of new cases was 780, old cases 3210, total 3990, daily average attendance 33.17, time devoted for each patient 3½ minutes.

(Continued from page 78)

- | | |
|---|---|
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(Courtesy: The Tuberculosis Association of India)

The figure under the column "untraced" includes those cases that did not turn up after some days.

Table IV shows the number of cases of Pulmonary tuberculosis who were declared fit to resume their duties at varying intervals. Even after resuming their duties, they are to attend the clinic regularly for the follow-up treatment.

THE WORKING METHOD

As soon as a patient comes, he is clinically examined, and the requisition is made for x-ray of the chest, the blood examination for Hb %, T.C.D.C., and E.S.R. and the sputum examination especially for A.F.B., as a routine and in selected cases examination of the stool and the urine. For the diagnosis of Tropical Eosinophilia other possible sources for eosinophilia are investigated for elimination.

Cases of Pulmonary Tuberculosis are treated and followed up for at least two years. Suitable cases are recommended for hospitalisation—especially who may require various surgical treatment.

Tropical Eosinophilia cases are treated with arsenic, Diethylcarbamazine and other drugs and our observations of the results with the treatment by the various drugs will be an object of future publication.

Bronchiectasis cases are generally advanced and there is hardly any scope for surgical treatment.

DISCUSSION

No doubt, the workers have received considerable benefit under the scheme, but we feel that the overall picture is far from satisfactory. There is a good deal of scope for further improvement and we would suggest the following :

- 1. There should be less number of patients and the daily attendance should not exceed 15, so that a little more time may be devoted for careful examination of each patient. At present, daily attendance is 33.17. A third unit (chest) should be opened to minimise the rush.
- 2. The cases that are sent to the chest specialist should be more properly screened by the panel doctors before hand, so that many vague cases may be eliminated.

3. At present there is very little scope for any surgical treatment—such as pneumo-peritoneum, Thoracoplasty, Lebectomy etc., and although some of our pulmonary tuberculosis cases are recommended hospitalisation for surgical interference, they get good deal of difficulty in getting into the hospitals and most of them continue to hang on indefinitely to our clinic.

4. We have been surprised to note that in certain cases, the employees suffering from pulmonary tuberculosis and advised 'absolute rest' by the chest specialist are allowed to work in the factory to the great detriment to their health and that of others. We fail to understand how this is possible and there should be a thorough check-up from the factory side.

5. We have found that many patients do not get the required number of injections and medicines prescribed by the specialist. As for instance, a patient has been prescribed Inj. Streptomycin 1G. I. M. daily x 30, when he comes after one month there is no record on the ticket whether all the 30 injections have been given regularly. Sometimes we have enquired at random and we have found that the patient has got only 15 injections or less. When we enquire why this is so, the answer is vague, sometimes the panel doctor is blamed for not having the injections regularly and sometimes the chemists are blamed for not supplying the medicines. This unfortunate affair can only be rectified if there is more close co-operation between the patients, panel doctors and the chemists.

To sum up it is our considered opinion that the E. S. I. Scheme can be a real boon to the employees, if three vital conditions are complied with :

- 1. Greater efficiency of all staff concerned.
- 2. Better organisation of the services—both domiciliary and hospital—with modern and adequate equipments.
- 3. Better organisation of all the various associated services, such as the Radiological Centres, the pathological laboratories and the chemists and druggists.

TABLE I

1955				
Month	New cases	Old cases	Total	Daily
August	32	84	116	29
September	156	134	290	32
October	112	277	389	49
November	91	200	291	36
December	75	237	312	44
	466	932	1398	190
	33.33%	66.50%	99.83	average 38
				daily average attendance = 38
1956				
January	96	193	289	36
February	91	216	307	38
March	104	276	380	42
April	82	283	365	40
May	105	337	442	55
June	103	422	525	66
July	144	440	584	73
August	231	323	554	61
September	196	302	498	63
October	139	508	647	72
November	147	453	600	75
December	73	654	727	80
	1511	4407	5918	701
	25.53%	74.46%	99.99	
				daily average attendance = 58.41

Table I—(Contd.)

Month	New cases	Old cases	Total	Daily
1957				
January	137	473	610	76
February	144	513	657	82
March	144	473	617	77
April	137	447	584	83
May	138	511	649	81
June	120	403	523	65
July	62	289	351	44
August	44	265	309	34
September	55	278	333	37
October	61	248	309	39
November	64	274	338	42
December	80	319	399	44
	1186	4493	5679	694
	20.88%	79.10%	99.98	
				average daily attendance = 58.83
1958				
January	63	277	340	38
February	66	238	304	43
March	84	274	358	39
April	45	191	236	39
May	54	209	263	33
June	67	268	335	37
July	77	284	361	40
August	87	321	408	50
September	64	321	385	43
October	61	247	308	44
November	67	291	358	50
December	45	289	334	42
	780	3210	3990	398
	19.54%	80.45%	99.99	
				average daily attendance = 33.17

TABLE II

Month	Chr. bronchitis	Emphysema	Eosinophilia	Bronchial asthma	Pleurisy	Bronchiectasis	Lung abscess	Cystic disease	Pneumonitis	Pneumo-thorax	Pulmonary tuberculosis	Bronchogenic carcinoma	Miscellane-ous
1955													
August	5	—	—	1	1	—	—	—	—	—	18	—	7
September	33	1	—	6	10	1	—	—	—	—	60	—	45
October	29	1	2	6	14	2	—	—	—	—	31	—	27
November	19	—	2	5	10	1	—	—	2	—	27	—	25
December	18	1	1	1	8	—	—	1	—	—	21	—	24
	104	3	5	19	43	4	—	1	2	—	157	—	128=466
=	22.32	0.64	1.07	4.08	9.22	0.85	—	0.21	0.43	—	33.69	—	22.47%
	%	%	%	%	%	%		%	%		%		=99.98%

1956

January	1	1	3	3	3	—	—	—	—	—	29	—	56
February	8	—	2	2	6	—	—	—	1	—	30	—	42
March	9	1	8	4	9	—	—	—	1	—	23	—	49
April	11	—	6	3	3	—	—	1	1	—	21	—	36
May	16	4	4	4	12	—	—	—	1	—	26	—	38
June	13	1	1	4	8	1	—	—	1	—	34	—	40
July	19	—	6	9	6	1	—	—	3	—	38	—	62
August	19	—	7	7	7	1	—	3	—	1	110	—	76
September	32	2	5	4	12	3	—	—	—	—	94	—	44
October	8	3	8	1	5	1	—	—	3	—	38	—	72
November	30	—	5	2	16	2	—	—	2	—	42	—	48
December	16	—	2	—	9	—	—	—	—	—	25	—	21
	182	12	57	43	96	9	—	4	13	1	510	—	584=1511
=	12.04	0.79	3.77	2.48	6.35	0.59	—	0.26	0.86	0.06	33.75	—	38.65%
	%	%	%	%	%	%		%	%	%	%		=99.96%

TABLE II—(Contd.)

Month	Chr. bronchitis	Emphysema	Eosinophilia	Bronchial asthma	Pleurisy	Bronchiectasis	Lung abscess	Cystic disease	Pneumonitis	Pneumo-thorax	Pulmonary tuberculosis	Bronchogenic carcinoma	Miscellane-ous
1957													
January	18	—	2	4	14	1	—	—	1	—	38	—	59
February	25	4	7	1	8	—	—	—	1	—	35	—	63
March	29	1	7	4	7	2	—	1	2	—	32	—	59
April	34	—	4	6	15	2	—	—	—	—	38	—	38
May	14	—	8	5	3	4	—	1	—	—	29	—	74
June	24	—	5	1	3	5	—	1	2	—	32	—	47
July	17	—	5	1	1	1	—	—	1	—	26	—	10
August	4	1	4	—	1	1	—	—	1	—	21	—	11
September	11	1	6	—	1	—	—	—	—	—	11	—	25
October	15	1	8	1	2	3	—	—	—	—	17	—	14
November	11	2	7	—	4	4	—	—	—	—	16	—	20
December	11	1	14	1	3	—	—	—	—	—	19	—	31
	213	11	77	24	62	23	—	3	8	—	314	—	451=1186
=	17.95	0.92	6.49	2.02	5.22	1.93	—	0.25	0.67	—	26.47	—	38.02%
	%	%	%	%	%	%		%	%		%		=99.94%

13

1958

January	18	—	15	—	2	—	—	—	—	—	18	1	9
February	4	1	7	—	3	—	—	—	—	—	22	—	29
March	1	1	6	1	3	2	—	—	2	—	18	—	50
April	5	—	5	—	2	—	2	—	—	—	10	—	21
May	4	—	3	2	2	—	—	—	—	2	17	—	24
June	7	—	11	—	3	1	—	—	1	—	24	—	20
July	7	—	7	—	1	1	—	—	1	—	23	—	37
August	4	1	3	—	3	—	—	—	—	—	22	—	54
September	12	1	3	—	2	—	—	—	1	—	14	1	30
October	4	—	4	—	1	1	—	—	—	—	17	—	34
November	5	—	4	—	1	—	—	—	4	—	21	—	32
December	4	—	1	—	1	—	—	—	1	—	13	—	25
	75	4	69	3	24	5	2	—	10	2	219	2	365
=	9.61	0.51	8.84	0.38	3.07	0.64	0.26	—	1.23	0.26	28.07	0.26	46.79%
	%	%	%	%	%	%	%		%	%	%	%	=99.97%

TABLE III
PULMONARY TUBERCULOSIS

	January	February	March	April	May	June	July	August	September	October	November	December	Total	Percentage
1955														
Open-cases								3	11	4	1	3	22	14.01%
Closed-cases								7	33	19	22	17	98	62.42%
Untraced								8	16	8	4	1	37	23.56%
TOTAL								18	60	31	27	21	157	99.99%
1956														
Open-cases	5	10	6	3	7	3	2	15	13	11	7	3	85	16.67%
Closed-cases	13	16	11	10	24	13	15	85	61	25	30	19	312	61.17%
Untraced	11	4	6	8	15	18	21	10	20	12	5	3	113	22.16%
TOTAL	29	30	23	21	46	34	38	110	94	38	42	25	510	100%
1957														
Open-cases	4	6	5	5	3	4	7	6	1	5	4	11	61	19.43%
Closed-cases	28	18	17	24	23	20	17	11	5	12	11	6	192	61.14%
Untraced	6	11	10	9	3	8	2	4	5	-	1	2	61	19.43%
TOTAL	38	35	32	38	29	32	26	21	11	17	16	19	314	100%
1958														
Open-cases	1	8	8	4	1	2	1	2	1	1	4	1	34	15.52%
Closed-cases	14	11	7	6	13	18	18	20	13	15	15	9	159	72.60%
Untraced	3	3	3	-	3	4	4	-	-	1	2	3	26	11.87%
TOTAL	18	22	18	10	17	24	23	22	14	17	21	13	219	99.99%

TABLE IV
Pulmonary Tuberculosis cases who resumed duties at varying intervals

	January	February	March	April	May	June	July	August	September	October	November	December	Total	%
1955														
A 1-3 months								1	9	6	14	7	37	37%
B 4-6 months								4	13	6	2	10	35	35%
C 7-9 months								3	7	4	3	-	17	17%
D 10 months-1 year								1	4	3	3	-	11	11%
E over 1 year								-	-	-	-	-	0	0%
													100	100%
1956														
A 1-3 months	8	5	6	3	10	4	4	61	38	8	9	5	161	60.29%
B 4-6 months	5	8	10	4	-	-	-	17	7	4	14	9	78	29.21%
C 7-9 months	3	1	-	-	-	-	-	6	2	3	-	4	19	7.11%
D 10 months-1 year	-	-	-	-	-	-	-	5	-	1	1	1	8	2.99%
E over 1 year	-	-	-	-	-	-	-	-	1	-	-	-	1	0.37%
													267	99.97%
1957														
A 1-3 months	8	5	6	8	11	2	2	3	3	8	2	2	60	37.26%
B 4-6 months	10	9	7	5	5	11	11	5	2	3	-	6	74	45.96%
C 7-9 months	2	3	1	2	4	3	2	-	-	1	1	3	22	13.66%
D 10 months-1 year	1	2	1	-	1	-	-	-	-	-	-	-	5	3.10%
E over 1 year	-	-	-	-	-	-	-	-	-	-	-	-	0	0%
													161	99.98%
1958														
A 1-3 months	4	4	4	4	7	7	5	6	5	2	7	-	55	37.41%
B 4-6 months	5	5	8	3	4	9	7	12	8	7	7	3	78	53.06%
C 7-9 months	-	1	1	1	2	-	3	2	-	-	-	-	10	6.80%
D 10 months-1 year	-	1	1	1	-	1	-	-	-	-	-	-	4	2.72%
E over 1 year	-	-	-	-	-	-	-	-	-	-	-	-	-	0%
													147	99.97%

A Reconsideration of Intracerebral Haemorrhage

By

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INTRODUCTION

THE term intracerebral hæmorrhage in this title is meant to include the solitary, subcortical encapsulated hæmatoma as well as an intracerebral clot which has communicated with a ventricle or has erupted onto the cortical surface but to exclude those cases with catastrophic hæmorrhage leading to rapid death. In other words, cases with cerebral hæmorrhage of limited degree but sufficient to constitute a space occupying lesion are grouped with those of intracerebral hæmatoma (as described by Buckley et McKinney, 1941) and this because of common problems of treatment.

Definition: Intracerebral hæmorrhage is an intracerebral clot which may remain encysted or communicates with the C. S. F. pathways and which behaves as a space-occupying lesion.

Incidence: This is perhaps greater than is generally appreciated and our series of 21 cases, to be discussed, were collected in a period of 18 months, representing the admissions to one Centre.

In another series of 100 cases of intracranial hæmorrhage treated conservatively 35 post mortem examinations revealed 34% to have large intracerebral clots and in a further 50 cases managed surgically 32% and intracerebral clots (Small et al 1953).

Aetiology: The breach in a cerebral vessel leading to hæmorrhage into the brain substance may be associated with the following conditions.

- | | |
|------------------------------|----------------------|
| (1) Trauma | Immediate
Delayed |
| (2) Congenital abnormalities | (i) Aneurysm |

- (ii) Angiomatous malformations macroscopic
microscopic

- (3) Arterial disease (i) atheroma
(ii) changes associated with hypertension.
(iii) polyarteritis nodosa, mycotic aneurysm and following embolic occlusion.

The cases labelled spontaneous in our series refers to those in which the precise ætiology was not determined and of 10 cases, the youngest was aged 44, and with one exception where documentation did not include a blood pressure reading, all were hypertensive.

The relatively advanced age of this group raises the possibility of a high incidence of arteriopathy in causation. The spontaneous group mentioned in the review of literature by Buckley and McKinney (1941) is a different one since all patients were of young adult age and in good health previously, and as Jewesbury (1947) pointed out, this type of case was indistinguishable from the delayed traumatic variety. Furthermore, out of a total of 40 cases of intracerebral hæmatoma, only 4 were associated with hypertension and arteriosclerosis alone. These differences would appear to be due to sampling according to the varying definitions mentioned in the introductory paragraph.

The effects of trauma may be immediate or the injury may precede the symptoms of an intracerebral hæmatoma by a period of days, months or years, e. g. 9 days—15 years (Pilcher 1941, Craig et Adson 1936, Buckley & McKinney, 1941). The relation of trauma is sometimes difficult to assess if the interval is long.

THEORIES OF CAUSATION

Of the delayed traumatic type numerous kinds of change in cerebral vessels and surrounding brain tissue at the time of injury have been proposed which predispose to a subsequent hæmorrhage, (appraised by Jewesbury, 1947). Congenital abnormalities and arterial disease may be considered as predisposing conditions to intracerebral hæmorrhage, and hypertension in conjunction with any one of them constitutes another predisposing factor.

In the presence of these conditions hæmorrhage commonly may be precipitated by exertion which presumably raises cardiac minute output volume and increases cerebral circulation. Trauma is another possible precipitating factor. The association of intracerebral hæmatoma with ruptured aneurysm became more obvious with the advent of arteriography and large vascular anomalies, including arteriovenous aneurysms, have similarly been demonstrated (Olivecrona et Rieves 1948, Dandy 1928). Margolis (et al 1951) reported a subcortical hæmatoma caused by a tiny arteriovenous angioma and suggested that unexplained hæmorrhage in children and adults may be due to microscopic deep seated angiomatous lesions and that some may be beyond demonstration, having been destroyed by the hæmorrhage.

PATHOLOGY

The sites of intracerebral hæmorrhage correspond to type of causation and those associated with ruptured aneurysm are commonly frontal or temporal, with trauma frontal, frontoparietal, temporal or multiple and in our spontaneous group the sites were predominantly frontal and frontoparietal. The internal capsule is seldom a site for traumatic hæmorrhage and involvement by hæmorrhage due to arteriopathy is frequently catastrophic.

Since arteriovenous angiomata occur in the posterior part of the cerebral hemispheres (Elkington 1935) this may also be an occasional site of hæmorrhage.

The contents of the cavity formed by intracerebral hæmorrhage vary from liquid altered blood to laminated clot which may ultimately calcify, and the surrounding brain tissue, initially œdematous, subsequently forms a granulation-like tissue which precedes glial formation.

An intracerebral collection of blood, regardless of cause, may increase steadily or by successive bleeds or may undergo slow shrinkage.

CLINICAL FINDINGS

Diagnosis

There may be a history of trauma, severe emotion or exertion preceding a sudden onset (except those due to the delayed effects of trauma which may present as slowly expanding lesion) of headache, vomiting and frequently a changed level of consciousness from drowsiness to coma depending on the site and extent of the intracerebral hæmorrhage. The changes in consciousness often fluctuate.

A focal fit or generalised convulsion may be associated with the development of a hemiparesis or hemiplegia, sensory changes, an hemianopia or dysphasia according to the region of cortex involved. Neck stiffness often but not invariably accompanies the presence of blood in the C. S. F. A pyrexia of up to 102°F for several days and a rise in the systolic and sometimes in the diastolic blood are not uncommon. False localising signs may arise because of tentorial herniation (Reid et Cone 1939, Beck 1954); that is the descent of part of the hippocampal gyrus between the edge of the tentorium cerebelli and the brain stem due to sudden increase of pressure above the tentorium. This may result in pressure on the optic tract or posterior cerebral artery causing an hemianopia or on the oculomotor nerve bringing about pupillary dilatation. Supratentorial intracerebral clot may produce a contralateral hemiparesis as would be anticipated by virtue of its site but the same effect can be produced by the pressure of herniated brain on the crus cerebri of the same side. Alternatively the brain stem may be displaced from the side of the clot and the opposite crus cerebri impinges on the edge of the tentorium cerebelli, an ipsilateral hemiparesis resulting.

INVESTIGATIONS

A case with focal signs and blood stained C. S. F. requires further investigation as soon as the general condition permits. The C. S. F. in intracerebral hæmatoma may be blood stained, show a raised protein and cell content or be quite normal.

Radiological procedures are:—Skull X-ray which may show a pineal shift, angiography which may

demonstrate both a space occupying lesion and the source of bleeding, and it is desirable that bilateral arteriograms are obtained since multiple vascular abnormalities may be present and the opposite circulation can then be assessed. Electroencephalography is a valuable preliminary investigation and intracerebral hæmatoma, in common with other space occupying lesions, may produce focal slow wave activity.

DIFFERENTIAL DIAGNOSIS

Some of the commoner conditions likely to be confused with intracerebral hæmatoma are:—

- (1) Subdural hæmatoma
- (2) Localised cerebral œdema.
- (3) Cerebral tumour.
- (4) Cerebral thrombosis.

Subdural hæmatoma may present a similar fluctuating course but the focal signs are often slight and more frequently bilateral. The two conditions may coexist in traumatic cases and rarely in those associated with ruptured aneurysm.

Rapidly expanding tumours can constitute an abrupt illness whilst the symptoms of intracerebral hæmatoma may develop insidiously so that an accurate clinical diagnosis may be impossible in some cases. Marked papilloedema, raised protein associated with a normal cell content of the C. S. F. and a normal blood pressure when present are in favour of a tumour but arteriography may be necessary to establish a definite diagnosis.

At onset cerebral thrombosis and intracerebral hæmatoma may be difficult to distinguish but steady improvement occurs in many cases of cerebral thrombosis. It is in the cases where the condition of the patient fluctuates or deteriorates that the real difficulty lies, especially if the C. S. F. gives no hint and the probability of extending thrombosis must be weighed against that of intracerebral hæmatoma. If the E. E. G. findings are equivocal, proceeding with investigations entails due consideration of the risks of angiography which can increase the liability to thrombosis and in these circumstances air studies may be a safer procedure.

Localised œdema of the brain following trauma may be indistinguishable from an intracerebral hæmatoma both clinically and on investigation.

TREATMENT

First Aid: Although seriously ill in our experience these patients travel well. In transit to hospital the patient should be on the side with a low pillow and light covering. A clear airway should be maintained and if there is a change in the patient's colour oxygen can be administered.

(1) HOSPITAL TREATMENT

- (a) Care of the unconscious patient includes:—nursing without pillows and with only light covering, semiprone each side in rotation, turning at not less than 2 hourly intervals. Suitable sedation for restlessness may be necessary.
- (b) Care of the skin—routine treatment of pressure areas.
- (c) Care of the bladder—spontaneous evacuation may occur but retention should be avoided and we have found polythene catheter drainage satisfactory in these cases.
- (d) Care of the chest—consists of physiotherapy and antibiotics and, in the event of an infection, frequent tipping can be carried out. Should any obstruction of the upper respiratory passages occur, tracheotomy should be performed.

Therapeutic lumbar puncture in subarachnoid hæmorrhage has been a controversial topic, some having stressed the dangers of medullary or tentorial coning and it is probable that there is a greater risk in the presence of an intracerebral hæmatoma than when diffuse hæmorrhage from the brain surface has taken place. It seems therefore a wise procedure in those cases of subarachnoid hæmorrhage presenting focal signs to perform only a single diagnostic puncture taking off a small amount of fluid, that contained in the manometer being sufficient for the first bottle and about another 1 cc. collected in the customary second bottle.

(2) FURTHER TREATMENT

The above measures may be continued with the hope that no further bleeding will occur and that shrinkage of the clot will take place with some coincident

restoration of function. The aims of neurosurgical procedures are first to evacuate the clot in order to preserve life and to reduce the likelihood of severe persistent disability and secondly where possible to deal with the source of hæmorrhage.

Brain damage in intracerebral hæmorrhage may be threefold.

- (i) Permanent dissolution of tissue by the passage of blood in the formation of a cavity.
- (ii) Pressure of surrounding œdema impairing the blood supply of adjacent tissue.
- (iii) Stretching of tissue over the mass of blood clot.

Treatment can only hope to restore function in tissues affected in the manner indicated in (2) and (3) and it is reasonable to assume that the chances are enhanced if these damaging factors are removed early.

INDICATIONS FOR OPERATION

Those suggested are deepening coma, progressive localising signs, presence of a space occupying lesion, presence of an aneurysm or other angiomatous malformation, age of the patient and his general condition.

Patients deeply comatose from the onset of the hæmorrhage have usually not benefited by early evacuation of the hæmatoma, but despite our unfortunate experiences to date it is difficult to withhold help in these patients, especially if they are in the younger age group. In patients over sixty years of age, especially those with hypertension, operation is not advised as an emergency procedure.

If arteriography indicates a large space-occupying lesion (with or without an aneurysm) which is accompanied by focal signs, and when the state of consciousness shows no tendency to improve, operation is advised.

In passing it is to be noted that a decompression carried out in cases which subsequent findings suggest the presence of localised œdema rather than a clot may not prove an adverse procedure and indeed may be beneficial, as suggested by Small (et al 1953), and this has been also our experience.

OPERATIVE PROCEDURES

- (1) *Burr Hole and Aspiration:* If the hæmatoma is likely to be fluid and no aneurysm is demonstrated on arteriography, it is often possible to aspirate the fluid hæmatoma through a suitably placed burr hole with a brain needle. This procedure may have to be repeated in a few days but often one aspiration is sufficient.
- (2) *Craniotomy and Evacuation of a Solid Hæmatoma:* In hæmatomata more than a few days old, especially if an aneurysm is demonstrated by angiography, a formal osteoplastic flap is elevated and the hæmatoma evacuated through a suitable cortical incision. The aneurysm is then appropriately dealt with and the wound closed. This operation may very conveniently be performed under hypothermia.
- (3) *Subtemporal decompression.* If following aspiration or evacuation of an intracerebral hæmatoma the brain is tight from œdema, a subtemporal decompression may prove life-saving. A vertical incision 4" in length is made 1" in front of the external auditory meatus on the side of the hæmatoma. The muscle is incised in the line of the skin incision and a circular piece of bone of 2—2½" in diameter is removed revealing the dura under tension. This is opened and can be left open if the brain is very swollen. The wound is then closed in layers.

The following small series of cases were admitted during a period of 18/12 to a neurological unit and a neurosurgical unit which were associated. They were considered to fall into the category of intracerebral hæmorrhage which has been described in the introduc-

tory paragraph. Those cases who died a short time after admission and were not amenable to surgical intervention and who could scarcely be regarded as treated conservatively were not included.

21 CONSECUTIVE CASES OF INTRACEREBRAL HÆMORRHAGE

Cause	Site	Age	Hyper-tension	Conser-vative	Opera-tive	Result	Time after onset
1. Aneurysm	Temporal	58	+	+	—	Recovered	
2. Spontaneous	Temporal	47	+	—	+	Recovered	
3. Spontaneous	Fronto-parietal	66	+	—	+	Recovered	
4. Spontaneous	Frontal	78	+	—	+	Died	22 hrs.
5. Aneurysm	Temporal	48	—	—	+	Died	3 days
6. Trauma	Frontal	14	—	—	+	Recovered	
7. Spontaneous	Frontal	74	+	—	+	Recovered	
8. Trauma	Fronto-parietal	10	—	—	+	Recovered	
9. Trauma	Temporal	26	—	—	+	Recovered	
10. Spontaneous	Frontal	44	+	+	—	Died	3 days
11. Spontaneous	Frontal	67	+	+	—	Died	11 days
12. Trauma	Frontal	49	—	—	+	Died	24 hrs.
13. Spontaneous	Capsular	60	+	+	—	Died	10 days
14. Spontaneous	Frontal	62	?	+	—	Recovered	
15. Trauma	Occipito-parietal	20	—	—	+	Recovered	
16. Trauma	Frontal	19	—	—	+	Recovered	
17. Trauma	Frontal & Temporal	35	—	—	+	Recovered	
18. Trauma	Fronto-parietal	62	—	—	+	Died	7 days
19. Spontaneous	Fronto-parietal	54	+	—	+	Died	10 days
20. Spontaneous	Fronto-parietal	58	+	+	—	Died	9 days
21. Aneurysm	Temporal	53	+	—	+	Died	7 days
CONSERVATIVE				6		2	4
OPERATIVE					15	9	6

With regards to survival rates the figures were not statistically significant in comparing the results of conservative and operative treatment but there was a trend in the direction of a favourable outcome from surgical treatment.

Assessment of the degree of improvement was necessarily subjective but there was an impression that function was materially improved by evacuation of an intracerebral hæmatoma.

The type of case comprising the spontaneous group is worthy of further investigation since the figures are of considerable interest, i. e. of 10 cases 5 were treated surgically and of these 3 survived while of the remaining 5 cases which were treated conservatively only one survived. With a small number of cases this can only be considered a pilot study but

should a larger series reveal a similar trend it might be recommended that a case of "cerebral hæmorrhage" in general practice or in the Medical Ward whose condition does not deteriorate rapidly should be submitted to further investigation.

SUMMARY

In this discussion the term intracerebral hæmorrhage is defined and includes intracerebral hæmatoma as well as hæmorrhage communicating with the C. S. F. pathways but excludes catastrophic hæmorrhages. The incidence, ætiology, and diagnosis of intracerebral hæmorrhage are reviewed. Management and neuro-surgical procedures, their aims and indications, are considered and the results of conservative and surgical treatment in a series of cases of intracerebral hæmorrhage examined.

ACKNOWLEDGEMENTS

We wish to thank Dr. A. M. Stewart-Wallace under whose care some of these cases were and also Dr. C. Riley for the pathological work involved in examination of this series.

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TABLE I
21 CONSECUTIVE CASES OF INTRACEREBRAL HÆMORRHAGE

Cause	Site	Age	Hyper-tension	Conser-vative	Opera-tive	Result	Time after onset
1. Aneurysm	Temporal	58	+	+	—	Recovered	
2. Spontaneous	Temporal	47	+	—	+	Recovered	
3. Spontaneous	Fronto-parietal	66	+	—	+	Recovered	
4. Spontaneous	Frontal	78	+	—	+	Died	22 hrs.
5. Aneurysm	Temporal	48	—	—	+	Died	3 days
6. Trauma	Frontal	14	—	—	+	Recovered	
7. Spontaneous	Frontal	74	+	—	+	Recovered	
8. Trauma	Fronto-parietal	10	—	—	+	Recovered	
9. Trauma	Temporal	26	—	—	+	Recovered	
10. Spontaneous	Frontal	44	+	+	—	Died	3 days
11. Spontaneous	Frontal	67	+	+	—	Died	11 days
12. Trauma	Frontal	49	—	—	+	Died	24 hrs.
13. Spontaneous	Capsular	60	+	+	—	Died	10 days
14. Spontaneous	Frontal	62	?	+	—	Recovered	
15. Trauma	Occipito-parietal	20	—	—	+	Recovered	
16. Trauma	Frontal	19	—	—	+	Recovered	
17. Trauma	Frontal & Temporal	35	—	—	+	Recovered	
18. Trauma	Fronto-parietal	62	—	—	+	Died	7 days
19. Spontaneous	Fronto-parietal	54	+	—	+	Died	10 days
20. Spontaneous	Fronto-parietal	58	+	+	—	Died	9 days
21. Aneurysm	Temporal	53	+	—	+	Died	7 days
CONSERVATIVE				6		2	4
OPERATIVE					15	9	6

Encephalitis Treated by Integrating Chinese Traditional and Western Medicine

By DR. HSU CHENG-WEN
Vice-Director of the Peking Children's Hospital

IT was a very hot morning. An anxious young couple were watching their 5½-month-old son, who had just been admitted to the Peking Children's Hospital. In a trembling voice, the mother asked, "Doctor, is he .. is ..?"

"We'll do everything possible," the doctor said reassuringly.

The child, Lin Chien-kuo, had a fever of 40.3°C. He was in a coma. The jaws were tightly locked. His limbs were making spasmodic movements and he had already stopped breathing several times. After a careful examination by traditional and Western-trained doctors, it was found he was suffering from type B Epidemic Encephalitis. He was in an extremely bad way. The next day, his temperature dropped suddenly, signifying a worsening of his condition. In the past, both traditional and Western-trained doctors would have considered the case practically hopeless. But the doctors of the Children's Hospital did not lose their confidence in saving the child. They adopted a plan incorporating both traditional and Western methods. The traditional doctors applied the methods of traditional medical science, while the Western-trained doctors used the modern medical science. The traditional doctors based their treatment mainly on the principle of the dialectical approach. They applied the four methods of diagnosis, namely: wang (judging from the patient's appearance), wen (smelling and listening), wen (inquiring) and chieh (taking the pulse), and judged by eight main symptoms, namely: piao (external), li (internal), han (cold), je (heat), hsu (insufficient), shih (excessive), yin and yang. The Western trained doctors helped with laboratory analysis and various emergency measures. Thus, by relying on each other's merits and making up for each other's deficiencies, the doctors of both schools tried every possible way to save the child. When Little Lin fell into a fit of convulsions, the traditional doctors at once applied acupuncture, one of the

methods of Chinese traditional medicine, in their efforts to relieve the child from this condition. When his breathing became difficult, the Western-trained doctors applied oxygen and gave him injections to help stimulate respiration. Meanwhile, a ginseng tonic (a traditional medicine) was given for the same purpose. The nurses kept a 24-hour watch over the child, and observed his symptoms closely. They discussed and studied his condition and complications, and took appropriate measures as occasion arose. When the child was unable to feed from the bottle, the nurses inserted a tube through the nostrils for feeding. They acted with great care and skill, knowing that any neglect or delay would aggravate his sufferings. When there was any sign of improvement, they breathed a sigh of relief. When his condition worsened, they quickly plunged into the fight again. After 16 days of persistent efforts, the child began to regain consciousness. The symptoms of type B Encephalitis gradually disappeared. On the 25th day, Little Lin was discharged with no after-effects whatsoever.

The Peking Children's Hospital has cured many patients by integrating traditional and Western medicine. Before they used this system, the average mortality from type B Encephalitis among the in-patients was about 20 per cent. Since 1955, when the system of combining the two schools was applied to type B Encephalitis, counting mainly on the Chinese traditional methods and prescriptions, the results have been encouraging. Mortality from such cases dropped from 6.7 per cent in 1956 to 5.9 per cent in 1958. In 1959, the entire staff of the hospital, inspired by the continuous leap forward in the nation's industrial and agricultural production, worked with even greater zeal and further cut down the mortality to 4.7 per cent.

The use of both traditional and Western medicine not only cures the sequelæ from type B Encephalitis,

(Continued on page 93)

NEW SULFA EFFECTIVE IN SINGLE DAILY DOSE

By A Special Medical Correspondent

A NEW form of the first modern chemical weapon against disease—the sulfa drugs—has proved effective in treating common bacterial diseases of children in a single daily dose.

The single-dose effectiveness presents two important advantages to patient and physician, according to a British scientist who carried out studies with the drug—Lederkyn sulphamethoxypyridazine—at the Royal Belfast Hospital for Sick Children.

The first of these, Dr. I. R. Wallace reported in the medical journal *The practitioner*, is that fewer side-effects such as nausea and vomiting were observed in children treated with Lederkyn compared to children given an older sulfa, sulphadimidine.

The second advantage is that the effectiveness of the drug in a single dose, compared to the need for administering the older sulfa at spaced intervals throughout the day and night, saves time on the part of the nursing staff.

In his study, Dr. Wallace treated 31 children suffering from such common diseases as bronchitis, tonsillitis and pneumonia with Lederkyn and a group of 30 children with similar infections with sulphadimidine.

He concluded that the drugs were equally effective in treating the infections and suggested that the lower incidence of side-effects with Lederkyn might be due to its single-dose feature.

"Children will tolerate medicine given once a day better than medicine given four times a day," he noted.

The first sulfa drug—sulfanilamide—was synthesized as early as 1908, but no one seemed to suspect its tremendous power as an inhibitor of bacterial growth. It was not until 1932 that German scientists uncovered the first sulfa used against human disease, which was tradenamed Prontosil.

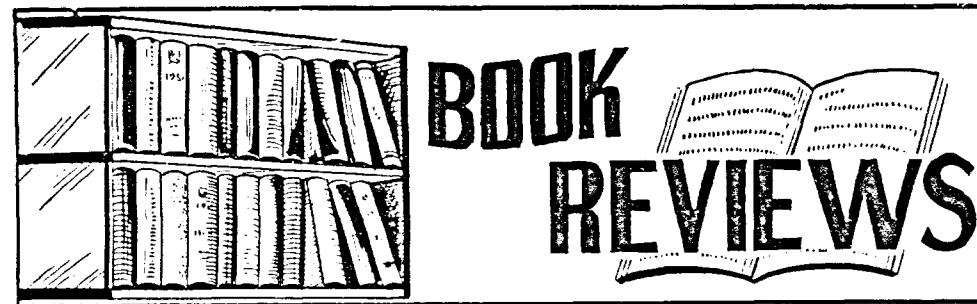
However, the advent of penicillin and later the broad-range antibiotics for a time threatened to eclipse the sulfas as weapons against disease. Scientific authorities were quoted as saying that the sulfas were "fading out of the picture".

Fortunately this pessimistic forecast proved untrue, and today physicians have available "super sulfas" like Lederkyn, which are more powerful at lower doses than their antecedents and which are free of the troublesome side-effects which once hampered the full effectiveness of the sulfa drugs.

(Continued from page 92)

but also reduces their incidence. Of 174 cases in 1958, nine had sequelæ, of which eight were completely or largely cured. In 1959, only two out of 102 cases developed sequelæ. In the past there was no way of dealing with these. Even if the child survived, he was often disabled or crippled, causing life-long misery to himself and great sorrow to his parents.

All the hospitals throughout the country are now treating type B Encephalitis by a combination of traditional and western medicine. They are also trying this approach on acute appendicitis, infantile paralysis and measles. The results are promising. Many children inflicted with these diseases have been relieved from pain and discomfort and restored to health.



A PRACTICE OF GENERAL ANÆSTHESIA FOR NEUROSURGERY

By Robert I. W. Ballantine with the collaboration
of Ian Jackson. J and A Churchill Ltd., London,
1960, Price 27 s. 6 d.

This 145 page book on a specialized subject is attractively produced by Churchills and contains 68 illustrations. It is divided into 11 chapters as follows: Chapter 1 on General considerations and problems is so brief and yet contains so much of value in it. Chapter 2 is on intracranial pressure. Figure 3 is an interesting table of examples of clinical conditions which may lead to cerebral damage by hypoxia and œdema. Chapter 3 is on premedication and anæsthetic technique. Chapter 4 is on different methods of lowering intracranial pressure. Chapter 5 is on controlled hypotension. Hypothermia is covered by Chapter 6. Chapter 7 and 8 deal with individual operations on the brain and on the spinal cord respectively. Chapter 9 is of general interest in that it concerns itself with the important problem of head injuries about which all medical men must necessarily know. Chapter 10 deals with radiological investigations. Chapter 11, again an important chapter deals with preoperative and postoperative nursing, care. I think Dr. J.E.A. O'Connell's admirable foreword sums up what the books is about. He writes "The pages do more than explain a technique, they reveal an attitude of mind. In the past, neurosurgical anæsthesia has appeared unattractive to some and was avoided for what was considered to be more rewarding work: the frequently long and sometimes dangerous operations no doubt partly explain this attitude. The present authors clearly regard themselves as being part of the neuro-surgical team, their interest in the patient commencing before his arrival in the anæsthetic room and being maintained after he leaves the operating

room. Preoperative assessment, supportive treatment during surgery and assistance with postoperative care have been accepted as among the anæsthetist's responsibilities. The value of such team work on the frontiers of surgery cannot be over estimated.

Truly this is a Bart's book and one should see the good work which is being done at the neurosurgical unit of St. Bartholomew's to appreciate the values of collaboration between the surgeon and the anæsthetists. The writer had the privilege of making this observations when posted there for anæsthesia training when he was a medical student at Barts.

The authors and publisher should be congratulated on this useful book and also Mr. N. K. Harrison of the Photographic department of Barts. Dr. A. M. Hall-Smith's drawings are very pleasing.

* * * * *

BLOOD TRANSFUSION: A GUIDE TO THE PRACTICE OF TRANSFUSION WITHIN HOSPITALS

By George Discombe, M.D., B.Sc. (Lond.) William
Heinemann Medical books Ltd., 2nd Edition,
1960. Price 6 s. net.

This 58 page booklet has a lot valuable material packed into so little space. The following subjects are dealt with. 1. The development of transfusion; 2. The regional transfusion centre; 3. Transport of blood; 4. Incompatibilities; 5. Avoiding errors; 6. Hæmolytic transfusion reactions; 7. Infected blood; 8. Other reactions and complications; 9.

Warming and freezing blood; 10. Indications for transfusion; 11. Organization within a hospital; An appendix considers The technique of ABO grouping, Rhesus grouping, The antiglobulin technique, Techniques for cross matching, Formulæ and practical notes and lastly Suggested record forms. This valuable booklet should be made available for ready reference wherever blood transfusions are being given to patients.

* * * * *

AN INTRODUCTION TO HUMAN BLOOD GROUPS

By Fulton Roberts, M.D., William Heinemann Medical Books Ltd., 1960, Price 9 s. 6 d. This 85 page booklet endeavours to clarify an extremely complex subject in which advances have been made. There are 13 chapters dealing with different aspects of the problem so:

1. Serological introduction; 2. The Rhesus factor; 3. Hæmolytic disease of the newborn; 4. Rhesus antibodies; 5. The Rhesus complex; 6. Some minor blood groups and their notation; 7. The MNS system; 8. The ABO system; 9. P and Lewii; 10. Blood groups and disease; 11. Blood groups and genetics; 12. Blood groups and anthropology and 13. Some growing points. The book has a bibliography and an index. The subject has been interestingly dealt with but it must be admitted that it will be of special appeal to those who have some specialized hæmatological knowledge and interest and not to the general practitioner.

* * * * *

BIOCHEMICAL VALUES IN CLINICAL MEDICINE

The results following pathological or physiological change By R. D. Eastham, B.A. (Cantab), M.D. (Cantab), D.C.P. Dipl. Path. John Wright and Sons Ltd., Bristol, 1960.

This pocket sized book of 144 pages attempts to provide an accurate summary of the ways in which various conditions effect many biochemical tests. The author is of the opinion that the clinician and the bio-

chemist should discuss the following subjects together: 1. clinical cases, 2. The methods of estimation used and 3. The ranges of normal values recognised by the particular laboratory.

It is not possible to review a handbook of facts and figures in detail but one example will, I think, illustrate the sort of material in this handbook. Take Urea for instance on P. 125. BLOOD UREA. Normal range 1. 1 week old 8—25 mg./100 ml. 2. Adult: 20—40 mg./100 ml. Physiological: Increase. The blood urea rises in normal people on increasing the protein content of the diet. Decrease. 1. The blood urea concentration is lower in the growing infant than in the adult. 2. During normal pregnancy the mothers blood urea is low. It is probable that in these two cases the amino acid nitrogen is immediately reconstituted into new protein and is therefore not treated as a waste product. 3. Normal person on low protein, high carbohydrate diet. This is the basis of conservative treatment of anuria. Pathological: Increase. 1. Excessive formation. a. High protein diet. b. Excessive body protein catabolism eg. fever, sepsis. 2. Faulty excretion. a. Prerenal failure. A low renal blood supply leads to reduced glomerular filtration eg. as in congestive cardiac failure. b. Renal failure. Damage to nephrons leads to faulty urine formation and excretion eg. Nephritis pyelonephritis etc. N.B. In the absence of pre and post renal failure the blood urea only rises after extensive damage has occurred i.e. less than 800,000 intact nephrons remaining. Obviously the rate of development of damage will be important, since slowly developing damage will allow some compensation to occur. c. Post renal failure e.g. urinary tract obstruction.

If you think this sort of information is useful in clinical practice, the book is full of the various types of biochemical investigations which are used by clinicians.

* * * * *

A SYNOPSIS OF PUBLIC HEALTH AND SOCIAL MEDICINE

By A. J. Essex-Cater, M.R.C.S., L.R.C.P., D.C.H., D.P.H., D.I.H., F.R.A.I., John Wright and Sons, Bristol, 1960, Price 55 s.

This book of 553 pages is made up of 17 chapters. Chapter 1 deals with The Health Services (in U. K.).

Chapter 2 is on History of Public Health and Social Medicine, Chapter 3 is on Medical Statistics. Chapter 5 deals with Epidemiology. The major causes of death is dealt with in Chapter 5. Communicable diseases are dealt with in Chapters 6 and 7, the first dealing with the bacterial and the second the virus diseases. Occupation and Health is the subject for chapter 8. Chapter 9 is on specific occupational disorders. Chapter 10 is on food and 11 on environmental health. Chapter 12 is on the Welfare Services. Chapter 13 is on Maternal and Child Care and under this head the following things are discussed: Antenatal care, Midwifery, Maternal mortality, Maternal morbidity, illegitimacy, Infertility, Care of the newborn infant, Infantile mortality, Prematurity and Infant welfare. Chapter 14 concerns the child at school and 15 the

Neglected child, an important problem. Chapter 16 is on mental health and chapter 17 on other aspects of public health and social medicine. An appendix contains a report of the working party on Social workers. The synopsis book is well got up and it is intended as the preface rightly states, for undergraduate medical and social science students, postgraduate students preparing for the Diploma examinations in Child Health, Public health, and Industrial health, nurses and other workers in ancillary interests. Like other synoptic volumes this work cannot replace standard textbooks; it is intended to be used in conjunction with them, as a means of quick revision and as an outline for persons not required to make a detailed study of the whole field of Public Health and Social Medicine.

HORMONE RELIEVES ASTHMA SUFFERERS

It looks as if medical science is well on the way to finding a cure for asthma. And the cure could easily be in the form of a new steroid hormone.

For according to a recent scientific report, fifty patients suffering from chronic bronchial asthma who could not be helped by any previous form of therapy all obtained relief when given a new steroid hormone.

Writing in the "New York State Journal of Medicine", Drs. Louis Levin and Emanuel Schwartz, both of the College of Medicine, State University of New York, detailed their experience with the hormone, called Ledercort triamcinolone. The patients received the hormone for between one and nine months.

"These patients were selected because previous available therapy had failed, and there was no other source of help," the physicians wrote. "These patients, for the most part, had suffered from chronic intractable bronchial asthma for years."

Ledercort was given by mouth in doses determined by the minimum amount required to relieve the patient of the wheezing and breathlessness characteristic of severe asthma, Drs. Levin and Schwartz explained. In most cases the doses were substantially lower than those required with older steroids.

The physicians stated that in those patients who were free of symptoms and remained so, the treat-

ment was regarded as excellent. If the treatment freed the patient from most symptoms, with only an occasional recurrence, the result was listed as good. Fair results were attributed where there still remained some wheezing, but where the amount and severity of symptoms "was so much less than the patient had been experiencing that the patient was very well satisfied..".

Drs. Levin and Schwartz reported that 52 per cent of the cases treated had excellent results this basis, 40 per cent good results, and 8 per cent fair results. In no instance was the response poor.

The New York physicians noted that in cases where the patient had been "futilely seeking relief, the administration of triamcinolone with the subsequent dramatic improvement in his condition gave the patient such a new and bright outlook that he co-operated enthusiastically in undergoing a complete study and search for the factors causing his asthma".

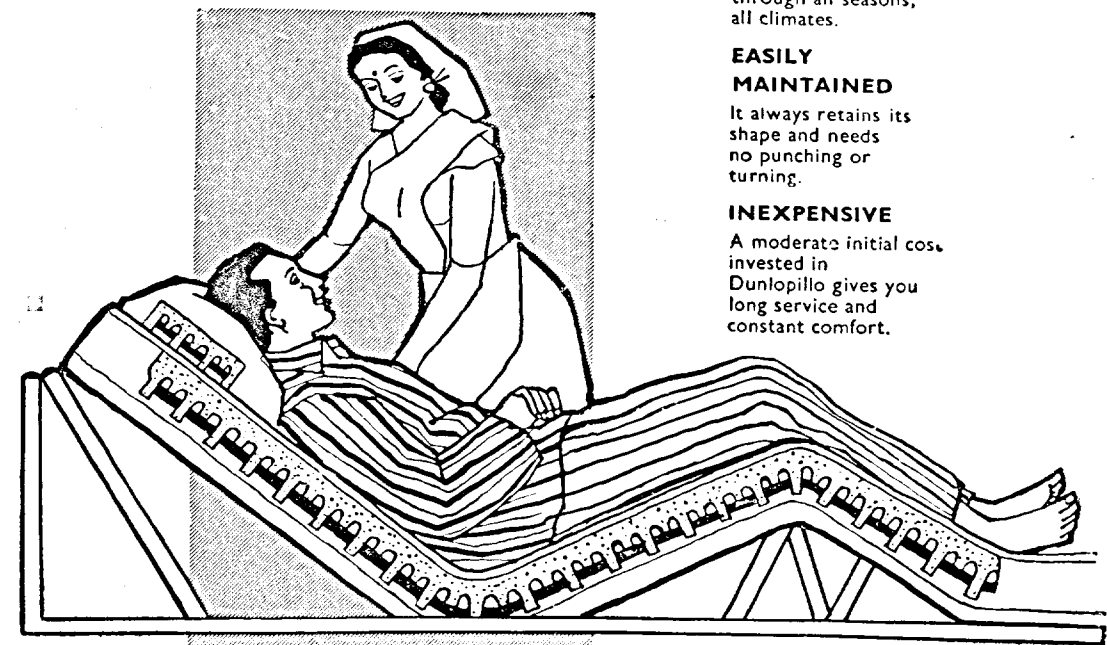
"This, after all", they declared, "is of prime consideration".

In conclusion, Drs. Levin and Schwartz stated that Ledercort is a useful drug in the management of chronic bronchial asthma because satisfactory relief of symptoms can be obtained with comparatively small doses. Also important, they added, was "the infrequency of severe side-effects".

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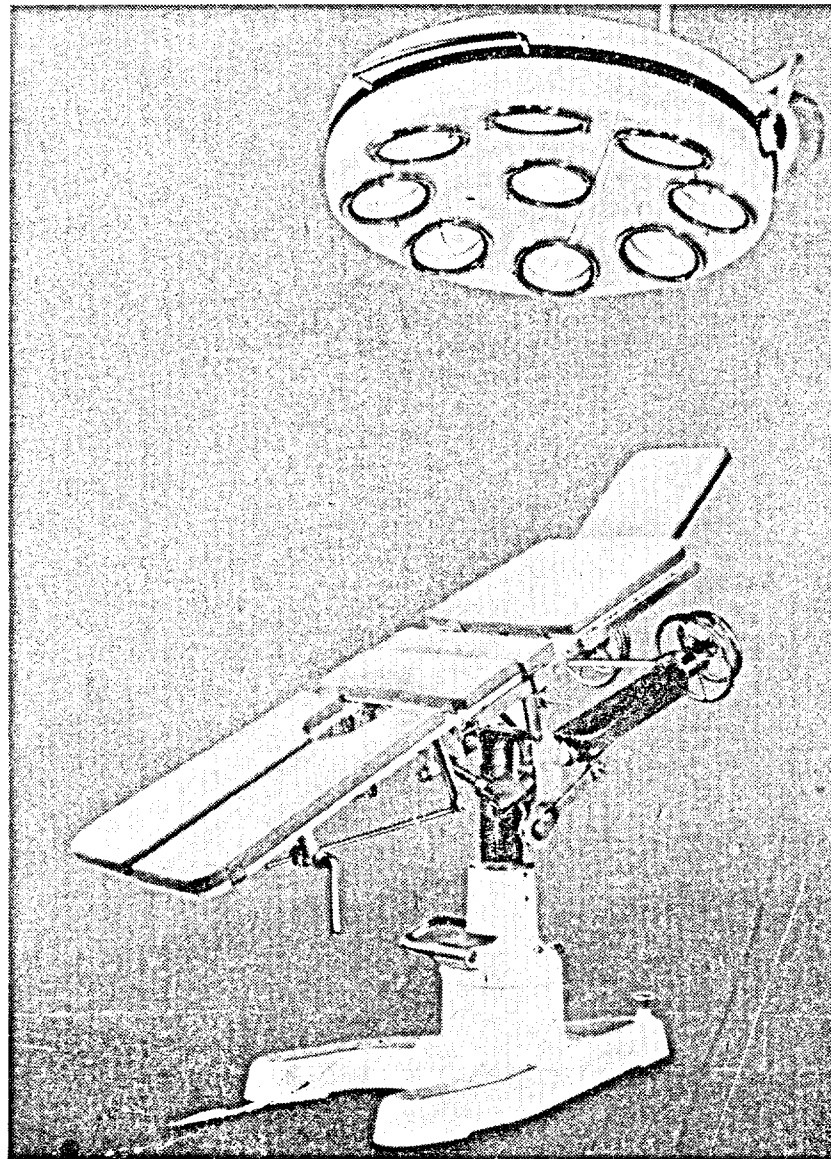
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