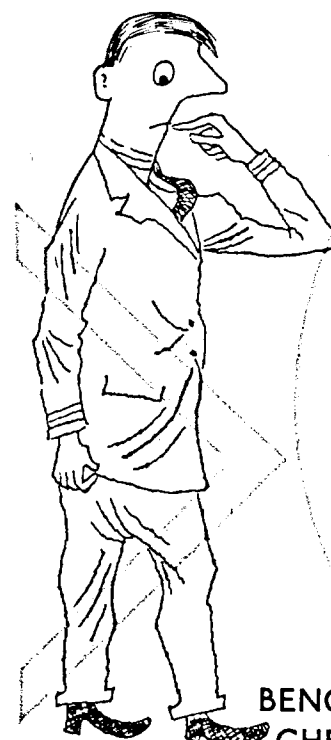


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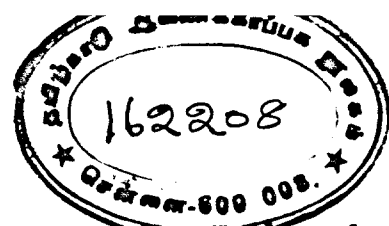
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Medical Colleges—The Basis for Selection of Students

“THE opening up of more medical colleges is not a real solution when more medical graduates are urgently required by the country. Going through the results of many medical colleges, one is surprised that only 10 to 20% of students pass through the entire course without a failure” said Dr. Rathnavelu Subrahmaniam giving his Chairman’s address at the All India Association of Physicians held in Madras on 13th January 1961. He attributed this to the disproportion in the ratio between the teacher and the taught as compared with the Western institutions. Efficient checks on the attendance and day-to-day progress of the students are very essential to ensure systematic and regular studies and application among the students. He was all in favour of conducting a series of periodical tests and clinical examinations with penalties for non-attendance and poor performances.

Making an editorial comment on this in Antiseptic, Dr. U. Krishna Rao stressed that admissions to the medical course should be made by stricter and more rational methods than obtained at present. This matter has been discussed frequently at various levels and the consensus of informed opinion would appear to be that instead of a strict adherence to definite principles based on merit and aptitude, other considerations which in effect run counter to the desirable modes of selection, come into play with the result that during recent years students who cannot cope with the arduous medical studies enter the college and are unable to leave it with the degree in anything under six or seven or even eight years.

In days gone by applicants to Medical Colleges were few and the number of places abundant that the problem was not of obvious misfits. To-day the number of candidates seeking a seat in a medical college is so great in relation to the number of available places that selection has become a grave problem. Who should be given a place and who forbidden?

The men who sit in judgment on the selection committee are entrusted with a great responsibility and an unenviable public duty to discharge. Faced with a hoarde of expectant candidates and a relatively short time to interview them, the Committee had to decide who they would admit and who they would bar. To say to some aspiring student of medicine ‘You may not enter medicine’ is a very serious thing; and any error of judgment would be the height of social injustice.

To accept some candidate who subsequently turns out to be unsuited is not so catastrophic because he gets to abandon it at some stage or other, may be often with less of a smile than the women students do when they find marriage a pleasurable alternative.

What are the motives for anybody taking to medicine as a profession to-day? With the paucity in State endowments and scholarships, the fast dwindling fortunes

of the middle class families and the great length of the course, it must be a brave and resolute person who embarks on this exacting study. A desire to study medicine must be backed by the command of adequate financial resources to achieve the end in view, assuming that it is possible to satisfy the selection board.

On what basis should selections be conducted? What qualities should a candidate possess to secure admission to a medical college?

It was my great good fortune to be present at the First World Conference on Medical Education sponsored by the World Health Organisation and held in London in August 1953. At this conference Medical Educationists from all over the world came to present their views on the different aspects of medical education, and it was to the great credit of India that the Vice-Chancellor of the Madras University Sir Arcot Lakshmanaswamy Mudaliar was one of the Vice-Presidents. My own teacher Sir Lionel Whitby in his Presidential address to the conference speaking of the qualities desirable in the ideal medical student, irrespective of the part of the world from which he might come, said, “He must be cultured, broadly educated in the Humanities, intelligent and intellectual, of transparent integrity and sympathetic, and, above all, one who will love his profession as well as his fellow men and all their weaknesses, their joys and their sorrows.” Sir Lionel himself confessed that not all students can attain such an ideal but all should have at least some of these qualities either inherent or capable of development—without it, however well the teaching may be, no man can benefit by it.”

There are two factors on which a candidate should be assessed. They are:—

- (a) Intelligence, and
- (b) Emotional stability.

By intelligence is not meant the sort of power by the use of which a candidate has the knack of passing examinations with marks ranging down from the maximum. Intelligence means an agile mind capable of abstract thinking, able to make logical deductions, to make observations of facts and critically analyse them. The candidate should be mature enough to think for himself, to judge for himself, and at the same time be humble enough to want to seek knowledge—for without this, no healthy pupil to teacher relationship can exist. Intelligence can be assessed to some degree by previous records at schools and colleges where men of integrity have judged the candidates; and further completed by personal interview combined wherever feasible by an intelligence test.

The candidate should be questioned carefully on the motives which prompted him to seek a career in medicine. In many cases it may have been parental pressure (the father may be a doctor and cherish the hope that the son will follow in his wake), or it may be social vanity, or just a desire to do something little knowing what the career implies.

Any one who has the illusion that one can make money in medicine should be dis-illusioned, for a man who makes money in medicine, would probably have made equally as much, perhaps many times as much, in any other walk of life. Some candidates may be led to think that medicine is glamorous (who can fail to be impressed by the popular film or story book version of a famous surgeon performing a heroic life saving operation taking all the credit for himself). Perhaps some are confirmed in this belief when they find that a prospective father-in-law in his quest for an eligible bridegroom having failed to land an Indian Administrative Service boy turns his search to the Medical College! Some are carried away by the craze for speciality which having ceased to be a paying proposition in the West is beginning to wane in India also, but for totally different reasons. Besides, how precarious must be the hope of entering a speciality these days with so many obstacles scattered in an already difficult path. Some there are, who, while accepting that India is perhaps one of the few countries where the young doctor gets a raw deal for all the energy and devotion and the many years he spends on study to qualifying for a medical degree, find satisfaction in knowing that there are other professions much worse of: this very feeling might motivate some to take up medicine.

At an interview a candidate's claims of having a high personal integrity or the possession of a special philosophy or aptitude can be assessed and dismissed for what it is worth.

Certain qualities there are which an understanding person may assess by talking to the candidate for a half hour. Does the boy (or girl) have common sense, resourcefulness, persistence, energy, a real interest in the subject and a sense of humour (this last being quite a valuable attribute)? Does he possess a stable temperament governed by reasonable optimism? Does he have an objective sympathy with human problems? Does he show a willingness and ability to express an opinion which can be understood quite easily by men in all walks of life? All this is comprised in the word "Personality" and the assessment of Personality is a very important factor in choosing prospective medical students. If one means all this by "Personality" surely the increased recognition that is given to this aspect is a laudable step in the right direction.

The boy who is very shy and non-communicative, the swank, the egoist, the aggressive and the mentally immature lacking in confidence are obviously unsuited to take up medicine because these qualities would adversely affect the future relationship with patients.

The time has surely come when we in India must attach less value to performance in examinations as a sole criterion for assessment of eligibility. *Nor should caste, creed or community a person belongs to the language or languages that he may speak, make any or difference to selection of the right candidate.* Let us concentrate all our effort to recruit to the medical profession those who are likely, first and foremost, to be worthy and useful citizens; and only next as people who by their special training and knowledge are able to put into use those skills to prevent disease and to relieve suffering.

ACCIDENTS AND THEIR PREVENTION

A STATEMENT BY DR. M. G. CANDAU
Director-General, World Health Organization

IN the world today, accidents cause more death than any single illness except cancer and cardiovascular disease. In many countries accidents kill more children from 5 to 19 than all other causes combined. They take a greater toll in young lives than any war the world has yet known.

Yet accidents have been less studied than has any fatal disease of equal gravity. It is only recently that scientific research on this subject has been undertaken.

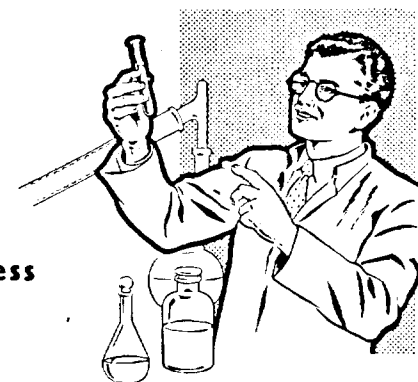
Too many people still unthinkingly accept accidents as misfortunes over which the individual has no control. "Accidents will happen", they say, as if that excused everything. Yet whenever studies are made of accidents in home or school, on the road, in

factory or farm, or of any other sort of accident, ways can always be found to reduce their number and seriousness.

Accidents are not chance events, they do not just "happen". Every one of them is the outcome of a chain of causes and most of them can be prevented.

There is evidence that the majority of accidents happen in situations which are generally thought to be "safe". About half of all accidents happen in the home, and children are the principal victims. Two-fifths of all fatal accidents to children between one and four years of age take place in or around the home. Prominent causes are burns and poisoning which, even if not fatal, are generally serious. Yet

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almost all could be avoided by a little extra vigilance and a few simple precautions.

A thousand people a day die on the world's roads—half of all accident deaths. Road accidents are the most talked-about and most written-about of all, yet little is really known of the multiple factors which interact to produce them. In only one or two countries have present prevention measures done more than stop the road accident rate from rising faster than the increase in vehicles or miles driven. Much more needs to be known about the principles underlying road safety.

Occupational accidents have been more thoroughly studied than any others, and in many industries strict safety regulations are enforced. Notwithstanding this, in the United States of America alone it is estimated that in 1959 the working time lost because of accidents was 220 million man-days.

Here then is one of mankind's greatest scourges. Yet in our era of scientific progress, we have scarcely begun to think about combating it.

Accidents have more in common with diseases than the simple fact that both can be deadly. The epidemiological methods used to study the distribution of disease can usefully be applied to accidents, but uniform methods of accident reporting must first be adopted. It will then become possible to define the situations in which they are likely to occur, in the same way as for the etiology of diseases.

It is not suggested that such research is easy, but it can and must be carried much further than at present.

In the meantime there is still much that can be done. Most countries already have a safety code for road

users; they have legislation intended to reduce occupational accidents and also, in some cases, regulations concerning the safety of home appliances, electric fittings, and so on.

The best present hope of accident prevention is certainly through safety education. Innumerable accidents are due, at least in part, to some action or omission on the part of the victim himself—the pedestrian who crosses the road without looking; the boy who tries to change a fuse without turning off the current; the workman who fails to observe the factory's safety rules. Safety should, of course, be taught in schools, but also in factories, on the farm, and, perhaps most important of all, in the home.

In economically developed countries some progress has now been made—accident statistics are recorded, although not in a uniform way; there is some safety legislation; there are accident prevention societies with active local committees; and education against accidents has begun.

But what of those countries in the process of rapid industrialisation, which do not yet have any statistics to guide them, where legislation is insufficient or not enforced and where the idea that anything at all can be done to prevent accidents is accepted only by a few? To them I would say: face up to this situation and act quickly, avoid the bitter mistakes made in countries where industrialisation began more than a century ago, and profit from the knowledge which they are now beginning to accumulate.

On World Health Day 1961, I would urge all peoples, whatever their stage of economic progress to open their eyes to the plain fact that accidents have now become a leading cause of death, disablement and economic loss, and to realize, once and for all, *that accidents need not happen.*

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You merely have to touch the body with one end of this thermometer, and the needle on its dial will immediately show the right temperature. Its pinpoint end is so small that, if need be, one can measure the temperature of a fly's eye. These properties make it possible to use the semi-conductor thermometer for biological research. The new thermometer has also been approved by medical workers, and with slight

modifications the new instrument will be used for the investigations of the internal organs of the human body.

The new semi-conductor thermometer was designed by Leonid Sterin, research worker of the Laboratory of Automation and Remote Control, Mining Institute, Siberian Branch, USSR Academy of Sciences.

THE FACTORY'S BEST PRODUCT IS ITS SAFETY

BY AN AUTHOR FROM W. H. O.

Each year in Europe, between one-ninth and one-quarter of all workers have a disabling accident. The proportion varies naturally in different places and different industries. Out of 10,000 workers, from one to four—and sometimes as many as 10—die as a result of accidents.

In the United States of America, out of a total of 91,000 accidental deaths from all causes, 14,000 are due to industrial accidents. In the same country, two million workers annually have occupational accidents resulting in incapacity for work. The number of work days lost in this way was estimated at 230 million in 1959, and the corresponding economic loss at \$ 4,200 million.

In France, a serious accident, causing death or permanent invalidity, occurs every two minutes, and even a small country like Switzerland has an annual toll of more than 200,000 occupational accidents of which between 300 and 400 are fatal. The number of work days lost annually is estimated at 8.5 million.

AN analysis of all types of industrial accident shows that only one in eight is caused by machines. Vehicles, electricity, sources of heat and similar causes account for one-quarter of the total. More than half is made up of what a British expert, Mr. W. T. McCullough, Chief Inspector of Factories, has called the Big Five: (1) falls from a height; (2) falls on the level; (3) handling of materials, etc.; (4) falling objects; (5) hand-tools. One technician has even claimed that today there are fewer risks in manufacturing nitro-glycerine than in transporting a heavy crate.

“DANGEROUS SITUATIONS”

“When dismantling a bench on which for years a large gas-ring had been fixed, it was found that underneath the asbestos sheet on which the burner stood, the wood of the bench was charred right through. The asbestos had been fixed tightly to the wood and had conducted so much heat to it that a sudden draught of air could easily have started a fire.”

Every day from the 110 factories and works of one of the largest chemical firms in Britain, a sheaf of pink report forms arrives on the desk of Mr. J. St. Brown, who is head of its Safety Division. Each reports a “dangerous occurrence” in which an accident

might easily happen. Copies of these reports are circulated to the Safety Committee in each of the company's factories together with precise recommendations in each case. For the situation described above the directive was: “A free space should always be left between the asbestos sheet that isolates a heating system and any inflammable material that it is supposed to protect”.

The results of this company's far-sighted policy speak for themselves. Among the 73,000 workers in the 110 factories for whose safety Mr. St. Brown is responsible, there were in 1959 only 386 accidents causing temporary absence from work, nine serious accidents and five fatal accidents. These were the lowest figures in the company's history, and showed more than 80 per cent improvement on the 1945 figures and 25 per cent on those for 1957. Such spectacular successes in the fight to reduce accidents are unfortunately rare.

THE NEED FOR BETTER STATISTICS

On the national scale it is much more difficult to collect such exact information as this. As Mr. Marcel Robert, Chief of the Occupational, Safety and Health Division of the International Labour Organization (ILO), said recently: “In compiling statistics, an accident is generally attributed to only one cause, the

most obvious one. In the great majority of cases this is completely misleading because potentially important accident factors are left out of account".

Nevertheless statistics are valuable, and are indeed indispensable for measuring the success of preventive efforts and discovering the weak points to which these efforts should be directed.

One ILO report published shortly after the last war showed that during the years 1939-1945 industrial accidents in the United States of America and the United Kingdom had killed more people than the war itself. Yet these two countries were already at that time leaders in industrial accident prevention.

A study of industrial accident rates since 1938 leads to the unexpected conclusion that in many industrialized countries the present situation shows little if any improvement over that existing before the war. Even in the United States and the United Kingdom the improvement between 1938 and 1958 is only 38 per cent.

In countries which are in the process of rapid industrialization on the problem of accidents has been growing increasingly important.

In India, for instance, the accident rate has increased from 100 to 240 between 1938 and 1958.

MAKING ACCIDENTS IMPOSSIBLE

Two different tendencies have developed in efforts to improve industrial safety. One is towards more and more detailed legislation and measures to improve the physical conditions of work. An English safety engineer recently said: "It is my job to see that even the clumsiest and least intelligent of our factory hands runs no risk of an accident".

The other tendency is to lay stress on the importance of education. According to partisans of "Education first", the evidence shows that a "human factor" is involved in more than 80 per cent of occupational accidents, and that therefore preventive measures should rather be directed towards the worker. Moreover, they say, when legislation and inspection procedures become too complex and cumbersome, they are no longer respected.

These two approaches are of course complementary. No accident is entirely due either to an outside cause or to a human failing. Most experts on the question agree today that industrial accidents, like all other accidents, have multiple causes.

"Most of these", says Professor Victor Raymond, Medical Adviser to the French *Institut National de Securite*, "are potential causes, they exist only as possibilities. No accident will actually happen unless in one given place and at one given moment, the different potential causes come into operation together."

One day at a certain moment a man falls into a hole. The hole is certainly a cause of the accident, for had there been no hole there would have been no accident. Yet it is only a *potential* cause, for plenty of people pass by unprotected holes without falling in. The man may also carry within himself certain potential causes of accident—for instance, a liability to feel dizzy or to day-dream—but this does not mean that he falls into every hole that he comes to.

THE "FATAL ACTION"

For the accident to cease to be potential and become actual, there must be this conjunction between the victim and the material cause, which supposes a precipitating factor. These factor, which determines or precipitates an accident, may be independent of the victim, as for instance in the case of a falling stone or other object, a plank that gives way, or machine that breaks down. But in a large number of cases, this factor is simply a movement or act of the victim himself. For this, Professor Raymond has coined the phrase "*le geste nefaste*"—the fatal action.

Most frequently, this fatal action is an uncorrected conditioned reflex. By their very repetition, many work movements become stereotyped. The man becomes a kind of robot, slave of the machines and objects he works with. His work movements become mechanical, and always follow the same pattern. Now suppose that the machine or the objects the worker is concerned with suddenly present some departure from the usual pattern. Unless the worker's conditioned reflex is quickly corrected, the "fatal action" will be made.

Fortunately for him, the human being possesses protective mechanisms against these "fatal actions".

First there are the primary reflexes which produce an "instinctive" withdrawal from a danger usually perceived through the sense of touch. Conditioned reflexes can also produce similar protective reactions. "Once bitten, twice shy" says the proverb—reaction to fire is the classic example. A child who actually touches a burning object will withdraw his hand by a primary reflex action. An association between the sight of fire and the sensation of burning is established, and a conditioned reflex is created which lasts throughout his life. Whenever he sees a burning object getting too close, he withdraws.

Such protective reflexes can be developed by creating associations between a danger and certain sights and sounds—warning by sirens or bells, and, very important, notices and labels.

Finally the instinct of self-preservation that everyone possesses can be strengthened and trained so that it corrects, checks or co-ordinates habitual actions and prevents them from becoming "fatal actions".

BUILT-IN SAFETY

Unfortunately this instinct of self-preservation cannot be relied on absolutely—there will always be occasional eclipses. Much can be done, however, to limit their effects by technical and mechanical safety measures. To be effective such measures should protect all workers alike and should require no effort or co-operation from the individual. They are based on the elimination of all risk. An example is the prohibition of the use of white lead in paint, which has automatically prevented white-lead poisoning among the people working with paint.

If safety devices are built into machines, fewer precautions are needed when using them. Of course the workers know about these safety devices and their role, and it sometimes happens that they resent them because, they say, they complicate their work. Therefore they sometimes remove them or put them out of action, temporarily or permanently. Machines should always be provided with an automatic stop that operates whenever its safety devices are not working. The less such a device interferes with the

worker's habits, the more easily it will be accepted and used by him.

These safety measures are collective in nature and do not require the co-operation of the individual worker. There are others which do require his more or less active participation. As we have seen, this is often problematical and such measures, even though necessary, are therefore less reliable.

VAGUE UNINFORMED FEARS

It is difficult enough to obtain even the worker's passive co-operation, for instance, in following certain rules, or going for a medical check-up. If he is asked to take more active precautions, like wearing gloves, special glasses or a mask, experience shows that the results are usually unsatisfactory.

It is of the first importance that each worker should know and understand the risks to which he is exposed. Instructions must be complete, detailed and precise in order not to create simply a vague, uninformed fear of accidents. For example, everyone knows vaguely that electricity is dangerous, but what is important is to know how dangerous and in what way. It is not enough for someone to know the dangers of lightning, or of high tension currents, if he does not realize the dangers of the common 110 volt or 220 volt household electricity supply.

Again, it is not enough just to tell people about such risks—they must really understand their nature. It is for this reason that too much dependence cannot be placed on rules, warnings, "forbidden" notices, etc. They become so familiar that after a while they have no further effect in preventing the "fatal action".

None of these "individual" safety measures can be really effective unless the person it is intended to protect is made to feel a partner in the scheme, and this will depend largely on the attitude of the works manager. He must set the pace. If he is genuinely concerned about safety measures, the engineers and foremen will follow suit, and the accident rate will soon reflect the success of their combined efforts.

100,000 Doses of Polio Vaccine to India

Mr. I. A. Benediktov, Ambassador of the USSR to India, handed over to Mr. Karmarkar, India's Health Minister, 100,000 doses of polio vaccine. This vaccine will be used for vaccination among the population in the state of Andhra Pradesh. The vaccination will be done with the help of Soviet doctors working at present in the Kalavati Saran Children's Hospital, the Research Practical Pediatric Centre in New Delhi.

GREEN LIGHT: GO FOR ROAD SAFETY

(A W.H.O. Feature)

Nine out of ten road accidents are the driver's own fault and only one in ten is due to defects in the car or the road. This frequently-heard statement may serve to awaken drivers to their responsibilities, but it is of little help to anybody making a serious study of traffic problems and traffic risks.

The truth is, of course, much less simple. Any traffic accident depends on three main factors—the driver, his vehicle and the road—although the degree to which any one of these may be involved will vary. There are certain subsidiary factors too, some constant and some not, which may be difficult to assess but which must nevertheless be taken into account.

THE part played by speed, for instance, has long been greatly over simplified. There is evidence that, taken over a driver's total mileage, most of his accidents on modern highways occur at the lower operating speeds. The proportion of accidents per driver drops with increasing speed, reaching its lowest value at about 65 m. p. h., but rises sharply again at higher speeds. It is true that accidents at high speeds are far more serious. However, the number of injuries on a miles travelled basis is at its minimum between 45 and 70 m.p.h. The fact that moderately high speeds are associated with lowest accident rates on highways should lead to the setting of more realistic speed limits.

Not all discoveries made in this field are quite so unexpected, and many of them confirm everyday experience. It has long been known that in all countries twice as many accidents occur at night as during the day, and that dawn is the most dangerous time of all. The holiday peaks in road accidents are recognized facts but no one has yet discovered the real reason for them. Investigations have shown only that the average number of accidents at holiday periods is 25 per cent greater than at other times, *even if all other traffic conditions are the same.*

It is also known that there are now fewer road accidents involving pedestrians than there were 25 years ago, and a number of reasons may be advanced for this. People walk less nowadays and many pedestrians are drivers as well and are more aware of the dangers; road signals are also better, both in towns and on the open road.

WHAT ROAD ACCIDENTS COST

The cost of accidents has been assessed from every angle. In the United States the Press has given wide publicity to the loss to the American economy from road accidents. Expressed simply, this amounts to a loss of a little over 2 dollars per mile of road, 116 dollars per car registered or 12½ cents per gallon of gasoline used.

But how to assess the economic loss due to the premature death of young drivers, at the beginning of their most productive period, for they are the primary victims of traffic accidents? Some 75 per cent of fatal accidents involve men; what are the effects on a family of the death of its bread-winner?

The answers to these questions are still not known—but basic research is being carried out in most countries of the world.

The Road Research Laboratory in Great Britain is by its very nature an organization admirably fitted to study certain of these problems. It has a traffic and safety section doing research on roads, vehicles and their users, an economic and statistical section, and a section dealing with road-building materials and methods. The great advantage of this organization is that all these aspects are centralized instead of being split up among different administrations, as is so often the case.

Among the first problems studied by the Road Research Laboratory have been the intensity and

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characteristics of traffic of different types, public lighting and skidding.

A large number of automatic counters are in continual operation to measure the distribution of vehicles on the roads. Observations from fixed points and from moving cars, as well as aerial photographs, are used to study cross-roads and roundabouts, to measure how often and how fast pedestrians cross the highway, and to assess the types and speeds of different road vehicles. An electronic brain gives precise information on the effect of traffic lights on the flow of traffic at cross-roads.

The Road Research Laboratory also undertakes statistical analyses of the effect of different types of road junctions, compares the frequency of accidents before and after changes in the design, surface or lighting of a road, and studies the influence on accidents of speed limits, pedestrian crossings, the removal of tram lines, the construction of double carriageways, etc.

Intensive research is being carried out on street lighting and road surfacing. Most objects in a lighted street are seen as silhouettes outlined against the road. The type of surface greatly influences the way the light is reflected, a rough surface giving a more even luminosity, with fewer highlights, than a smooth one, particularly when the road is wet.

MAKING ROADS SKIDPROOF

The most remarkable work of the Road Research Laboratory has perhaps been in connection with road surfaces and skidding. Step by step each aspect of road surfaces is minutely examined to reveal defects and show the way to improvements.

More than a thousand tests are carried out every year on wet roads (a wet road being more slippery than a dry one) in a car equipped with a fifth wheel connected to a special recording device. A portable apparatus has been devised by which road engineers or public works departments or firms can measure the skid-resistance of roads without having recourse to laboratory studies. Tests have also been made with a car travelling at different speeds over a surface covered with a thick film of water.

A number of sections of roads, selected to be as representative as possible of the British road network,

has been tested every fortnight for three and a half years. As a result it has been possible to measure, and to some extent to predict, seasonal variations in the skid-resistance of roads.

The summer months appear to give more trouble than the winter, for when a road which has long remained dry is moistened by a sudden shower, it becomes infinitely more slippery than one subjected to regular rains. After the cold, wet summers of 1956, 1957 and 1958, there was a quite exceptional drought in the British Isles starting in May 1959. The Automobile Association, advised by the Road Research Laboratory, was able to warn road-users that the slightest rain after the beginning of August would make roads far more slippery than they had been for three years.

The Road Research laboratory has also come to the conclusion that special non-skid surfaces could become more slippery than smooth surfaces if the sharp edges of the gravel used in them became worn down. Far from improving the grip of tyres on the road, they would, on the contrary, act like smooth beads and increase the risk of skid. Even the best of surfaces, of course, will not prevent an accident caused by weak braking or worn tyres.

Research probes into each accident factor separately but the final solution must be a function of all the factors involved. At the Road Research Laboratory the behaviour of a vehicle and the qualities of the road itself are, therefore, studied in close conjunction, one of the essential aims of the work being to ensure that in an emergency the driver of a car can pull up in the shortest possible distance without danger to himself or to others.

But the ideal is still a long way off. The first studies carried out by the Road Research Laboratory showed that the average braking distance for a car travelling at 30 m.p.h. is 75 feet; for 10 per cent of the cars tested it was over 100 feet. The Highway Code lays down a distance of 45 feet. Moreover, when a driver brakes in an emergency the wheels frequently lock, and this not only upsets the stability of the car but reduces the effectiveness of the brakes to zero, the course of the vehicle being slowed down only by the resistance offered by the road.

A number of attempts have been made to find a way of preventing wheel-locking. R. D. Lister and R. N.

Kemp have carried out a long series of tests on a car fitted with a device, known as "Maxaret", which is used on aircraft. They conclude that it considerably shortens the braking distance, particularly on wet roads, and gives greatly added stability to a car, even with worn or badly-adjusted brakes.

Other experiments have conclusively shown the importance of tyres for road safety. It is common knowledge that worn tyres are highly dangerous, but few people realize that a complicated tread is of no particular advantage. All that matters is that the tread be deep.

One new discovery made by the Road Research Laboratory in cooperation with Dr. D. Tabor of Cambridge University, is that highly effective non-skid tyres can be made of what is known as "dead" rubber. This rubber, which was once a source of despair to the manufacturers, has the characteristic property of absorbing a considerable amount of energy when subjected to strain.

This is one example of the value of "pure" research carried out with no immediate profit or application in view.

WHAT ABOUT THE DRIVER?

Finally there is that great unknown, the human factor. Here, too, there is need for research or at least co-ordination of research. If the psychologist is to put forward anything better than mere theories, he must work closely with the engineer, the policeman and the doctor.

Some not very successful attempts have been made to draw up a composite picture of the man who is "accident-prone" on the roads, as has been done for other types of accidents. It has not been possible to establish any certain link between accident-proneness and physical or psychophysiological failings. One series of tests will show that quick reactions lead to accidents, while another demonstrates that quick reactions and slow reactions cause about the same number of accidents. One medical report will state that it is dangerous for people with high blood pressure to drive; another that persons with low blood pressure are liable to accidents. The one conclusion to be drawn from these few examples is that

interpretations of tests of psychomotor ability seem peculiarly liable to error.

There is both a simpler and a better way of looking at the human factor. As an expert of the Harvard School of Public Health has put it, "People drive as they live". Dr. L. G. Norman, Chief Medical Officer to the London Transport Executive, considers that a man's temperament and his psychosocial qualities—were they measurable—would make a better yardstick by which to tell a "bad" driver.

From experience with London bus drivers, Dr. Norman observes that given equal experience, the older driver (even over 65 years old) is a better one than the younger man, despite slower reactions and less acute sight and hearing. He is more watchful and takes more care to anticipate dangerous situations, and this more than makes up for any deficiencies due to age.

According to another expert, marital status has a definite influence on accident-proneness. Married persons are less liable to accidental death than widowers, who are in turn safer on the roads than divorcees. The only exceptions to this rule are people under 20 years of age; they have a higher percentage of accidents when married than if they are single.

Over-indulgence in alcohol, fatigue and sheer lack of attention are, obviously, responsible for a very large number of accidents but little systematic study has been made of the causes underlying these factors, whether physiological, psychological or social.

Until a clearer light can be thrown on these obscure matters, more limited but more immediately realizable goals may still be pursued. The Road Research Laboratory, for instance, has just begun a study on "the driver", in the course of which they propose to investigate, separately and together, the driver's receptiveness to instruction, his control over the car, and his behaviour at the wheel. A special car will record and transmit his reactions over four simultaneous radio circuits. This experiment is still in a very early stage and its importance cannot yet be judged but at the very least it will be a first step towards a real, rather than a theoretical and subjective, picture of the car-driver's personality.

Other contributions to a more thorough knowledge of the road-user include a study of the overtaking

driver, which is now well-advanced, and research into the behaviour of pedestrians.

Finally, since 1956 the Road Research Laboratory, and more recently the Birmingham Accident Hospital, have organized squads of technicians, doctors and photographers to study accidents as they happen.

These squads have so far examined 300 accidents on the spot and card-indexed their findings.

When all possible information has been obtained, it may at last be possible for effective prevention to be undertaken and for the green light of safety to shine on the roads of the world.

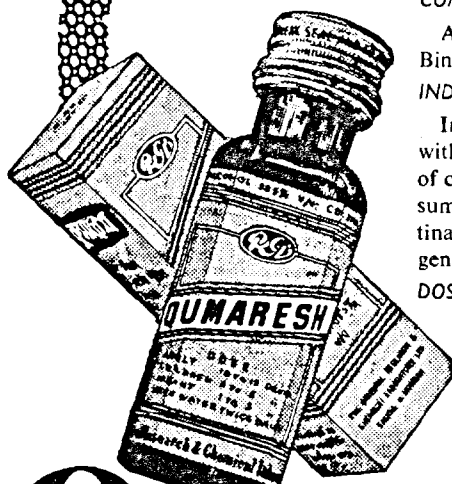
ELECTRIC ANAESTHESIA USED IN U.S.

Electricity has been successfully used on two patients to produce anaesthesia during surgical operations, *The Journal of the American Medical Association* has reported.

It is believed that these two cases are the first in which controlled electric current has been used as an anaesthetic in any successful major surgery, according to the authors of the report. They say that two

advantages of the use of electricity are the rapid recovery of the patients and the absence of after-effects from the anaesthesia. The method warrants further study, they believe.

The operations for which the electric method were used were performed at the University Hospital of the University of Mississippi Medical Centre at Jackson, Mississippi.



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14th World Health Assembly—Delegates Tell of National Successes in Health Programmes

Ceylon calls for attack on world problem of drug addiction

THE world-wide and distressing problem of drug addiction was stressed by Mr. J. P. Obeysekere, Chief Delegate for Ceylon, who was the first speaker when the general debate on the Director General's report on the work of WHO in 1960 was continued at session.

"Have we assessed the magnitude of this public health problem?" he asked. "It is clamouring for a solution. Whatever we do to combat it is bound to enhance our reputation as the greatest international co-operative adventure".

Ceylon had already controlled malaria and was now in the second year of its eradication campaign. With WHO assistance, smallpox also, Mr Obeysekere said, should be eradicated in the island and in the S. E. Asia Region within the next few years.

Dr. J. Anouti, Chief Delegate for Lebanon, described the success his country had achieved in fighting smallpox. No case had appeared since 1957, he declared, but nevertheless a campaign was carried out from April to September 1960 during which more than one million people, or 76 per cent of the total population, were vaccinated.

His country was moreover, he believed, the first in the Eastern Mediterranean Region to have completely interrupted the transmission of malaria over the whole of its territory.

In conclusion, Dr. Anouti handed over a cheque for five thousand pounds as his country's contribution to the WHO Malaria Eradication Special Account.

The main task of the Assembly and the Organization, according to Dr. V. Djukanovic of Yugoslavia, was to strengthen the aid given to the newly-independent states and those under-developed countries in the process of accelerated economic and social development. All international bodies had the

obligation to aid these countries. In the process of emancipation of peoples in under-developed areas, political, social and economic elements were closely linked, he said.

WHO should, he believed, pay special attention to assisting work for the control of smallpox, tuberculosis and cholera and also to the problems of sanitation, air pollution and control of insect carriers of disease. With regard to malaria, the results already achieved should not be compromised by financial difficulties and he urged the Assembly to take a specific decision on the financing of WHO's malaria eradication programme.

Dr. Ngobeh of Sierra Leone said that on the eve of its independence his country was looking forward to an era of great health improvement with help from international organizations. Already hospital attendances were on the increase although previously people had had to be persuaded to come for treatment. They had made progress in controlling yaws and leprosy, but for this as well as for widespread diseases such as tuberculosis, onchocerciasis, malaria and kwashiorkor they needed outside help in personnel, funds and equipment.

"It is the duty of the World Health Organization to show its authority in the matter of protecting mankind's health against the harmful effects of ionizing radiation and atomic energy", declared Dr. J. Plojhar, Chief Delegate of Czechoslovakia. Describing health progress in that country, he said that they now had one doctor for every 570 inhabitants. Medical research was carried on in more than thirty institutes, nine medical faculties and many other health institutions.

While appreciating the work done by the Organization, Dr. Plojhar said there were certain defects. Four-fifths of the senior posts in the secretariat were occupied by the USA and its allies. Great Britain, he

said, occupied the same number of posts as all the neutral countries of Asia and Africa together.

Another defect was the fact that a world map showing only the WHO Member States would have too many blanks. His delegation intended to submit a resolution asking the Director-General to invite all those States which were not yet members to consider the usefulness of joining the Organization. Only then could WHO justify its name as a truly "world" body.

It was essential, he went on, that the World Health Assembly, as the leader in the struggle for health, should take up an unequivocal attitude concerning disarmament and atomic warfare.

Dr. M. Escalona Reguera, Chief Delegate of Cuba, emphasized the health progress made in his country in the two years since the revolutionary government took over. The yearly expenditure on health had risen from \$ 21 million to \$ 71 million, while there had been an 80 per cent increase in the number of hospital beds. With help from the Pan-American Sanitary Bureau, WHO Regional Office for the Americas, malaria eradication had been almost completed in some sectors. For many years there had been no smallpox cases in the island.

Dr. Sook Bang, Chief Delegate of Korea, stated that his country was particularly grateful to WHO for its assistance in starting a malaria eradication programme which was now very close to success.

Dr. S. Al-Whabi, Chief Delegate of Iraq, said that the concept of universality was the cornerstone of

WHO. "We anxiously look forward," he added, "to the end of colonialism once and for all so that all peoples may take their rightful places as members of WHO."

Dr. Al-Whabi concluded by referring to the atomic tests in the Sahara and his country's strong objections to them.

Professor P. Muntendam, Chief Delegate of the Netherlands, said that he hoped that India, which was carrying out the largest national malaria eradication programme in the world, would succeed in freeing its people from the disease. He also stressed that his Government was opposed to financing the worldwide malaria eradication programme by means of a special account.

Dr. A. C. Andriamasy, Delegate of Madagascar, one of the new Member States of WHO, asked for more assistance from the Organization in solving some of his country's health problems.

Dr. D. Samonte, Chief Delegate of the Philippines, thanked the Assembly for electing him one of its three Vice Presidents.

The last speaker of the morning's session was Mr. W. Ibrahim, Chief Delegate of the Federation of Nigeria, who stated that his country had great confidence in WHO. He joined previous speakers in expressing concern about atomic test explosions, especially in the Sahara, which, he said, made a complete mockery of the humanitarian efforts of organizations such as WHO.

NEW HORMONE FOUND

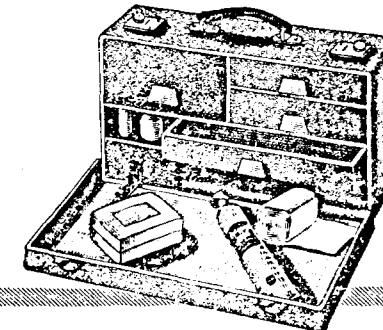
Dr. Daniel Rudman of the Goldwater Memorial Hospital in New York City has discovered a new pituitary hormone, which tests have shown to be more powerful than the well-known ACTH in making fat move in or out of body tissues.

Further experimental work with the new hormone, which is as yet unnamed, may yield new facts concerning the cause of atherosclerosis, a widespread form of hardening of the arteries, which is now under intensive study in the United States.

For the time being the new hormone is being called "Fraction L." It has the properties of a protein, made up of a long sequence of amino acids. It will not be finally named until more is known about its biologic actions.

Meanwhile, Dr. Rudman and his associates will endeavour to relate their findings in experimental animals to human disorders. To date, in tests conducted with rabbits, they have found that the fatter the rabbit, the more responsive the animal is to the action of Fraction L.

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14th World Health Assembly—Assembly Invited to meet in Argentina in 1963

*\$4,750,000 gift by USA to aid WHO malaria eradication,
water supply and medical research programmes*

AN invitation to the World Health Assembly to hold its 16th Session in Buenos Aires in 1963 was made by Dr. A. Martinez Marchetti, Chief Delegate of Argentina, during an evening session of the World Health Assembly.

A day earlier the Assembly had been invited by the Chief Delegate of the USSR to hold the 16th Assembly in Moscow.

Continuing the general discussion on the Director-General's Report, Dr. Leroy E. Burney, Chief Delegate of the USA, stated that his country fully supported the Director-General's proposed programme and budget for 1962. It was his government's firm purpose, he said, to expand help for newly-emerging states. In addition to the USA's share in the regular budget of WHO, a sum of 4,750,000 dollars would be voluntarily contributed to help WHO's programmes of malaria eradication, community water supply and medical research.

With regard to malaria, Dr. Burney said "We cannot allow the eradication programme to be jeopardized". His country had made voluntary contributions amounting to 25 million dollars to the Malaria Eradication Accounts of WHO and its Regional Organizations.

Congressman John E. Fogarty, USA, announced that his government was making a further contribution of 500,000 dollars to WHO's Medical Research programme.

Colonel M. K. Afridi, Chief Delegate of Pakistan, warned the Assembly of the danger of spreading the Organization's effort into new fields before earlier, basic programmes, had been sufficiently consolidated, and called for a closer examination of Priorities.

Professor E. Aujaleu, Chief Delegate of France,

congratulated the Director-General on taking long-term as well as emergency action to assist the Congo (Leopoldville) to rebuild its health services. There were now 60 Congolese health workers completing their medical training in France, and a number of students taking the full medical course, he said, while WHO had also assisted in strengthening existing facilities for training medical students in the Congo itself.

A global attack was now possible on diseases such as malaria, smallpox, trachoma and yaws, said Dr. G. E. Godber, Chief Delegate of the United Kingdom, and other communicable diseases would certainly come under control in the future. The progress in dealing with mental ill-health in the U. K. had received an added stimulus, he said, from WHO's activities in this field.

Dr. J. A. Scharndorf of Ghana asked WHO to promote investigation into herbal medicine. Various indigenous systems of medicine could, he believed, provide valuable assistance to countries like his own in improving the health of their peoples.

Dr. I. Birzu, Chief Delegate of Romania, stressed the importance of WHO's programme for intensified medical research and of the work of the Organization's Expert Committees.

D. B. R. Tandan, Delegate of India, spoke of his country's malaria eradication programme which, he said, had been assisted on a magnificent scale by the International Co-operation Administration of USA and WHO and on which India herself had spent more than 200 million dollars. He stressed that for the eradication programme of India to be successful it was important that neighbouring countries intensify their malaria eradication campaigns. Dr. Tandan also mentioned the efforts of India to provide safe water for her people and suggested that WHO should help

obtain loans from international sources for the provision of safe water supplies. He concluded by urging WHO to give its share to the study of the problem of population pressure.

Dr. L. Stoyanov, Chief Delegate of Bulgaria, said he hoped that international agreement could be reached on disarmament and that funds thus freed would be used primarily for the development of public health in all countries.

Dr. Y. Ben Abbes, Chief Delegate of Morocco, joined several previous speakers in expressing concern about the continuation of atomic test explosions.

Mr. A. Raohq, Chief Delegate for Poland, said that the central problem for WHO, as for other international organizations, was that of peace. This Organization, whose duty it was to watch over the health and welfare of the peoples of the world, must remain vigilantly on the side of peace and disarmament.

TWO MAIN COMMITTEES MEET

The Assembly's two main Committees held their first meetings. The Committee on Programme and Budget met under the chairmanship of Dr. W.A. Karunaratne (Ceylon) and elected Dr. L. Stoyanov (Bulgaria) as Vice-Chairman and Dr. A. M. Kamal (United Arab Republic) as Rapporteur.

The Committee on Administration, Finance and Legal Matters, whose Chairman is Dr. H. Van Zile Hyde (USA), elected as Vice-Chairman Dr. R. Vannugli (Italy) and as Rapporteur Mr. A. B. Sar (Senegal).

Reviewing the Organization's work in 1960 in the administrative, financial and legal fields, Mr. Milton P. Siegel, Assistant Director-General said: "I am pleased that I can again assure you that, in terms of the regular budget, the financial position of the Organization is sound".

However, this was not the case with the malaria eradication programme. Despite all the Director-General's efforts, Mr. Siegel went on, only a few of the economically more privileged countries had contributed or promised contributions to the Malaria Eradication Special Account.

Analysing WHO's total expenditure in 1960, Mr. Siegel said it amounted to more than 28 million dollars. This was made up of the regular working budget of almost 17 million dollars; WHO's share of the United Nations Technical Assistance Funds, of nearly 6 million dollars; more than 4 million dollars from the Malaria Eradication Special Account; half a million from other special funds and more than one million for emergency action in the Congo, this last item being reimbursable from the United Nations.

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(Sd.) **B. S. Amruta**
Signature of Publisher

Dated: 1—3—61

OBSTETRICS AND GYNAECOLOGY

(A Method of Maintaining Records)

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.

FOR quite some time now my mind has been toying with the idea of designing an obstetric and gynaecological case sheet wherein an accurate and detailed record may be kept of unusual and interesting cases of academic interest. Finally I devised a case sheet. Despite its many imperfections which I am still trying to remedy I had it printed for my own private and personal use. This case record is a very elaborate and long one and is not at all meant to serve for use in routine gynaecological practice. It is reproduced here with the hope that readers may be able, after patient study, to offer constructive criticism as to the ways in which it could be improved and to point out any glaring omissions that are present. Post-graduates who are required to make a thorough study of a specified number of cases for their higher Degree examinations in Gynaecology (and Obstetrics) may find this form of considerable interest and some use. The case record is actually designed to encompass both Obstetrics and Gynaecology. In some places overlap is inevitable. Here the part pertaining to Gynaecology is emphasized.

The record begins with an initial panel wherein essential facts may be summarised. After the usual particulars are obtained concerning Name, Age, Religion, Address, Occupation, Income group and Status, the patient is encouraged to relate her complaints in her own words. A history of her present illness and its duration is next obtained. A very important part of gynaecological diagnosis lies in taking a good history. Much time and patience should be devoted to this part of the procedure for this may be of very great value especially when physical signs are scanty. An accurate Gynaecological history and Marital and Obstetric history should be taken along lines indicated in the record. Although many authors have attempted to deal with this subject in their books, I doubt if any one has equalled the skill with which the chapter on "Gynaecological diagnosis" has been written in Shaw's "Textbook of Gynaecology".

Gynaecological symptoms may be dealt with as follows: Bleeding, Pain, Discharge, Pruritus; Dyspareunia, Frigidity and other Sexual disturbances; Infertility, Sterility; Swelling, Tumour, Prolapse or other allied complaints. Symptoms relating to obstetrical conditions; Symptoms relating to general diseases which may complicate pregnancy, labour or the puerperium; Symptoms arising from systematic manifestations of gynaecological or obstetric diseases and Symptoms of general diseases which may or may not be related to gynaecological disorders. As far as the last two are concerned one cannot equal the brilliant exposition of Isidor Rubin in his "Symptoms in Gynaecology—Etiology and interpretation with notes and diagnosis" (Gynaecological and Obstetric monographs, D Appleton and Co. New York and London 1931) and later in his "Integrated Gynaecology" edited by him jointly with Josef Novak in 1956, in the section on the "Relationship between Reproductive and other body systems".

The case record then considers Family history, Social history, Medical history and Surgical history and there is a tabulated column for Special comments on past obstetric or gynaecological history.

The next section includes a record of both symptoms and signs in the general examination of the patient with particular reference to Obstetrics and Gynaecology. The systems of the body have been arbitrarily arranged by me under the alphabets A—Z, Z encompassing the female genital tract.

This section makes provision for recording findings obtained by gynaecological and obstetric examination. As far as abdominal examination is concerned the excellence with which it is described by Crossen in his "Diseases of Women" remains unchallenged to date. I have included the section on Abdominal Examination under 'Digestive system' and reproduced a chart devised by Howard Kelly to depict abdominal tumefaction in three dimensions. It is surprising why

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this chart seems to have gone out of current use for it is ingenious and has great utility; it appears of course in Howard Kelly's "Gynæcology" (1928).

Some of these systems and their relationship to Obstetric and Gynæcological practice have already been considered in some detail not only in previous numbers of this journal but in others (See references). It is planned to consider in detail some of the systems and other sections left over in future numbers of Surgical and Medical News.

The genital tract has been divided into seven parts. 1. Vulva (including urethra) 2. Vagina 3. Cervix uteri 4. Pelvic supporting structures 5. Uterus 6. Fallopian tube and 7. Ovary. Beneath each part have been printed all the known diseases affecting the female genital tract as recorded in the "Nomenclature of diseases drawn up by a joint Committee appointed by the Royal College of Physicians of London-7th edition (1948) and published by His Majesty's Stationery Office. The purpose of including all these diseases is that it helps in considering "Differential diagnosis" and gives an indication for its appropriate classification. The form next considers special investigations and tests. Both these parts will be reproduced in a future number of this journal. The section dealing with pre-operative care, operation and post-operative management in gynæcology which follows has already been considered in Surgical and Medical News of January 1961.

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OBSTETRICS AND GYNAECOLOGY

Obstetric and Gynaecological unit.

Hospital reference :

Date :

Admitted for :

Gynæcological complaint/Obstetric condition

Ante-natal/Labour/Puerperal

Delivery Normal/Abnormal

If abnormal : Vaginal/Abdominal

Treatment given :

Operation performed : Vaginal/Abdominal

Diagnosis

Index number :

Admitted on :

Discharged on :

Name

Age

years.

Religion : Hindu/Mohammedan/Christian/Other

Address

Occupation :

Income group :

Status : MarriedSingleWidowRemarried

Complaint :

History of present illness and duration :

Gynæcological History

Menstruation

Age of onset (puberty)

years.

Normal cycle

days.

Duration

days.

Amount (Estimate in pads or towels)

Excessive / moderate / slight / normal/ diminished.

Colour

Consistency Normal/abnormal/clots/other

Inter-menstrual bleeding present/absent

Inter-menstrual pain present/absent

Vicarious menstruation

Menstruation : Normal/Abnormal

Last menstrual period :

Amenorrhœa : primary secondary

Duration days/ weeks/ years.

Dysmenorrhœa : present/absent

Abnormal uterine hæmorrhage

Marital and Obstetric History

Married at the age of

years.

Husband Status Health / Whether previously married

Sexual history

Dyspareunia/Frigidity/Other sexual disturbances

Infertility or Sterility

Previous pregnancies

None (Nullipara)

One

More than one (Multipara)

PARTICULARS

NUMBER OF CHILDREN

1

2

3

4

Complications of pregnancy

Complications of labour

Complications of puerperium

Other

SYMPTOMS AND SIGNS IN THE GENERAL EXAMINATION OF A PATIENT (OBSTETRICS AND GYNAECOLOGY)—(Contd.)

- M. Arteries: Pain, intermittent claudication/gangrene/embolism/hæmic and vascular murmurs/hypertension/hypotension/other
- N. Veins: Varicosity/pain/swelling/other
- O. Capillaries: Purpura/Hess's test/other
- P. Blood: Blood loss/coagulation defects/other
- Q. Hæmopoietic System: Pallor / dyspnœa / œdema / koilonychia / dysphagia/glossitis/other
- R. Lymphatic System: 1. Spleen 2. Lymph nodes 3. Lymphatic channels
Splénomegaly / Lymphadenitis / Lymphadenopathy / Lymphangitis, acute, chronic/other
- S. Digestive System:
- | | | |
|------------------------------|-------------------------|--|
| 1. Mouth | 8. Adenoids and tonsils | 15. Anus |
| 2. Lips | 9. Oesophagus | 16. Liver |
| 3. Tongue | 10. Stomach | 17. Gall-bladder and bile passages |
| 4. Teeth and gums | 11. Intestine | 18. Pancreas |
| 5. Palate and uvula | 12. Colon | 19. Abdomen |
| 6. Salivary glands and ducts | 13. Appendix | 20. Peritoneum |
| 7. Pharynx | 14. Rectum | 21. Portal, hepatic and mesenteric vessels |

Dyspepsia/ nausea/ vomiting/ hæmatemesis/ regurgitation/ heart burn/ dysphagia/ appetite: decreased (anorexia), increased (polyphagia), perverted (pica)/ acute and chronic constipation/ acute and chronic diarrhœa/ rectal pain/ tenesmus, pain on defæcation/ incontinence of fæces/ melaena/ rectal bleeding/ tenderness, tumour/other

General abdominal pain: labour/acute general peritonitis/acute or chronic gastro-enteritis/ colitis/ bacillary dysentery/ amœbic dysentery/ food poisoning, acute intestinal obstruction/ acute appendicitis/ tuberculous peritonitis/ Other

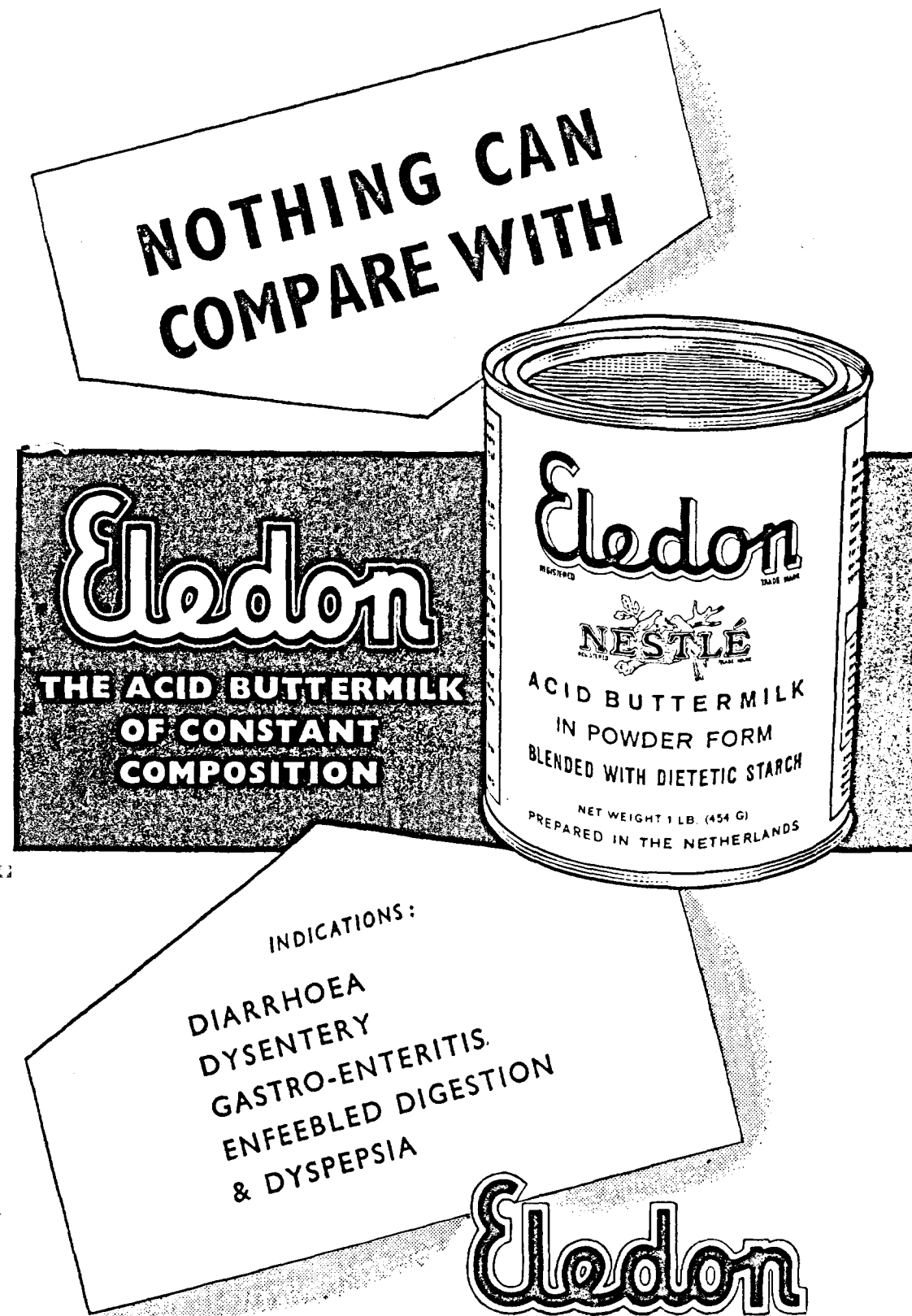
General abdominal tenderness: acute general peritonitis/ toxic gastritis/ acute intestinal obstruction/ tuberculous peritonitis/ gastro-enteritis/ other

Examination of the Abdomen

Inspection: General appearance, contour, normal fullness, swollen, protruberant, sunken, retracted, general enlargement, bulging or distension (fat, fluid, flatus, fæces, foetus, or new growths), distension in anteroposterior and transverse diameter, local enlargement (specify zone in which it is present). Does swelling move with respiration? Pulsation in the epigastric region—present/absent. Movement of the abdominal wall—present/absent; normal/abnormal. Peristaltic movements—present/absent (specify direction) / Foetal movement—present/absent. Abnormal pigmentation or discolouration—present/absent. Surface of the abdomen—smooth/glossy/striæ/abnormal surface vein pattern/caput medusæ. Umbilicus depressed, on level with surface/everted/protruberant/oozing, discharge, discolouration, swelling of navel/other

Hernial orifices—normal/abnormal

Palpation: Tension of the abdominal wall/resistance/general and localized rigidity, hyperæsthesia/absence of abdominal and skin reflexes, local or general tenderness.



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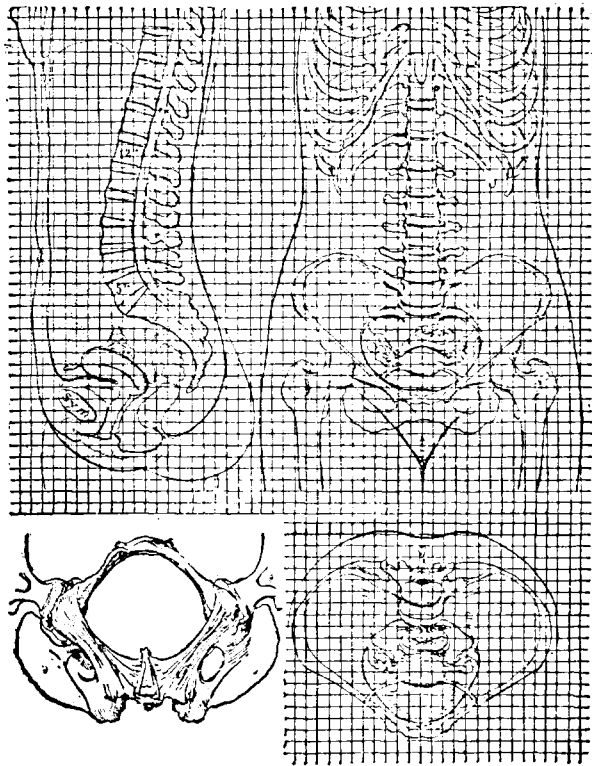
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SYMPTOMS AND SIGNS IN THE GENERAL EXAMINATION OF A PATIENT
(OBSTETRICS AND GYNAECOLOGY)—(Contd.)

- Does viscus harden under examining hand?
- Abdominal swelling—present / absent.
- If present is it general or local?
- Is the tumour on the abdominal wall or within the abdomen?
- Is it abdominal or abdomino-pelvic?
- Is it tender?
- Does it move with respiration?
- Does it appear to be related to any abdominal organ?
- If it moves in which direction does it move?
- Size: small / medium / large / enormous.
- Situation and position (Indicate on figure)
- Measurement (in cms. / ins): Circumference of the abdomen (in cms. / ins):
- Shape: spherical / ovoid / other
- Attachment
- Contour: smooth / lobulated / irregular / other
- Consistency: hard / solid / cystic / fluctuant / other
- Other features: (specify)
- Hepatomegaly, Splenomegaly, Enlargement of the kidney, other
- Percussion: Resonant / tympanitic / shifting dullness / fluid thrill / other
- Auscultation: Borborygmi—present/absent (silent) / murmurs/foetal heart sounds / other
- General abdominal swelling / Local abdominal swelling
- General abdominal swelling: Pregnancy / obesity / ascites / acute or chronic intestinal obstruction / retention of urine / gastroptosis / enteroptosis / large ovarian cyst / tuberculous peritonitis / splenomegaly / psueudocyesis / dilated colon/tympanitis/other

(Clinical Photographs may be affixed here)

SYMPTOMS AND SIGNS IN THE GENERAL EXAMINATION OF A PATIENT
(OBSTETRICS AND GYNAECOLOGY)—(Contd.)



REGION	Pain	Tenderness	Swelling	Other
Epigastric	..			
Right hypochondriac	..			
Left hypochondriac	..			
Umbilical	..			
Right Lumbar	..			
Left Lumbar	..			
Hypogastric	..			
Right iliac	..			
Left iliac	..			
Right inguinal	..			
Left inguinal	..			

SYMPTOMS AND SIGNS IN THE GENERAL EXAMINATION OF A PATIENT (OBSTETRICS AND GYNÆCOLOGY)—(Contd.)

T. Urinary System : 1. Kidney 2. Ureter 3. Bladder 4. Urethra

Renal pain / dull ache in costovertebral angle / renal colic / ureteral colic/frequency of micturition—diurnal, nocturnal / polyuria / oliguria / anuria / pyuria / hæmaturia / hæmoglobinuria / chyluria / glycosuria / suprapubic ache / vesical pain / urethral pain (dysuria) / stranguria / acute or chronic retention / retention with overflow / incontinence true, tonic, or false / stress incontinence / total incontinence / stream-continuous, hesitancy, impaired, interrupted, force of projection / post urinary dribbling / dribbling in addition to normal micturition / details of the act of micturition / character of urine / other.

U. Endocrine System : 1. Pituitary 2. Thyroid 3. Parathyroid 4. Adrenal 5. Thymus 6. Pancreatic islets of Langerhans

Dwarfism / gigantism / impotence / sterility / obesity / other

V. Nervous System :

- | | | |
|-------------------------|--------------------------------|---|
| 1. General | 4. Brain | 7. Vessels of the spinal cord |
| 2. Vessels of the N. S. | 5. Vessels of the brain | 8. Peripheral nerves including cranial nerves |
| 3. Meninges | 6. Spinal cord and nerve roots | 9. Autonomic nervous system |

Headache / pain / fits and other transient disturbances of consciousness / vision / mental and emotional state / speech / comprehension / expression / apraxia / cranial nerves / Sensory and motor disturbances / reflexes / sphincters / skin, nail and joint changes / other

W. Eye : Eyelids / conjunctiva / cornea / sclera / eyeballs / pupils / lens / vision / fundus (Ophthalmoscopic findings) / retinal vascular changes and retinitis / optic neuritis / optic atrophy / black, white or patchy spots on retina / other

X. Ear : pain / tenderness / swelling / deafness / other

Y. Diseases not associated with a single anatomical system : Toxins / metabolic disorders / dietary deficiencies / other

Z. Genital Tract : (Gynæcological and/or obstetric diagnosis).

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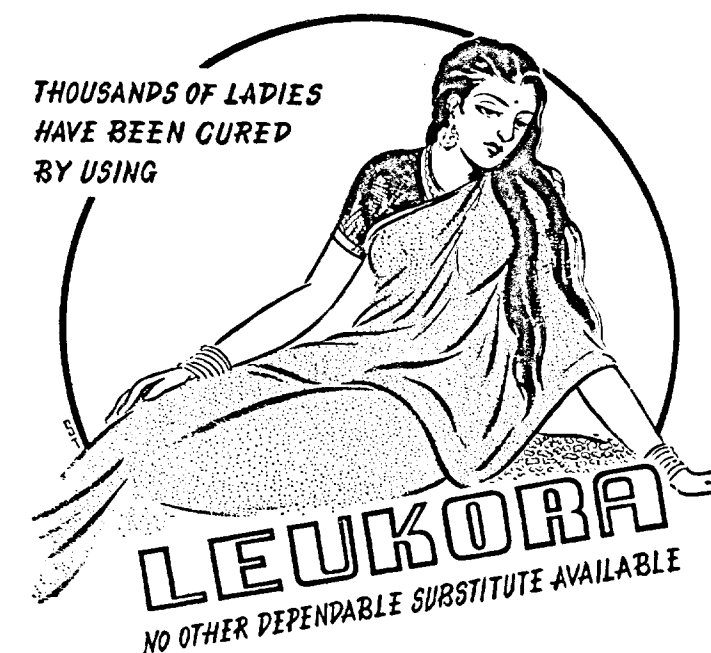
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INTERNATIONAL WORK IN CHOLERA

1. Past and present distribution of cholera*

The term "huo luan", the present name for cholera, is found in the Nei Ching and other old chronicles, but it appears that it does not refer to the disease we now recognize as cholera. There is little doubt that in the past this term has been used to cover a group of affections... and cholera might have been mixed up with them. A significant point, however, is that no one, until a late period, alludes to the epidemic character of the disease.

WONG & WU LIEN-TEH¹

THE vast pandemics of cholera that swept across Asia, Europe and the Americas during the nineteenth century marked a sudden transformation in the character of a disease that appears to have been endemic in parts of Asia for centuries. Indeed, it is probable that cholera has been present in India, in the region of the Ganges delta, since time immemorial. The clinical manifestations of the disease may be closely imitated, however, by other gastro-intestinal infections, and it is therefore difficult to identify it with certainty from early descriptions of diarrhoeic diseases.

An epidemic among the Athenians, described by Thucydides in the fifth century B. C., may have been true cholera, since it is stated that the contents of the bowels ran out "like pure water", but in general the early Greek writers mention bilious discharges, and the word *Χολέρα* found in Hippocratic writings is thought to refer to a disease different from that now recognized as cholera. Similarly, much uncertainty exists regarding the interpretation to be placed on descriptions of cholera-like diseases to be found in ancient Indian medical literature. There is evidence that in Lower Bengal the people have long worshipped a goddess of cholera, coming from all parts of the country to Calcutta to pray at her shrine. This

suggests that the disease must have raged at times with considerable violence. Susruta, an Indian physician of the seventh century A. D., has described a disease characterized by diarrhoea and vomiting, stabbing pains, cyanosed lips and nails, sunken eyes, and a weak voice. Although this closely fits the clinical picture of cholera, there is nothing to indicate that it refers to the epidemic form of the disease, commonly known today as Asiatic cholera.

On the other hand, from the sixteenth century onwards, detailed descriptions of cholera in India were given by European observers, the earliest referring to the province of Goa, on the west coast of India, where the first Portuguese landings were made. During the seventeenth century, Dutch, French and British observers reported epidemics from other areas of the west coast, and by the last quarter of the eighteenth century the disease had been encountered on the east coast as well, and even beyond the confines of the sub-continent.

It seems likely that early importations of cholera took place from India into neighbouring countries, particularly into Burma, and it is claimed that in 1639 it was carried into China. The first reliable reports of cholera outside India relate to an epidemic in Ceylon in 1732, severely affecting the British fleet anchored at Trincomalee, and to an outbreak in Burma in 1783. At the same time an epidemic was raging on the right bank of the Ganges in north-west India, killing 20,000 pilgrims in less than eight days at the holy town of Hardwar. During the remainder of the eighteenth century, there were frequent reports of epidemics in various parts of India, often involving European troops, and there was a violent outbreak in Bengal in 1814. Ceylon was again affected in 1804.

* This is the first of a series of articles intended to give a concise account of the public health aspects of cholera, and to outline present trends in its control. Those wishing to go more deeply into the subject are referred to a comprehensive monograph recently published by WHO: *Cholera*, by R. Pollitzer (with two chapters written in collaboration with W. Burrows and S. Swaroop), Geneva, 1959 (*World Health Organization: Monograph Series*, No. 43), 1019 pages.

¹ Wong, K. C. & Wu Lien-teh (1936) *History of Chinese medicine...*, Shanghai

CHOLERA* BECOMES PANDEMIC

In 1817, cholera suddenly flared up with hitherto unprecedented virulence and began to spread to parts of Asia that had previously been free from the disease. This violent eruption is believed to have had some connexion with the unusually heavy rainfalls and disastrous floods of 1815 and 1817, and the fact that the intervening year, 1816, was excessively hot and dry. Probably originating in the hinterland of Bengal between the Ganges and Brahmaputra, the epidemic had reached Calcutta in early August, and a month later the magistrate of the city reported that it had been "far more fatal than at any former period within the recollection of the oldest inhabitants". Within three months the whole of the province of Bengal—nearly 200,000 square miles in area—had been affected, scarcely a single town or village escaping the ravages of the disease. The infection also overran the Bundelkhand, to the south of the former United Provinces, causing great havoc among troops stationed in the area.

In 1818, the disease extended north-eastwards into Nepal, westwards into Bombay, and south into Hyderabad, Mysore and Madras. Towards the end of the year, it reached Trincomalee in Ceylon, spreading over practically the whole island during the following year. Burma also appears to have been invaded by the land route in 1819, and epidemics of sea-borne cholera broke out in 1820 in various parts of the Malay peninsula as well as in Java, Borneo and other islands of the Indonesian archipelago. At the same time, the disease reached several ports in China, spread along the Yangtze valley, and invaded the north of the country the following year. Further outbreaks occurred in northern and central China in the period 1822-24. The disease first appeared in Japan in 1822, exacting a terrible toll of lives in Osaka and some other cities.

A British expeditionary force sent from India to Oman in 1821 carried the infection to Arabia. From Oman, cholera spread up the Persian Gulf into what is now Iran and across to the southern shore of the Caspian Sea. At Basra, in present-day Iraq, it killed more than 15,000 people in less than three weeks. Carried up the Tigris by boat and caravan, the disease caused terrible havoc among the Persian army attacking the city of Baghdad. The following spring, cholera broke out along the Euphrates as well as the Tigris and eventually reached Tiflis and

Astrakan on the Caspian Sea. There the pandemic came to a halt, as a result, it is believed, of the severe winter of 1823-24.

CHOLERA CROSSES THE ATLANTIC

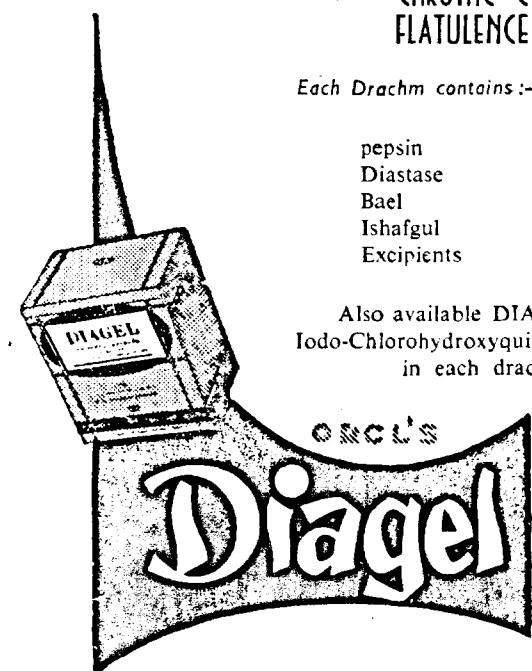
In the meantime, the original epidemic in India had also subsided. The respite was short-lived, however, and by 1826 cholera was again showing signs of increased violence and activity in Bengal. By 1829, it was rampant in Afghanistan, penetrated again into Persia, and was also present around Bukhara and Khiva. From there, it seems to have been carried by caravans to Orenburg in the south-east corner of European Russia and soon started to spread north-eastwards. The Second great pandemic was under way. In the spring of 1830, cholera began to advance on a wide front, ultimately invading not only most parts of Europe but also large parts of the Americas, as well as Arabia and East and North Africa. In spite of rigid quarantine measures, by 1831 the disease had progressed as far north as Archangel in Russia and

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entered Finland. Poland, Austria and parts of Germany were affected in the same year, and ships carried the infection from the Baltic ports to England, where a number of outbreaks occurred in late 1831 and 1832. In the latter year, cholera not only broke out in Ireland, France, Belgium and the Netherlands, but also crossed the Atlantic and appeared in Canada and the USA. Subsequently, it spread into Mexico and other countries of Central and South America. In Europe, recrudescences of the disease continued every year until 1837. Spain was affected in 1833, in spite of exceptionally severe quarantine measures, and from there cholera spread along the southern shores of France and into Italy and Switzerland. In 1834 and 1835, French troops carried the disease into Algeria. Outbreaks had already occurred in Egypt, as well as in Syria and Palestine, in 1831. These are believed to have been started by pilgrims returning from Mecca, where cholera had taken a heavy toll of life earlier that year.

In India, fresh outbursts of cholera occurred in Lower Bengal in 1837 and again in 1840. Troops that had been assembled in Calcutta and Madras carried

the disease in 1840 to the Straits Settlements and China, where the pandemic raged with great ferocity during the next two years. A further serious recrudescence of cholera in Lower Bengal in 1845 was followed by the invasion of Madras and Ceylon on the one hand, and of the Bombay area on the other. From there the disease spread westwards and in 1846 invaded almost the whole of the Arabian peninsula. The following spring, cholera again appeared along the shores of the Caspian and the Black Sea and advanced rapidly across Russia. After a lull during the winter, it resumed its march early in 1848, reaching Norway in the north, the Balkan countries in the south, the British Isles in the north-west and Spain in the south-west. Pilgrims returning from Mecca once more imported the disease into Egypt, and it also reappeared in the USA. During 1849, it overran practically the whole of the States lying east of the Rocky Mountains, made inroads into Canada and was carried into Mexico and Panama. In 1850 and again in 1851, cholera raged with great violence in Cuba and Jamaica.

The second pandemic had barely subsided when a

fresh pandemic broke out in 1852, attributed by some to the persistence of a focus of infection in Poland, but undoubtedly reinforced by fresh waves of infection from India. This pandemic lasted until the end of 1859, affecting at first mainly Europe and North America. In 1855, the infection spread from Arabia into Syria and Asia Minor and also appeared in Egypt and other parts of North Africa. Furthermore, while North America now remained apparently free, cholera broke out in Venezuela and Brazil. China and Japan suffered severely during the period 1857—59, and in the latter year a serious recrudescence of the infection in Bengal was followed by a fresh wave of infection in Russia and various parts of Europe.

NEW TRAFFIC ROUTES SPREAD CHOLERA

The fourth pandemic, which began in 1863, differed from the first three in that the disease penetrated into Europe by new traffic routes, via Arabia into Egypt, Constantinople, Southern France and Italy. In May 1865, cholera broke out with extreme violence at Mecca, where some 90 000 pilgrims were assembled for the jubilee year. It has been estimated that at least one third of them fell victims to the disease. Returning pilgrims disseminated the disease in various parts of Arabia, Iraq, Syria, Palestine and Egypt. From Alexandria, the infection was carried to Istanbul, Marseilles and other Mediterranean ports. Cholera appeared at widely scattered points in Europe during 1865 and 1866, the most serious ravages being in Russia, Germany, Austria-Hungary, Italy, Belgium and the Netherlands. Between 1866 and 1873, sporadic outbreaks of limited extent were of frequent occurrence throughout Europe, and a number of major epidemics also occurred, particularly in Russia. In the meantime, the disease had been spreading southwards from Abyssinia into Africa. By 1869, it had reached the region of Kilimanjaro, and from there it advanced south-westwards across Lake Tanganyika to the upper reaches of the Congo, and south-eastwards to Zanzibar Island, where 70 000 persons succumbed to the disease in 1869. By May 1870, cholera reached the city of Mozambique and was then carried to the Comoro Islands, Madagascar and the Seychelles. Cholera was also rife in the north of Africa, and Morocco had a violent outbreak in 1868. It seems likely that caravans carried it from there to French West Africa, and thence the infection spread to Gambia and Portuguese Guinea.

Cholera was rampant in New York in 1866 and the

newly built railways facilitated its spread to other parts of the USA. Large-scale troop movements also assisted the dissemination of the infection. Nevertheless, the number of deaths was far lower than in earlier pandemics. Canada remained almost free from the infection, but the disease made several appearances in Central and South America from 1866 to 1868. In the USA a serious recrudescence of the disease occurred in the area of New Orleans and the Mississippi basin in 1873.

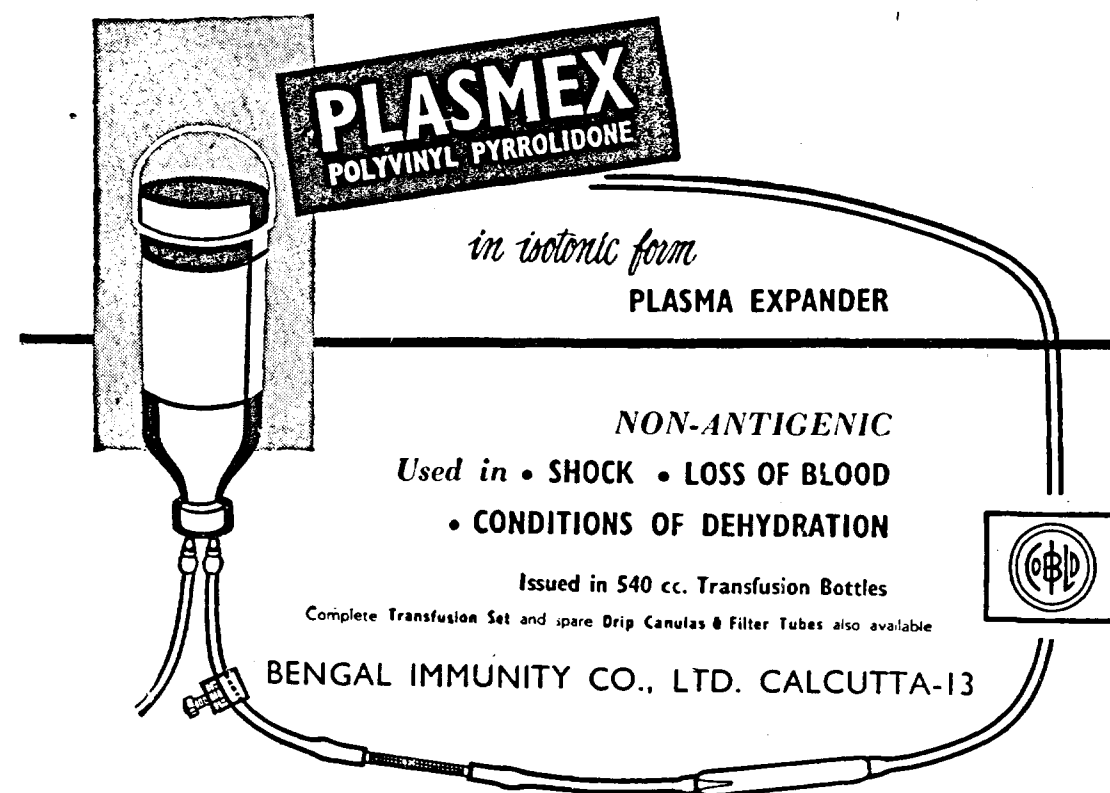
Cholera raged with particular violence in India in 1875, and other Asian countries also suffered severely during the concluding years of the pandemic. Information is scanty regarding the fate of countries to the east and south-east of India at this time. Cholera is stated to have been widespread in China in 1862, in the Indonesian archipelago in 1863 and 1864, and in China and Japan in 1864—65. Serious outbreaks also occurred in Japan in 1877—79.

THE PANDEMICS DECLINE

The fifth cholera pandemic, which lasted from 1881 to 1896, caused much less havoc than its predecessors, although wide areas were affected. It was during this pandemic that an important advance was made in the study of the disease: Koch succeeded in proving that cholera is caused by a specific gastro-intestinal infection. As in the case of the previous pandemic, the infection was first disseminated by pilgrims returning from Mecca, where epidemics occurred in 1881 and 1882 following a serious exacerbation of the cholera situation in India. In 1883, cholera broke out in Egypt among visitors to a fair at Damietta and soon spread to other parts of the country. Between 1884 and 1890, a number of epidemics occurred in France, Italy and Spain, but the rest of Europe remained practically free from the disease. The failure of cholera to become entrenched in Great Britain at this time was attributed to adequate preventive measures and the provision of wholesome water supplies.

The spread of cholera to the USA was narrowly averted in 1887 by rapid laboratory diagnosis of the disease among the passengers of a steamer from Marseilles—the first occasion on which use was made of bacteriological methods in combating the scourge. Serious outbreaks took place, however, in Argentina and in Chile between 1886 and 1888.

In 1892, cholera flared up in Afghanistan and



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Persia and spread rapidly across Russia, claiming some 800 000 victims in 1893—94. At the same time, an explosive outbreak occurred in Germany at Hamburg, owing to the distribution of unfiltered water from the River Elbe. Sporadic cases of cholera also occurred at many other places in Germany as well as in France between 1892 and 1894.

Throughout the pandemic, cholera continued to be prevalent in India, and there were repeated epidemics in the Indonesian archipelago, as well as in China and Japan.

An increase of cholera in India in 1899 ushered in a new pandemic which lasted until 1923. Violent outbreaks occurred in Calcutta and Bombay in 1900, with extensions of the disease westwards into Afghanistan and the Persian Gulf area and eastwards into Burma and Malaya. By 1902, the pandemic had spread to the Philippines, Korea, Manchuria, China and Japan. In the same year, pilgrims assembled at Mecca were once again struck down in large numbers and despite every precaution the disease was carried back into Egypt where it claimed 34 000 victims in three months. In 1904 cholera spread from Baku on the Caspian Sea into Russia and during the next few years gradually extended its hold on the country. In 1910 there were over 230 000 cases with almost 110 000 deaths, but for the next ten years the disease tended to be sporadic, with slight exacerbations in 1915, 1918 and 1920. There was a sudden flare-up in 1921, with more than 200 000 cases, but thereafter the disease declined, and in 1924 and 1925 there were only a few sporadic cases. Since then Europe has remained free from cholera.

This sixth pandemic was much more limited in extent than its predecessors. The Americas escaped entirely and in Western Europe only sporadic cases or abortive outbreaks occurred. On the other hand, the pandemic assumed serious proportions at times in central and south-eastern Europe. Thus, frequent and often serious outbreaks occurred in the Balkan peninsula, where the spread of infection was facilitated in 1912 and 1913 by local wars and later by the First World War.

There are some areas that remained unaffected by any of the six pandemics. These are especially the northernmost and southernmost parts of the globe. Thus, in Western Europe, Iceland, the Færø, Shetland, and Orkney Islands, the Hebrides, Norway, north of

SURGICAL & MEDICAL NEWS

Bergen, and Lapland were spared. So also were Northern Siberia and Kamchatka, Greenland, and the regions of North America beyond the 50th parallel. Similarly, the Southernmost parts of Chile and Argentina remained free from the disease, as did the southern parts of Africa. It does not appear that any of the pandemics ever reached Australia and there is no reliable evidence that the Islands of the Pacific were affected, with the exception of New Guinea and the Bismarck Archipelago, which were affected during the fifth pandemic.

CHOLERA SINCE 1923

As remarked above, Europe has remained free from cholera since 1923. In fact there has been no westward spread of cholera beyond Afghanistan, apart from sporadic outbreaks in Iran (1927, 1931 and 1938—39) and Syria (1947—48) and a serious epidemic in Egypt in 1947 which caused more than 20 000 deaths in a period of three months. Unlike earlier epidemics in Egypt, this outbreak was not initiated by pilgrims returning from Mecca, since it began in September, before the pilgrims returned. Though various possibilities were suggested, the origin of the epidemic could not be satisfactorily traced. The first cases occurred at the important trading centre of El Korein in the Delta Province of Sharkiya, where merchants from all over Egypt had congregated to attend the annual date fair. The infection spread rapidly, and within two weeks all the Delta provinces except Beheira were affected, as well as the governorates of Cairo, Damietta and the Canal, and the province of Giza in Upper Egypt. The epidemic continued to extend, reaching its greatest height during the fifth week. It then declined steadily, and by December cholera had practically disappeared from Egypt.

This epidemic in Egypt occurred at a time when the newly constituted Interim Commission of WHO was about to undertake initial preparations for revising,

MEDICAL EDUCATION IN THE USSR

As many as 80 medical institutes are training doctors for the Soviet public health services. Enrolment in these institutes aggregate more than 170,000 young men and women. These figures, testifying to the successes scored in medical education, are given in the latest statistical volume, "Public Health in the USSR," published in Moscow. At present the Soviet people

are better provided with doctors than the population in any other country in the world. The USSR has five more doctors per 10,000 of population than, for instance, in the United States of America. People say that the best way to evaluate the present is to review the past. Tsarist Russia, and especially her national outlying territories, ranked among the most backward of States.

unifying and strengthening existing international sanitary regulations. It provided the Commission with a unique opportunity for testing the effectiveness of these measures. The Commission co-operated closely with the Egyptian health authorities and kept other countries, particularly those closely in contact with Egypt, regularly informed of the epidemiological situation. It also undertook the bulk ordering of cholera vaccines and other supplies from various sources and supervised the application of the International Sanitary Conventions, the provisions of which were found to be adequate; many countries, in fact, had to be discouraged from taking unnecessarily drastic action, in excess of these provisions.

For India and Pakistan, the years shown as epidemic are those in which more than 100 000 deaths were recorded, but even in the intervening years, with the exception of 1954, there were always between 50 000 and 100 000 cholera deaths. The worst year was 1943, with nearly 460 000 deaths, while in each of the years from 1927 to 1930, as well as in 1924, 1944 and 1945, the total of deaths approached or exceeded 300 000. Incidence and mortality varied considerably, however, from province to province and even in different parts of the same province. The highest average endemicity for the period 1901—45 was in the province of Bengal at the mouth of the Ganges delta, and this area has been called "the major endemic home of cholera". There are marked seasonal fluctuations in incidence.

Since 1955, cholera has been confined to India, Pakistan, Nepal, Burma and Thailand, with small outbreaks in Cambodia and Afghanistan. The gradual retreat of cholera, first from the west and more recently from countries to the east of the Indian peninsula, is due to complex causes, but undoubtedly vigorous public health action, especially the provision of wholesome water supplies and stringent application of the International Sanitary Regulations, has played a major role.

USSR INVITES ASSEMBLY TO HOLD 16TH SESSION IN MOSCOW

WHO delegates report on health progress in their countries

IN the general debate on the Director-General's report of the work of WHO in 1960 during plenary session, the chief delegate of the USSR delegation, Dr Sergei Kurashov, invited the World Health Assembly to hold its 16th annual session in Moscow.

The debate on the Annual Report was opened by Professor B. Papanicolaou, Chief Delegate of Greece, who stated that his country was pushing ahead with its successful malaria eradication campaign and expected to achieve eradication within two years. Commenting on WHO's assistance to countries in developing health services and training personnel, he said he felt that, when WHO assistance to a project was withdrawn, arrangements should be made for future periodical inspection at intervals of about two years, to ensure that the aims of the project were still being pursued in accordance with the original agreement between the Government and WHO.

Dr. C. Mode, Chief Delegate of Haiti, reported rapid progress in health improvement in his country. More hospitals had been built and better training provided for medical personnel. Dr. Mode invited medical students from Africa to study at universities in his country. In Haiti, he said, yaws had been almost wiped out but malaria appeared to be on the increase. However, the Government was mobilizing all its resources in order to combat the disease, with assistance from UNICEF and WHO. Dr. Mode concluded by calling the attention of international agencies to the problem of malnutrition in Central America.

Dr. J. Stralau, Chief Delegate of the Federal Republic of Germany, expressed his satisfaction that WHO was devoting much energy to the study of "modern" diseases such as cancer and cardiovascular diseases. Commenting on the shortage of funds for the world-wide malaria eradication campaign,

Dr. Stralau expressed the hope that the part of the cost of this campaign borne by WHO would be included in the Organization's regular budget.

Mr. I. Pirosky, Delegate of Argentina, said that the malaria eradication campaign in his country had reached a stage of consolidation in 60 per cent of endemic areas, and it was expected that eradication would be achieved within two years. Argentina was pushing ahead with a number of internationally assisted health projects, and its own determination was shown from the fact that for each dollar spent by WHO in these projects, Argentina herself spent 81.

On behalf of his delegation, the Chief Delegate of Israel, Mr. I. Barzilay, welcomed the new countries of Africa which had recently joined the international community and paid tribute to the WHO Director-General for his leadership in the WHO action in the Congo. Mr. Barzilay felt that the most important task for WHO today was to assist the newly independent states to solve their health problems. To do so effectively, he suggested that the Assembly charge the Organization with the task of setting up a special committee of experts to work out a programme of new means and techniques to meet these countries' public health needs. In the work of the proposed committee, representatives of the new countries should participate.

Dr. Sergei Kurashov, Chief Delegate of Soviet Russia, joined the previous speaker in greeting the new members of WHO and said that the Director-General's Annual Report showed that WHO had achieved certain successes during the past year. However, the Organization had opportunities for still more effective work.

The main purpose of the work of WHO, he said, should be to assist the less developed countries which had

attained independence, and to this end the Organization should revise its budget.

The countries in the African Region, Dr. Kurashov said, where the training of medical staff from the indigenous population was of primary importance, had received the smallest allocation for that purpose. Between 1949 and 1959 WHO provided the African Region with only 569 fellowships out of a total of 10,000-about 5 per cent.

Dr. Kurashov also felt that in order to improve the assistance to newly independent countries it would be advisable to have more representatives of the indigenous population on the staff of the executive bodies of WHO, for they were better acquainted with the problems of their own countries.

He concluded by pledging continued support by his country to WHO and by asking the Assembly to approve that the 16th World Health Assembly be held in Moscow.

Dr. J. S. Saleh, the Chief Delegate of Iran, stated that 70 per cent of his country's malaria eradication programme had now been accomplished. However, he said, the last 30 per cent was the most difficult and he expressed concern about the state of the Malaria Eradication Special Account. Recalling the cholera outbreak in two of Iran's neighbouring countries last year, Dr. Saleh said that as a result of the great efforts of the countries concerned cholera was prevented from coming to Iran. This was the first time in the history of Iran that this disease had reached the frontier and had been arrested there.

Dr. P. E. Moore, delegate for Canada, invited delegates to attend the 16th biennial meeting of the International Union against Tuberculosis which this year would meet in Toronto, Canada.

The Chief Delegate for Afghanistan, Dr. A. R. Hakimi, thanked the S. E. Asia Regional Office of WHO for the assistance rendered to his country in many different health fields and said how grateful they were also to the USSR, India, Iran and other countries for providing medical aid and vaccines which had prevented the 1960 cholera outbreak in Afghanistan from becoming a serious epidemic.

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PIONEERS IN FIGHT AGAINST MALARIA HONOURED

Darling Foundation Award for Sir Gordon Covell and Dr. Arnaldo Gabaldon

THE President of the 14th World Health Assembly, Dr. A. L. Mudaliar, presented the seventh award of the Darling Foundation medal and prize to Sir Gordon Covell, of the United Kingdom, and to Dr. Arnaldo Gabaldon, of Venezuela.

The Darling Foundation Prize is granted on recommendation of the Darling Foundation Committee for "outstanding achievements in the pathology, etiology, therapy, prophylaxis or control of malaria". It honours the memory of Dr. Samuel Taylor Darling, whose premature death by accident when on a mission for the Malaria Commission of the League of Nations cut short a long career devoted to research in the control of disease, particularly malaria.

In presenting the award, Dr. A. L. Mudaliar said: "Sir Gordon Covell's important contributions to malariology led, in 1936, to his being appointed Director of the Malaria Institute of India—a post which he held until 1947. During the second World War his own battle against malaria was carried on vigorously, and resulted in the saving of many lives in many theatres of operation.

"Afterwards, having reached an age at which many men retire, he became Adviser on Malaria to the British Ministry of Health and Director of the Malaria Reference Laboratory at Horton Hospital, Epsom, Surrey. His numerous writings include studies on the life history of malaria parasites and on the incidence, clinical aspects and ecology of malaria. He was a joint author of the valuable Monograph on the Chemotherapy of Malaria which was published by WHO in 1955.

"But his greatest services to mankind may well be those that he has given as a teacher, an adviser and a director of research on malaria. The seeds which he sowed so carefully and tended so laboriously have borne rich fruit in malariologists throughout the world.

"Dr. Gabaldon's magnificent services in the struggle against malaria are well known. As Director of the Division of Malariology at Maracay, Venezuela, he has guided large numbers of WHO fellows and other students, from all over the world, along the right path. He carried out, and described in the scientific press, a technically pioneering scheme of epidemiological study and executive control leading to the first declaration of eradication of malaria from a large area in the tropics.

"This alone is a pioneering activity of outstanding significance, but Dr. Gabaldon has also contributed materially to general epidemiological understanding. His scientific knowledge, practical experience, far-seeing strategy, buoyant enthusiasm, dynamic energy and faith in the progress of public health have contributed enormously not only to the significant advances of malaria eradication in the Americas but also to the general acceptance of idea of world malaria eradication."

In accepting the award, Sir Gordon recalled that when he was Director of the Malaria Institute of India, the Terai area in the State of Uttar Pradesh was used as an example of how devastating the effects of malaria could be. A huge fertile valley lay waste because of the ravages of the disease. Since the Terai area had been freed from malaria it had become prosperous farmland.

In the absence of Dr. Gabaldon, the delegate of Venezuela, Dr. D. Castillo, received the award on his behalf. In a message to the Assembly, Dr. Gabaldon expressed his gratitude for the award and recalled how in 1936, when he was a young doctor, he had read writings on malaria by the then already well-known Dr. Gordon Covell.

"I had never thought," Dr. Gabaldon said in his message, "that the disciple and the master would ever receive, at the same time, the highest award given to malariologists".

LIVE ANTI-POLIOMYELITIS VACCINE

By Professor A. Smorodintsev,

Corresponding Member, U.S.S.R. Academy of Sciences

THE pathogene which causes poliomyelitis is a tiny virus that enters the human body through the mouth and multiplies in the intestinal tract. In the most susceptible persons, it enters from the intestines into the blood and thence into the central nervous system, destroying the nerve cells. This leads to paralysis of the muscles of the arms, legs and trunk. The widespread incidence of this disease in the world has been a source of great anxiety in the last few years.

In view of the growing danger, scientists turned their efforts to the discovery of preventive methods. It has been known for a long time that persons having once suffered from poliomyelitis remain immune to further infection. Scientists have, therefore, striven to find a method of creating artificial immunity through vaccinations. They were particular that the virus of poliomyelitis entering in the composition of vaccine must entirely be harmless to children and not cause any symptoms of the disease or any other less dangerous reactions.

The first effective anti-infant paralysis vaccine was developed by the American scientist, Jonas Salk, in 1954. He reproduced highly pathogenic viruses of poliomyelitis in cultures prepared from the living cells of the nephric tissue of apes, after which he killed the reproduced viruses with formalin. The vaccine, thus rendered harmless, was injected three times subcutaneously or intramuscularly. This vaccine reduced fatal cases among millions of children inoculated by about 75 per cent.

TOO EXPENSIVE

Salk's vaccine has some substantial defects too. The proportion of children whom it protects from poliomyelitis is not over 75 per cent of those who are inoculated. The rest remain susceptible and may fall victims to the infection. The immunity acquired after three injections of the dead vaccine does not last long, so that the injections have to be repeated every two or three years. The preparation also is very complicated and expensive. It is prepared on the nephric tissue of

apes brought by plane from India and China. At least 1,500 apes are needed to prepare a million doses, whereas the number of children and juveniles requiring vaccination in the U.S.S.R. is about 80 million.

These serious drawbacks naturally increased the scientists' interest in the study of live vaccine, a preparation affording better prospects. It is composed of specially obtained harmless viruses, deprived of the capacity of developing in human nerve cells and injuring them. When live vaccine, containing millions of active virus particles, is injected, for example, into the brain of apes (who are much more susceptible to the pathogene of poliomyelitis than human beings) the animals, as a rule, are not observed to develop any pathological reactions.

A great advantage of live vaccine is that its preparation is simple and inexpensive: 100,000 doses can be prepared from the kidney of one ape.

Live anti-poliomyelitis vaccine was developed and studied by the joint efforts of American and Soviet scientists. After many years of work, the American virologists, I. Koprovsky and A. Sebin, obtained weak poliomyelitis viruses which, as has been said, became harmless to the anthropoid and lower apes not only after oral administration, but after direct injection into the brain.

But extensive observations were still necessary before the harmless nature of the live vaccine and its effectiveness could be finally established. Its effect on a mass vaccination had to be studied. This was done in the Soviet Union. "Why is it necessary to search for live vaccine," said the opponents of the new method, "when we already have an entirely harmless and widely tested dead vaccine?"

The great work accomplished in the course of the last four years by the Leningrad Institute of Experimental Medicine of the U.S.S.R. Academy of Medical Sciences has given an answer to this and many other questions. In 1956 we prepared a consignment of live vaccine from the weakened viruses of Dr. Sebin and

began observing its effect from the beginning of 1957.

SOVIET TESTS

In 1958 1,250 infants were vaccinated with this new vaccine. The same number of children, who were in constant close contact with those who had been inoculated, did not get any vaccine. Clinical observations gave additional proof that the vaccination was completely harmless, both for the children who were inoculated and those who were in contact with them.

A new objection was raised: admitting that the live vaccine had proved harmless for 2,500 children, the figure was too small for the solution of so important a problem. At least 100,000 children ought to be inoculated before it could be pronounced harmless.

In the first quarter of last year about 20,000 children and in the second quarter one and a half million more

(Continued on page 45)

children up to 14 years of age in Byelorussia, Latvia and Moldavia were vaccinated. The Institute for the study of poliomyelitis of the U.S.S.R. Academy of Medical Sciences has been doing similar work since 1959. By the end of last year there were already 12 million children in the U.S.S.R. inoculated with the live vaccine and there was among them not a single case of poliomyelitis caused by vaccination. In the epidemic season (June–November) the number of poliomyelitis cases among the children who had been inoculated with live vaccine was 10 times less than among those who were not vaccinated. Two or three injections to susceptible children proved entirely harmless and were much more effective in preventing the disease than Salk's dead vaccine.

TOWARDS ERADICATION

Pathogenic stray viruses are not found in inhabitants inoculated, since the necessary conditions for reproduction of the pathogene are absent in the intestinal tract of vaccinated children. Poliomyelitis retreats rapidly under the onslaught of live vaccine and the

CARDIAC SURGERY IN THE USSR

By Professor B. Khromov

THE unusual intricacy of the anatomical structure of the heart and lungs, their tremendous, vitally significant role, the exceptional sensitivity which, during operations on these organs makes the condition of the patient especially grave, the danger of air entering the pleural cavity and the particular danger of infection—all these prevented the successful development of thoracic surgery. It took many years of persistent work to overcome these difficulties.

The first attempts to suture the heart were made in the eighties of the last century. These experiments were first conducted on animals. Later, operations were performed on men suffering from injury to the heart. Since then the human heart has ceased to be considered "out-of-bounds" for the surgeon's scalpel.

It should be emphasized that the suturing of a wounded heart results in recovery in over 70 per cent of the cases. Blood transfusions also play a significant part in saving the patient's life.

Soon after the first successes in suturing the heart, surgeons attempted to remove foreign bodies from this organ.

These operations are now a matter of history, but the experience gained laid the foundation for the further development of thoracic surgery.

Nowadays surgeons in all countries are intensively studying new intricate problems concerning the surgical

treatment of various diseases of the heart, including its congenital and acquired defects.

MODERN METHODS OF DIAGNOSIS

Of great significance in cardiac surgery was the development of modern methods of diagnosis of various diseases, such as X-ray examination of the heart and the blood vascular system with the introduction of contrast substances and the study of cardiac activity by delicate instruments like the electro-cardiograph. The cardioscope, a new interesting optical instrument which makes it possible to see and even photograph heart cavities and to conduct various operations within them under visual control, has come in existence recently. Experiments on artificial circulation and the creation of various apparatuses for this purpose, such as "artificial heart and lungs" may also be mentioned. Such experiments began in the Soviet Union as far back as 1928. A number of models of "artificial heart and lungs" have already been tested in the Soviet Union. One of the models, designed by a group of engineers and surgeons of the Research Institute of Surgical Apparatuses and Instruments, has proved the best.

Hundreds of operations for removing congenital heart defects have already been performed, and, as a rule, they have resulted in the complete recovery of the patients.

The surgical treatment of various acquired heart defects, which are mainly due to rheumatic

(Continued from page 44)

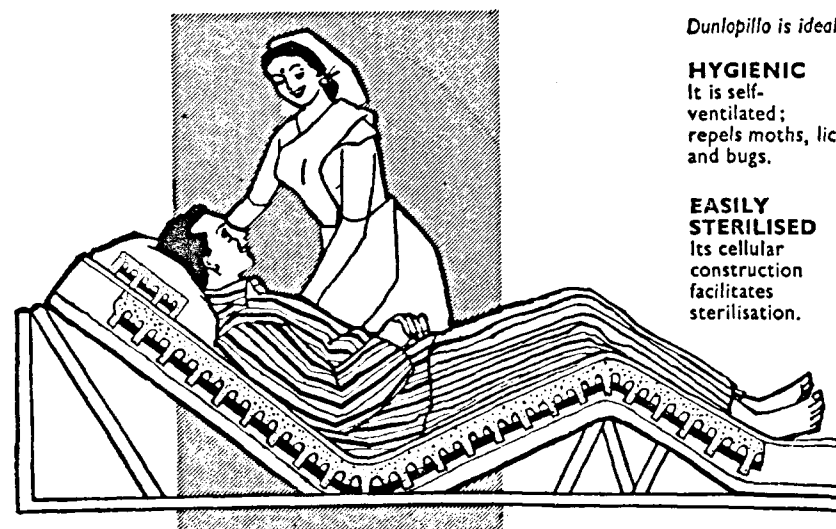
danger of new epidemics is steadily heading towards complete eradication.

Live vaccine is now produced by the Moscow Institute for the study of poliomyelitis in the form of a liquid which can be taken in with a spoonful of sweet syrup of water, or in the form of candy. When the vaccine is administered orally as a liquid or a candy three times (at monthly intervals), immunization

becomes an easy and even pleasant process.

The whole juvenile population of the Soviet Union up to the age of twenty is to be vaccinated against poliomyelitis within a few months. This energetic attack on poliomyelitis with the aid of highly effective live vaccine is conducted for the first time and shows to the whole world the advantages of the Soviet medical system.

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endocarditis, is a much more difficult and complicated task.

It may be noted that acquired heart defects occur more frequently than congenital, and constitute 97 per cent of all heart defects.

Years of experimental study by eminent Soviet surgeons like I. P. Dmitriev, N. N. Terebinsky, A. I. Yarotsky and others, have preceded modern operations on the heart. Special instruments provided with an electric lamp and optical system, making it possible to see the heart valves and to perform operations under visual control, are available at present for intracardiac surgery. Hundreds and even thousands of such operations have been successfully carried out up to the present time. The results of surgical treatment of mitral stenosis are quite satisfactory: about 50 per cent of the patients undergoing this operation are able to resume work.

OPERATING ON "DRY" HEART

Attempts to operate on a "dry" heart with its temporary "exclusion" from the circulation by occlusion of the venæ cava are very promising. When combined with certain new methods of anæsthesia such occlusion of the veins makes it possible to "exclude" the heart from circulation for 15-20 minutes and even longer. However, the use of the apparatuses mentioned above for inducing artificial circulation and thereby ensuring the complete exclusion of the cardiac function during an operation has opened even greater possibilities for cardiac surgery. Such a brilliant operation was performed for the first time in the USSR by the famous Soviet surgeon Prof. Vishnevsky at the end of 1957. He successfully operated on an 11 year-old boy who suffered from a grave congenital heart disease.

Professor P. A. Kuprianov, an outstanding Soviet surgeon, performed some time back another most intricate intracardiac operation—and a successful one—for the repair of congenital interauricular septal defect. Such operations are a new step in the further development of intracardiac operations.

In 'decompensated' heart defects when surgery

of the heart is contraindicated, a number of other operations are employed. These operations, such as ligation of certain large veins in the abdominal cavity, considerably improve the circulation of blood. The positive effect of these operations sometimes lasts several years.

ANGINA PECTORIS

There have been very interesting attempts at surgical treatment of angina pectoris or of coronary insufficiency due to a spasm or sclerosis of the blood vessels supplying the heart. Conservative treatment by medicines is indicated in a majority of cases of angina pectoris. However, surgical treatment is required in grave cases with frequent severe attacks of pain.

Various methods of administration of novocaine solution into the mediastinal cellular tissues are employed (novocaine block). This is done to relieve the suffering of the patients by affecting the nerve plexuses of the heart. In a number of cases substernal cellular tissue, various muscles of the lungs or omentum, i. e. the tissues rich in blood vessels, are sutured to the heart muscle to improve its circulation. Finally, the heart veins are ligated and certain operations on the pericardium are done for the same purpose.

Attempts at surgical treatment of the severe malady known as myocardial infarction (that is, a sudden obstruction of the vessels of the heart with acute disturbance of the cardiac function) are of great interest. The first experiments on animals lead one to assume that in time surgical methods of treatment of myocardial infarction will occupy a due place in medical practice. Thoracic surgery in the USSR has already attained considerable success and is advancing rapidly. The achievements of outstanding specialists in this field are becoming widely known to practising doctors. It is especially satisfying to note that complicated operations on the heart, lungs and the œsophagus are now performed not only in clinics and hospitals of the capital, but more and more frequently in many other cities of the Soviet Union.

FOURTEENTH WORLD HEALTH ASSEMBLY

THE Fourteenth World Health assembly was held from 7 to 24 February 1961 at Vigyan Bhavan, New Delhi, India. It was attended by delegations from 99 of WHO's Member States, as well as representatives of the United Nations, specialized agencies, and non-governmental international organizations in official relations with WHO. The delegates were welcomed, on behalf of the Government of India, by Mr. D. P. Karmarkar, Minister of Health, who said that the holding of the Assembly in New Delhi was a significant event for his country, particularly as it was the first World Health Assembly to be held in Asia.

In his opening address, the outgoing President, Dr. H. B. Turbott, Director-General of Health of New Zealand, welcomed the Honourable Mr. Jawaharlal Nehru, Prime Minister of India, and other distinguished guests, as well as the participants in the assembly, in particular the delegates of those States which had become full Members of the Organization during the preceding year. After reviewing the work of WHO during 1960, Dr. Turbott went on to say:

"Our organization stands for equality for all in health. The counter to much of the world's disease lies in fighting malnutrition, intestinal diseases from faulty sanitation, and general ignorance... of healthful living. We have the knowledge and health educational skills to deal with these killers, but we must await that economic and social development that will make possible improved national feeding and sanitation. Meanwhile we WHO Members who 'have' must encourage our countries in those international measures, financial, agricultural, and cultural, aimed at stimulating social progress and better standards of living in Members who 'have not'. Public health lags without money; economic development drags without health. It is our joy that our successes against specific diseases have helped to break this vicious circle, enabling disease-free people to cultivate more land, produce more food, and have a higher standard of living. But, because public health, economic development, and social development march hand in hand, we must ever be willing to give understanding co-operation to sister

agencies of the United Nations, WHO being entrusted with one facet, albeit an interlocking one, of the needs of our developing Members."

The Assembly was then addressed by the Honourable Mr. Jawaharlal Nehru, Prime Minister of India:

By acclamation, Dr. Arcot Lakshmanaswami Mudaliar, Vice-Chancellor of Madras University and Chief Delegate of India, was elected President of the Assembly. Dr. A. Martinez Marchetti (Argentina), Dr. J. Plojhar (Czechoslovakia), and Dr. D. Samonte (Philippines) were elected Vice-Presidents.

In his presidential address, Dr. Mudaliar said that, "among the many international organizations set up by the United Nations, the World Health Organization has come to occupy a foremost place in its efforts to improve the conditions of the millions of people in all parts of the globe". He recalled the early days of the Organization and the part played by the Indian delegation to the First World Health Assembly in moving a resolution for the constitution of regional offices to facilitate the promotion of health in the different parts of the world. The subsequent establishment of the various WHO regional organizations had "contributed not a little to bringing the work of the Organization... more directly into contact with the countries concerned" with significant success.

"One of the great and spectacular changes that were made in the approach to problems of health was in the decision arrived at that henceforth the World Health Assembly should have as its policy and motto not the control of certain diseases but the eradication of these diseases, particularly diseases whose causative organisms are well known and in respect to which effective steps could be taken. It is owing to the genius of the present Director-General and his staff that the problem of malaria control was changed to one of malaria eradication... I need not go into the many steps that have been taken in the promotion of this objective, but the significant decline in the incidence of malaria in many countries of the world shows not only how effectively this campaign has been carried on but it gives hope and cheer to the

nations of the world that with regard to other diseases, also of a communicable nature, the word 'eradication' may well be writ large as a significant sign for the manner of tackling these diseases. I refer in particular to diseases like smallpox, cholera, several of the water-borne diseases and to many other diseases which are carried by insects."

Dr. Mudaliar then referred to the work of WHO in various parts of the world stricken by natural or man-made disaster, and in particular to the organization's emergency action in the Republic of the Congo (Leopoldville).

Of the tasks facing WHO in the future, Dr. Mudaliar said:

"Great as has been the work of the World Health Organization during the last thirteen years, considerable as have been its achievements, significant as has been its effect on the reduction of morbidity and mortality in most lands, no one can deny that the World Health Organization has yet a greater part to play. It cannot afford to rest on its laurels. There are still many diseases which require its constant attention and intensified activity. Prominent among the four priorities established by the First World Health Assembly is tuberculosis and, although much has been done, much yet remains to be done in a constructive way to control this widespread scourge. It is of significance that, recently, experiments have been carried on in South India in the city of Madras, which tend to give us a ray of hope that by domiciliary treatment it may be possible to control the disease and to prevent its spread. I am glad indeed that the technical discussions this year will be on the subject of tuberculosis.

"Yet another disease which, in this region and in neighbouring regions, has caused a great deal of concern because of its method of insidious onset and the large numbers that are affected by it is leprosy. One need hardly say that from early times it has unfortunately been the practice to think of those suffering from this fell disease as persons who should be beyond the pale of society. Fortunately for them and fortunately for the conscience of humanity, the remedies that have been discovered have made it possible for such persons to be comparatively free of some

of the obvious manifestations of the disease and, by suitable treatment or rehabilitation, to make them once more useful members of society. The work involved however is tremendous and it would be well for the World Health Organization to concentrate upon the eradication of leprosy also and to seek the co-operation of all governments and of the general public for the radical removal of this ancient scourge, which has from biblical times been dreaded by humanity.

"Yet, as disease after disease is being controlled, the problems of world health are becoming increasingly complex. New diseases have unfortunately come to light and some diseases have become much more common now than before. The stress and strain of modern civilization, the constant dreads which society has to bear from the action and reaction of world politics and the conditions prevalent in highly industrialized society, have unfortunately increased the cases of mental illness, fatigue and irritability and, what is more disquieting, this factor is as important in the young as in the old. As new discoveries are made and new remedies are placed in the hands of the medical profession, one has to realize that the goal of public health work in respect of most diseases which affect the masses of the people will be more of prevention than cure and that control and eradication are measures which must be thought of only when the diseases actually set in. And therefore it is that the World Health Organization has always insisted upon those factors which are conducive to the prevention of diseased conditions."

In conclusion, Dr. Mudaliar said:

"No organization is so singularly devoted to the welfare of humanity as the World Health Organization. It has no other ideology, on other aims and no other objectives. And, so long as it is inspired by these high and noble ideals, I feel sure that it will command the sympathy and support of all countries in the world—a fact that is amply borne out by the very large number of countries that have become Members of this Organization. Let us continue this great task with humility but with the firm determination to render unto the people what is their due, to make life healthy and happy with a purpose, to be of greater and greater service to humanity at large."

Mr. S. M. Keeny, Director of the Asia Regional Office of UNICEF, then read a message from Mr. Dag Hammarskjöld, Secretary-General of the United Nations:

"I wish it were possible for me to be with you in person. The work of the World Health Organization is of special significance to the development of the United Nations system and of international co-operation in general. In particular it has helped to lay the foundations for progress in the direction of a multi-lateral approach to questions of economic and social development, through its continuing efforts to meet and overcome problems in the field of health as instanced by its malaria and smallpox eradication programmes, and through its encouragement, as defined in its Constitution, of 'the attainment by all peoples of the highest possible level of health'.

"WHO can look back on a year of solid achievement, but it has before it problems of vast significance to the welfare of mankind. Close relations between WHO and other members of the United Nations family are of vital importance if the social and health aims outlined in Article 55 of the United Nations Charter and spelled out in resolutions of the Economic and Social Council and of the General Assembly are to be achieved. The attainment of higher health standards on a world-wide scale depends not only on health measures, but also on measures to raise standards of living and social conditions in general, in which the United Nations and other international agencies have an important role to play. In this common effort each can be successful only with the assistance of the others. I might illustrate this point by referring to a matter that is to be a subject for discussion at this Assembly, namely, assistance to the Republic of the Congo. The civilian operation of the United Nations family in the Congo has been a remarkable instance of co-operation on a large scale among international agencies involved. As stated by my special representative in the Congo in his first progress report to the Security Council last September: 'For the first time in the history of international organization the United Nations and the specialized agencies have collaborated in the Congo as a single team under the mandate of the Security Council, to meet the economic emergency following the country's independence.

They have put together, in a little over a month, the largest civilian team they have ever had in one country at one time.'

"In the effort to meet a critical situation, new forms of international assistance are being developed. The operations have been based partly on the tradition pattern and methods of technical assistance and the provision of operational and executive personnel, but new ground has had to be broken. In addition to technical assistance proper, activities on a higher level of administrative responsibility under new and special arrangements have had to be undertaken by international officials in the Congo.

"The contribution of WHO to this operation cannot be over-estimated. Having been requested by the Security Council to render assistance, WHO has responded, under the terms of its Agreement with the United Nations, both promptly and in a spirit of helpful and practical co-operation. It has provided a senior consultant in health to the Consultative Group of the operation and has assigned a sizeable number of its staff members, who are responsible, with the Ministry of Health of the Republic, for co-ordinating all health work in the country. Its health teams and those provided by the Red Cross have carried out their tasks with devotion and a sense of self-sacrifice, under conditions of great difficulty. The long-term plans for the development of appropriate medical cadres and the training of medical personnel, elaborated by WHO, should become the basis for an improvement in the health of the population throughout the country.

"There are a number of other areas of mutual interest which deserve particular mention. Of special importance in my view is the assistance rendered by WHO in Africa, especially to newly independent countries, in response to resolutions of the General Assembly and the Economic and Social Council. The participation of WHO and other Members of the United Nations family in the long-term programmes in the field of community development, urbanization and housing provides significant examples of effective, concerted action at the international level. Mention should also be made of the fruitful contribution of WHO to projects of the Special

Fund and the aid recently provided by WHO when disaster struck on a large scale in Chile and Morocco. Lastly, let me add that the co-operation of WHO in the work of the Asian population conference, scheduled for late 1962 or early 1963, under the auspices of the Economic Commission for Asia and the Far East, will be warmly welcomed.

"In concluding these remarks on some of our common endeavours, I have great pleasure in conveying to you my warm greetings and sincere good wishes for the success of your deliberations."

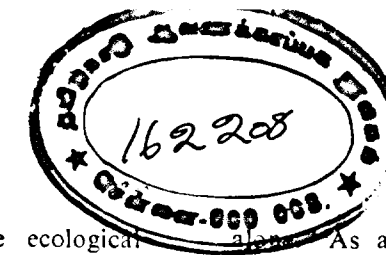
Presenting his report on the work of WHO during 1960, Dr. M. G. Candau, Director-General of WHO, commented first of all on the action taken by WHO in the Republic of the Congo (Leopoldville) immediately after that country gained its independence in July 1960. This was the first time that the Organization had had to combine emergency measures to satisfy immediate needs with long-term programmes

to maintain and develop the basic health services. Dr. Candau told the Assembly that WHO was now in the process of recruiting 130 health workers of all categories needed to fill key positions in the medical-surgical centres of the Republic. The task of assisting the country in the education and training of its own health personnel has also begun well: 61 *assistants médicaux* were studying in various universities of France to complete their full medical training, while 7 students from the Congo had commenced medical studies in France and in Switzerland. At the request of the Rector of the University of Lovanium, through the Government of the Republic, WHO was recruiting a number of professors in order to complete the teaching staff of the medical school and of the school of nursing. Dr. Candau stressed the fact that WHO had been able to carry out its work in the Congo without any serious difficulty.

With regard to malaria eradication, Dr. Candau expressed the hope that the Assembly would find a lasting solution to the financial difficulties that impeded the execution of the programme and might soon jeopardize the results already achieved. Recently there had been indications of additional, and hitherto unexpected, benefits that might come from a successful all-out war on malaria. *Anopheles* mosquitos had for the first time been incriminated as vectors in a virus epidemic—the outbreak of o'nyong nuong fever, a disease carried by *Anopheles funestus* and *A. gambia*, which started in East Africa in 1959 and had so far affected about 750 people. Thus the attack directed against the malaria vector should also significantly reduce the transmission of this other disease.

Another important feature of the activities described in the 1960 report was the continual stress laid on research. Despite certain financial difficulties, the intensified programme of medical research had been launched, with the highest priority given to the communicable diseases, particularly those prevalent in the tropics:

"One of the facts which augur well for the future of work in this field is that scientists and field workers are increasingly adopting the ecological approach to the study of insect-borne diseases. Indeed, we know now that many costly failures could have been avoided in the past if the control of certain diseases had been based on sounder ecological principles. It is



therefore most fortunate that the ecological concept of communicable disease is now being expanded beyond the phenomena of transmission to take into account the climate, geology and the whole structure and behaviour of animals and man and their inter-relationship. Furthermore, a change in man's environment affecting his agricultural and industrial activities often results in a change in the very pattern of a disease. A comprehensive study of any communicable disease must consider all these factors in order to establish practical measures ensuring adequate control and eventually complete elimination of that disease."

Other features of the international research programme included efforts to improve the tools available for the investigation of the disease-carrying arthropods. The use of isotopes had been extended to studies of insect physiology and the mechanism of transmission, and it was hoped that it would help to solve the biochemical puzzle of the resistance of insects to insecticides.

Another part of the programme was cooperation with the chemical industry to find new compounds that could be successfully applied to problems of public health:

"We now have a five-stage programme involving six laboratories in different parts of the world and a research team established in Lagos, Nigeria. This programme is destined to test as many as 300 compounds a year, and at present more than 120 are being examined. Already a number of promising new chemical groupings have emerged from this undertaking, and we are about to use them in carefully controlled field trials on the vectors of trypanosomiasis, typhus fever, onchocerciasis, filiriasis, Chagas' disease, and plague."

Dr. Candau next referred to the new prospects for the control of trachoma opened up by the isolation of the virus, and to the progress in poliomyelitis research which had made it possible to envisage the eventual elimination of the disease. Nevertheless, the development of live vaccines still left many problems to be solved in laboratories and in the field.

More countries had achieved independence in 1960 than during any one year in the past—17 in Africa

As a result the membership of WHO had increased to 160 with 104 full Members and 2 Associate Members. Dr. Candau went on to speak of "the opportunities which lie before the international community in assisting the newly developing countries in their economic and social development". It was, he said, the duty of the Assembly to emphasize the indissoluble relationship between health and economic and social development:

"We in WHO believe... that the tragic and all too familiar cycle of ill health leading to poverty and poverty causing ill health must be broken through the concurrent and concerted action of all branches of science and technology. Only then can we be sure that our Organization may make its modest but essential contribution to the great undertaking launched in our time to eliminate poverty, disease and ignorance from the face of the earth, so that the people of all races and of all nations can build the healthy, prosperous and peaceful international society which still the cherished dream of all of us."

THE CONTEXT OF HEALTH

Address by the Honourable Mr. Jawaharlal Nehru, Prime Minister of India, to the Fourteenth World Health Assembly

We feel honoured by this World Health Assembly meeting here in this old city of Delhi. It is an honour, for [WHO], in the brief course of thirteen or may be fourteen years, has done much good work and has such achievements to its credit and, what is more, has laid the foundations of so much good work in the future.

There are many world organizations today, a number of them stemming from the United Nations, as does WHO. Without meaning any disrespect to any of the others, I might say that the World Health Organization has probably steered clear of many of the controversies and conflicts that afflict some of the other organizations, and that come in the way of their successful achievement of the tasks before them.

The list of achievements of WHO is formidable. It is impressive. But I imagine that, apart from the practical achievements, if I may say so, the other achievement—not something that you can

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easily grasp, but nevertheless which is there and which is very evident—is the consideration of international problems in a peaceful way, not dividing yourselves into national or other groups and rather by-passing the main task because... other conflicts come into your work. That is a great achievement, because perhaps the most important thing in the world today is to achieve that objectivity in considering problems, that spirit of co-operation, which sometimes we sadly lack.

I suppose it may be said that most of the problems that afflict mankind today—not all, but most, and certainly the primary problems of health, education, the general welfare of the community, food, clothing, housing and such problems—are capable of solution by the means at hand in the world, not in each country at the present moment, but in the world as a whole. We have the means at hand to solve these problems and build up a measure of welfare throughout the world, a measure of health, a measure of education. We have that, and we have it in recent times for the first time in history. Going back a generation or a little more, that statement could not have been made. The world was not in a position to grapple with these problems and solve them. But today the world is in that position theoretically, and to some extent practically. But other things come in the way, other obstructions, with the result that the capacity for work which it undoubtedly possesses is not fully used and sometimes our efforts do not succeed and a sense of frustration comes over us. Now that perhaps applies less to the work of WHO than to other great organizations. And, therefore, WHO helps—as other organizations too, but perhaps more so WHO—in this vital task of promoting a spirit of co-operation, of making people realize, as I believe it is stated in your approach to these problems, that the world is becoming progressively one unit in regard to its major problems. It is difficult enough to solve any major problem of the world by taking bits of it apart and ignoring the rest, whether it is disease, whether it is anything. If that is difficult, it becomes even more difficult when the different bits pull against each other and come in the way of each other. You are of course engaged in this great Assembly in an important task of spreading physical health, but in an even more important task of creating an atmosphere

conducive to the mental health of the general community. As every doctor I believe knows, physical health is very much dependent on mental health. You can hardly separate the two. The world today, which can deal with the problem of physical health satisfactorily enough, though it may take a little time, has still to find ways of dealing with the mental health of nations, groups and communities. I hope that this Assembly, this organization, though perhaps it cannot tackle their problems directly, will nevertheless indirectly make that approach and help those forces, those elements in the world today which are trying to reach this state of mental health of the world community.

The achievements of WHO are very considerable, partly I think because the intrusion of mental conflicts has not come there: it is a straightforward course of dealing with problems—some of them very difficult problems, but nevertheless there is no mental obstruction coming in the way as it does in other matters, political and economic. I think one of the reasons why this success has been considerable is this absence of mental obstruction which comes from pulling in different directions. We hope that that will lessen and then the progress that you or other great organizations make will be very considerable, much more so even than now.

In our country, in the last thirteen years since we became independent, we have been rather overwhelmed by problems. Not that we are afraid of problems, and they did not come to us suddenly without notice: they were there. We inherited them and we had to deal with them. And remember that almost every problem that we have to deal with has to be multiplied by 400 million. So we get a large figure: that is, the population of this country. We think of these problems in terms of the 400 million, not in terms of some inchoate mass of humanity or some concept of the state apart from the individual, but in terms of the welfare of the 400-odd million people in this country. So the problems increase in size and become very big. We are directly dealing with them; we shall continue to deal with them, with a measure of success I think, and indeed the odd thing is that, as we succeed, other avenues open out and other and more difficult problems face us. That is a measure of success. It is only those

people or those communities that are not moving and that are stagnant that have practically no problems before them.

Well, we are moving in India, I believe, and moving fairly fast, and with a certain dynamism behind that movement, and so problems surround us. Health is one of them, education another basic problem, and behind it all economic betterment, which gives us the capacity and the means to deal with these other problems. We have to choose, and often enough it is a hard choice, whether we should devote more of our resources to education, to health, to agriculture, to industry and so many other things. The fact of the matter is that everything is interconnected and we can only see it properly in the context of other things: they cannot be separated. Therefore we go in for planning, trying to understand the whole picture in a connected way. Naturally it is not easy and we fail to understand it fully, because life is too complicated, life in a huge country like India struggling out of the past into the present certainly, but almost into the future at the same time—because in India we live simultaneously in all the centuries of the past and in the present, and with our foot in the future. It is a fascinating spectacle, a fascinating experience and an exciting one; and every success that we achieve naturally gives us greater strength to face the future.

Now it is odd that success itself sometimes, as I said, leads to greater problems. The President in his address mentioned the fall in infant mortality, which is very considerable. I remember many years ago, in the 'twenties as far as I remember...reading about the expectation of life in India. It was then said to be, I believe, 24 years, which is fantastically low, a chiefly because of infant mortality. Round about 1947, when we achieved independence, it had gradually crept up to 32, which is low enough. In the last thirteen years it has come up to 42, which is a fairly substantial advance in this period; and it is going up and up, which in itself is a measure of the cumulative effect of the various health measures that have been taken by us, and in which I am happy to acknowledge the help of the World Health Organization.

So we are progressing along those lines and as we progress towards better health, our population rises more and more. Deaths are relatively fewer and the death-rate goes down. The ratio increase

of the population goes up, presenting us with another basic problem. I mentioned how all our good efforts sometimes lead to new situations which become rather overwhelming. That is bound to happen, and therefore we have to see all these various problems in a connected way. We shall struggle on with faith and hope and with a certain confidence in our future and the world's future. But there is one thought which I should like to share with you. It is not a problem of the present in India, because in India or in the under-developed countries our problems are how to provide the basic necessities of life to our people, whether it is food, clothing, or housing, as I mentioned, or health and education. These are the basic necessities which every human being should possess. That is our problem, and the problem of every undeveloped country.

But in the case of industrially or economically advanced communities, in the case of nations which have largely developed affluent societies, problems are different. They have got the basic necessities of life, by and large, and so they have to face entirely different problems. That is why, in trying to understand the state of the world today, we sometimes get rather lost in political divisions, political arguments and the like, important as they are in their right place. But the most important thing is, in considering the world, the division of the advanced, the prosperous communities of the world and those that are under-developed and therefore poverty-stricken, where even the basic necessities of life are lacking for many people. That is the real division in the world, and that is a division which is not only bad in itself, but which brings dangers in its train—political dangers, economic dangers, social dangers, all kinds of things. I believe it is now being recognized more and more that this question of dealing with those countries is not merely one of doing a good thing, but something which is necessary from the points of view of the health, the political health, the social health, of the world community as a whole.

We are struggling, as I said, for the basic things of life in India, and in many countries of Asia, and in many countries of Africa, in various degrees—some may be a little more developed than others, but basically they are under-developed—we are struggling for that. In the other countries, the industrially and economically more advanced countries, there seem to be new

dangers arising. I mention them as a layman merely, as I know not much about them. New dangers, almost you might say sapping the health of the community; dangers of the mind and the spirit, a neurosis let us say. There is no lack of the normal good things of life, but somehow the flavour of life, the spice of life, the sense of adventure, the sense of facing problems, becomes less when everything happens as planned; and may be a sense of frustration comes into the minds of people. I do not know, I just put it to you for consideration. There is more leisure and people do not know how to utilize that leisure. All this you know better than I do.

Anyhow that is not our problem, and that is not the problem of countries that are under-developed. I am very glad that they are a number of new Members of this assembly from the independent States of Africa. As we all know, this last year... stands out among other things perhaps more specially because of the developments in Africa. Africa is a vital, dynamic place. There may be trouble there and there may be conflict there, and there may and will be, I am sure, advance in many ways; but one thing is certain, that it is today, and is going to be, a vital, dynamic place, for good or bad as you like. It is good that it has come out of that morass in which it was stuck; it has come out perhaps in some places in a bad way; by a bad way, I mean that the

manner of its coming out showed how badly prepared it had been in the past. Whatever that may be, the fact is that the countries of Africa are of vital importance in the world, to the health of the world, apart from their own problems. And I think that all countries that are favourably circumstanced, I mean India and other countries like her which are struggling with their own difficult problems should, so far as is possible for them, stretch out their hand of help to these countries of Africa which have newly come into this world community and face these difficult problems.

You drew attention, Mr. President, in your remarks to the help given to the Republic of the Congo by WHO. Undoubtedly that is very considerable help, and it has come at a time when it was most needed. The success of this help compares rather favourably, if I may say so, with the political aspect and the political problems there and the conflicts that have taken place and still are unresolved. It shows how the work of the World Health Assembly, lacking as it does the political motive, is much healthier than the work of other organizations. And I hope it will always keep away from these political motives and political conflicts and deal with the problems in the spirit of a common humanity. Till that spirit prevails all over the world, in all our problems there will be difficulties and conflicts.

SCIENTISTS CONFIRM FAVORABLE RESULTS WITH ANTI-CANCER DRUG

Researchers from the National Cancer Institute reported that a five year study has confirmed their previously published findings that the drug methotrexate does control some cases of choriocarcinoma, a rare but highly malignant form of uterine cancer. Dr. Roy Hertz and associates told scientists gathered for the 52nd annual meeting of the American Association for Cancer Research that 30 of 63 patients treated with methotrexate are now free of evidence of the disease. Several of these women have had no indication of return of the disease for up to five years since their treatment was completed, according to the government scientists. The disease is extremely rare, however, affecting approximately 300 American women each year.

Of particular significance, they said, is that in all these cases the tumor had spread outside the uterus into other parts of the body, most frequently into the lungs. They termed this response "uniquely favorable" and indicated that complete return to good health for periods of five years following chemotherapy for a malignant tumor has not been previously observed.

Methotrexate belongs to a class of drugs called folic acid antagonists which so closely resemble the vitamin folic acid that,

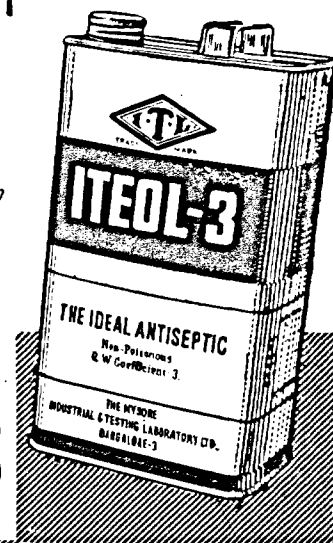
in effect, they "trick" the cancer cells into absorbing. But once absorbed, the antagonists provide no nourishment for the cancer cells and seriously interfere with their growth.

The drug was discovered and developed at Cyanamid International's Lederle Laboratories under the direction of the Indian-born scientist Dr. Yellapragada Subba Row as part of Lederle's 22 year cancer research activities. It was initially used in the treatment of leukemia and often helps prolong the lives of its child victims by several years. Dr. Hertz' research with the drug began in 1956. By utilizing large doses of the drug and by administering it early in the disease, he was able to report "considerable success" in treating 17 patients in 1958. However, this disclosure represents the first report of a five-year follow-up study on the disease. In addition to methotrexate, the researchers reported treating 14 of the women for short periods of time with a recently developed plant derivative called Vincetukoblastine. These medications have severe side effects, but the doctors described their methods for insuring the complete recovery of their patients from such undesirable and somewhat hazardous effects. Assisting Dr. Hertz with the study were Drs. John Lewis, Jr. and Mortimer B. Lipsett.

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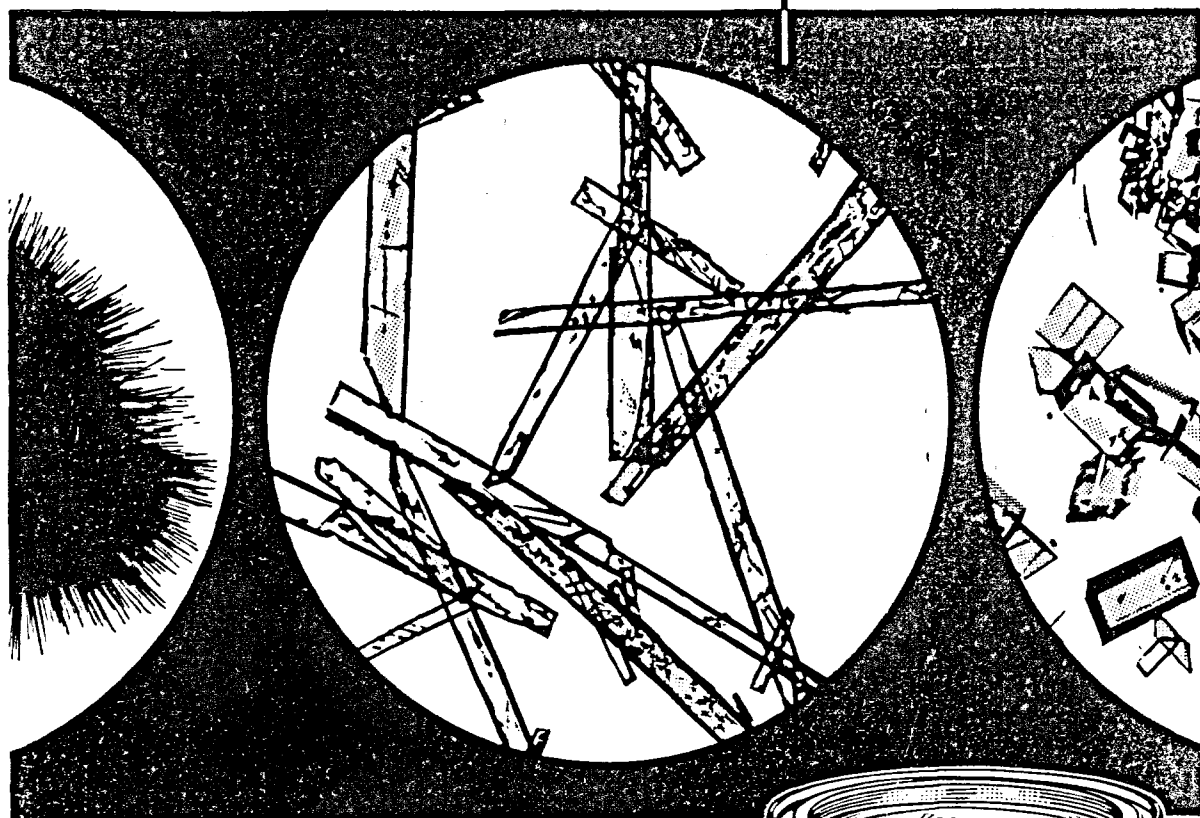
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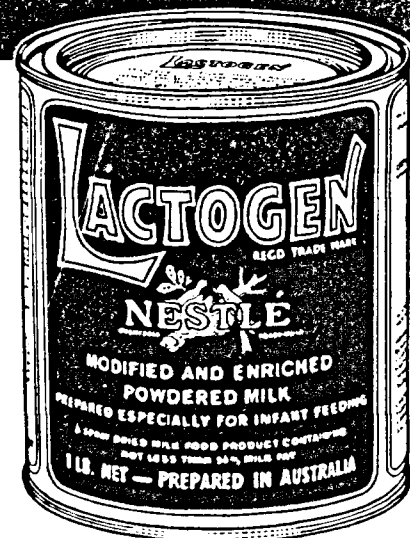
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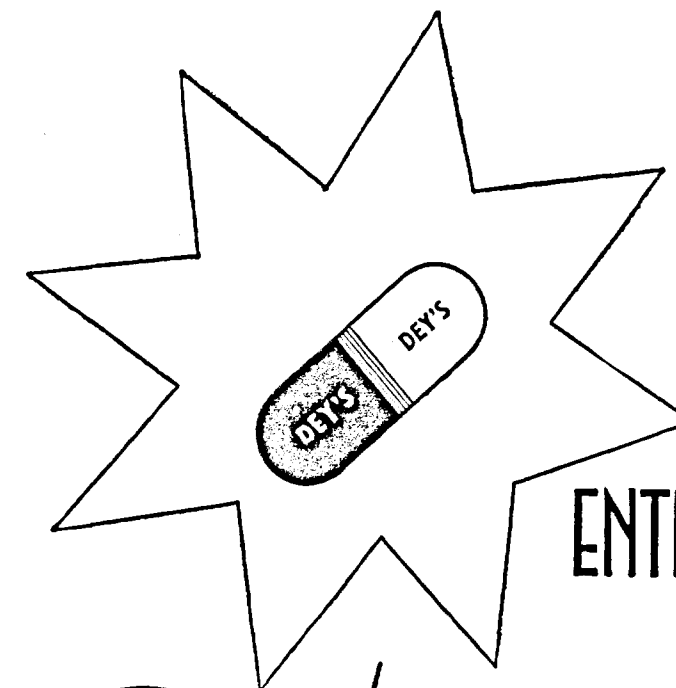


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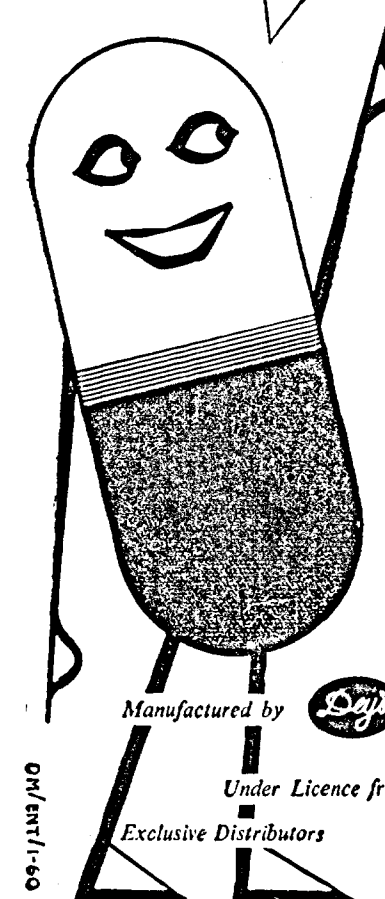
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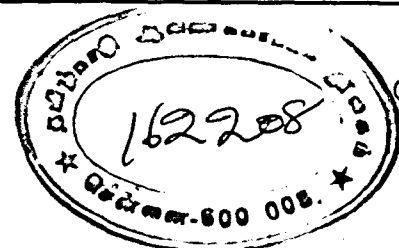
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DOCTORS FOR VILLAGES

"A HALF baked doctor will do, for there are no doctors at all in the village" said the politician to his friend the Professor of Medicine. The discussion came to an end because he had to take his own child to see a highly qualified medical specialist in the big city. He did not pay any heed to the Professors argument that it would be better to have no one than to have a semi-qualified person and thus lower standards of medical education. There was something to say on both sides but the fact is that many a village has to go without any doctor at all. This problem of finding medical aid for villages is a very serious problem and a real challenge which the nation has to meet.

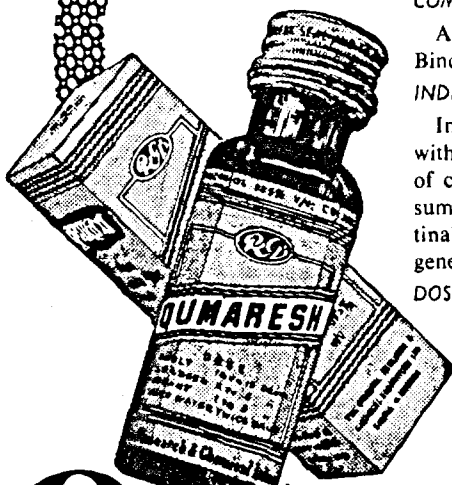
It appears that the Govt. of Mysore has more or less decided to start four medical schools to start training students for the diploma course in Medicine, in spite of protests from the custodian of standards of medical education, the Indian Medical Council.

This is nothing new for quite a number of years there were licentiates in medicine manning rural and urban clinics and hospitals until the system was abolished in the interests of bringing a unified standard of medical practice. In fact about 19 schools turning out about 1000 licentiates a year was closed down and the main reason for this was that the schools were most unsatisfactory. The training was far from adequate, and there were grave deficiencies in equipment libraries and museums, clinical facilities and laboratory services. The Bhore committee which studied the set up of medical education in India also went into this matter and believed that the absence of a central body to govern medical education resulted in much divergence in standards of medical education. In 1942 the Indian medical council adopted a resolution that all such schools be abolished and converted into colleges in order to have a uniform standard of medical education. This was widely welcomed and finally an end was put to the schools training licentiates. The decision to revive this by Mysore is interesting and everyone, both medical men and the general public cannot but look at this experiment with keen interest. The schools which are being started are to be somewhat different in the sense that the shortcomings which made the system fall into disrepute has been eliminated as far as possible. For instance it is proposed to start the licentiate training schools only in such places where there will be adequate training facilities and equipment. The course has of necessity been abbreviated and it would be a matter of interest to see if this type of imperfectly trained doctor will remain in the service of rural India or whether they will migrate to complete with their fully qualified brethren. As far as the general public is concerned they may not be able to distinguish between the imperfectly qualified and the fully qualified doctors.

Short term courses with semi-qualified medical personnel evidently has been used with some success both in the Soviet Union and China to solve their problems of finding medical aid for rural populations. In India too the proposal to train "medical assistants" to serve under medical practitioners in the villages has been under serious

consideration. Mysore seems to have taken the view that it is better to have imperfectly trained doctors for the villages than no doctors at all and the prospects of obtaining fully trained doctors for the villages under the present set up being somewhat remote. Besides it is thought this is not a perfect solution but something which is expedient and it is also believed that these imperfectly qualified personnel may at a future date be allowed to appear for a condensed course and become fully qualified doctors.

There may be something to be said for the experiment being tried out by Mysore but one would have to judge on the results because it remains to be seen how imperfectly trained men will be made to stay on and serve in rural areas and whether the public itself will accept a reduced standard of medical service for those who live in villages. It remains to be seen whether this proposition will solve the problem because there is no doubt the problem has to be solved. It would appear that it might be better to give adequate inducements to fully qualified medical personnel to settle and practice in villages as is being done by certain States and to popularize the scheme of having a well equipped and complete medical and surgical team to visit outlying villages in mobile units. By this means a high standard of medical aid may be given to the villages instead of giving them half baked doctors, and to say that these will be better any day than no doctors at all.



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Children	2 to 5 "
Infants	1 to 3 "

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Epidemiology of Tuberculosis with Special Reference to Dusty Industries

BY DR. M. N. GUPTA

(Deputy Chief Adviser, Factories (Medical), Ministry of Labour and Employment)

IN large industrial towns, thousands of active open cases of tuberculosis are detected every year. A very large majority of these cases are found amongst workers engaged in various occupations. Surveys in special groups of industrial workers as textile; jute; tobacco; dusty industries, like potteries, metal grinding, metalliferous mining, stone cutting, stone breaking, etc., have revealed high incidence in particular industries and localities. These special investigations have helped in providing information about the epidemiology of tuberculosis and morbidity resulting from it.

In the epidemiology of tuberculosis a large number of factors play an important part—like, a low standard of living, malnutrition, unhealthy housing conditions, ignorance of the laws of hygiene, etc. But all these factors get accentuated when urbanisation and industrialisation increase in a country, and this is what is happening in India today. The rural and semi-rural population (tribals) which is composed of highly vulnerable people, is migrating in large numbers, in search of employment to highly tuberculised industrial and urban localities, where chances of infection exist.

It has also been said that the tuberculosis mortality curve has not yet reached its peak in India in the sense that it was reached in Great Britain in 1950. This fact combined with another important fact that demographic and health-statistics, especially in industry, are most inadequate, do not allow of a qualitative and quantitative assessment of tuberculosis in industry. Our growing industrialisation is producing a picture of "pathological urbanism", the consequences of which will be considerable on tuberculosis epidemiology in general and especially in industry.

It is also unfortunate that industry has shown no marked interest in the use of X-rays as an aid in diagnosing diseases of the chest among employees and applicants for employment. This attitude of industry can be said to be influenced largely by the opinion of industrial physicians.

EXPOSURE TO DUST

In considering the general epidemiology of tuberculosis in industry it is necessary to refer to early records on the subject.

The making of stone implements by pre-historic man represents the first industry with an industrial hazard, i.e., dust. Lyell (1) makes mention of a prehistoric flint knapping factory at the site of one of the Swiss lake dwellings, and also the fact that some of these persons engaged in making flint implements suffered from respiratory diseases. Collis (2) reports that flint Knappers of Brandon suffered high mortality from phthisis induced by flint dust generated in their work. Carozzi (3) states that it is certain that pre-historic man suffered from a disease of the nature of tuberculosis if not an occupational pneumoconiosis.

Dusts of various kinds are present in the atmosphere everywhere and these, after inhalation produce inevitably some changes in the lungs (the pigmented lung of city dweller as shown by Kettle) (4).

The air under different conditions has varying amounts of dust as shown in the following table by Landsberg (5).

TABLE 1

Kind of air	Particles of dust per cubic centimetre (large particles only)
Mountain	2
City residential quarters	15
City business centre	100
Cement factory	1200
Granite cutting	2100
Bituminous coal mine	3900
Anthracite Mine	4400
Grinding shop	6700

He also states that the air inhaled by a normal person during a working day contains roughly about 12 million particles.

Our own figures in various industries where dust counts were carried out were as follows (6) :

TABLE 2

Pneumatic drilling in Mica Mines	800	mppcf
Grinding of Mica	133	"
Silica brick manufacture (various operations) (Range)	9-112	"
Fire clay Brick Manufacture (various operations) (Range)	4-1700	"
Cutlery grinding (Range)	36-110	"
Ceramics & Pottery industry (Range)	4-429	"
Cement Factories (Packing) (Range)	46-166	"
(Lime Stone Crushing) (Range)	15-90	"
Coal Pulverising (Range)	7-150	"
(7) Magnesite (concentrating plants) (Range)	1.2	"
(7) Chromite (concentrating plants) (Range)	1.7-114.2	"
(8) Lead dust (Manufacture of Storage Batteries)	0.5-60.4 milligrammes per 10m ³ of air.	

The chemical and physical characteristics of the dusts, their composition and particle size, concentration of particles in the atmosphere breathed and the duration of exposure, all play an important part.

PHYSIOLOGICAL EFFECTS OF BREATHING DUST

The weight of air turned over in the lungs in the course of a day is of the order of 60 lbs. or about 10 cubic metres during an eight-hour shift work of an industrial worker, a much greater weight than that of food ingested, and if it should contain any harmful substances in the form of dangerous dusts, a significant amount may be absorbed. The importance of this

route of absorption of silica dust and other dusts lies in the fact that they have a direct effect on the lung itself. One million particles of one cubic micron size are obtained from grinding one cubic centimetre of a stone piece, and if these are dispersed over a volume of 10,000 cubic feet (a room 25 ft. X 25 ft. X 16 ft.) would give an average concentration of 100 million particles of dust per cubic foot of air.

The effect of chronic conditions like chronic tracheitis bronchitis, bronchiectasis and bronchiectasis and asthma in diminishing the ability of the lung to rid itself of foreign material by way of the tracheo-bronchial tree is too well-known to be described here.

The relative incompetence of the lymphatic drainage system in workers in dusty trades and other hazardous trades has also been described in literature.

The description of respiratory syndromes associated with exposure to mineral substances and their inorganic compounds in industry can be found in books on Industrial Occupational diseases.

The role of air pollution and irritant gases found in industry is also described in such books.

Now these factors play an important part in the etiology of tuberculosis in industry especially so in dusty industries.

The oldest account of the harmfulness of exposure to dust is one written by Pliny (9) who says "Miner Refiners in the factory envelop their faces with loose bladders, which enable them to see without inhaling the fatal dust". Celsus, a Roman medical writer, in the first century stated: "By far the most terrible form of emaciation is that which the Greeks call phthisis. It spreads to the lungs. On top of this ulceration occurs and a slow fever which at times disappears and at other times reappears".

Mavrogordato (10) says that in writings of early writers dust phthisis is frequently mentioned. Agricola in his book *De Re Metallica* (11) says, "in the Carpathian mountains there are women who have married several husbands, all of whom this dreadful disease has brought to an early grave". Ramazzini (12) was the first to recognise the social significance of industrial diseases from harmful dusts and chemicals. Pancost (13), a recent author, states "the condition

pneumoconiosis is a more or less necessary risk of commercial development in the progress of civilization in recent years". His monumental work in this field started the roentgenological and clinical investigation of pneumoconiosis.

The first (Transvaal) Miners' Phthisis Commission in 1902 reported that 15.4 per cent miners were affected with miner's phthisis. In 1916, there was instituted the Miners' Phthisis Medical Bureau of the Union of South Africa and the work of this Bureau has helped to bring into prominence the incidence of silicosis and tuberculosis amongst miners.

Several special investigations carried out in certain industries in the United States (14) have attracted attention to the high death rate from tuberculosis, specially in mining, grinding, granite work foundries, cement, pottery, silica and firebrick manufacture.

Almost all other highly industrialised countries like Canada, Netherlands, Australia, France, Germany, Italy, Russia, have reported high incidence of tuberculosis in dusty industries. Now all this increase in dust has happened since the invention of the pneumatic drill, the Jack hammer, the mechanical coal cutting machine, sandblasting and electric welding, etc.

Also, the importance of the subject has increased since large scale social reforms stirred up the dust in the minds of men and roentgenology increased its value in the diagnosis of dust diseases.

Collis (15) has shown that when a country whose population is established on a rural basis moves into industry a rise in tuberculosis mortality occurs, principally in young men. Stabilization is only very gradually reached and the peak of mortality recedes from the young to the middle-aged to the elderly and the rate begins to fall.

We, in India, are seeing now an increase in industrialisation, trade and communications and industrial transformation of semi-urban areas, which is causing the sudden aggregation of persons in industry and this means evolution of new social and economic structure favourable for the growth of tuberculosis phenomenon. This also means an exchange of disease and in the case of tuberculosis the young adult is the first to fall a victim. But several factors interplay here. First the succeeding batches of young

adults coming to industry are no longer the unsalted rural workers, they were rapidly acquiring resistance or dying from the effects of the appalling hygiene in industrial areas, towns and slums.

The average infection rate as reported by Bogen (16) at different ages in India are not yet much lower at the younger ages as contrasted with countries where the opportunities for exposure to the germ have diminished. Also the majority of adults now yield positive rates, but since more than half of the population of India is still under 25 years of age, the majority of all ages have not yet been affected.

TYPES OF INJURIOUS DUSTS

Silicosis constitutes only a facet of a very large question—the prejudicial effects of dusts in general upon the human subject. These dusts may be described as follows:—

TABLE 3

- (a) those having effect only in massive concentrations as
 - carbon (graphite) in the manufacture of crucibles and electrodes
 - iron (fumes) (in welders)
 - Calcium and barium compounds
 - silicate dusts—fuller's earth
 - synthetic abrasives.
- (b) Dusts causing fibrosis of lungs
 - silica (SiO₂) as quartz, flint, sand, sandstone, Kieselguhr as in mining, quarrying, potteries, foundries, refractories
 - Asbestos.
- (c) Dusts causing inflammation of lungs
 - cadmium
 - beryllium, vanadium, uranium, manganese, cobalt.
- (d) Dusts contributing to lung cancer
 - Radioactive dusts in mining of uranium, nickel
 - chromate dusts
 - Arsenic, nickel.
- (e) Dusts having undetermined effect on lungs
 - Talc, Mica, Diatomaceous earth.

Storage of inert dust is not harmless; mechanical interference with respiration occurs and predisposition to disease, such as tuberculosis may result. Some of the other dusts bear a special relationship to development of tuberculosis; the trades with which these dusts are associated are well known. Certain dusts have a direct bearing on the incidence of tuberculosis, as has been shown in studies carried out by the author.

There are also groups of non-dusty occupations which have a mortality from respiratory tuberculosis which is higher than that of the general population of the same age-group, e. g., composers, printers, shoemakers, etc.

The etiology of pulmonary changes caused by many organic dusts is still obscure. Although less important than organic dusts, from the point of view of mortality, they cause in the aggregate, much suffering and economic loss. The part played by mould infections, by vegetable dusts in causing asthma of allergic type has not been investigated very much in this country.

Chronic bronchitis stands out as chief of dust diseases and during middle life causes much recurrent invalidity and incapacity and after middle life high death rates. Dust bronchitis cannot be distinguished clinically from bronchitis due to exposure at hot furnaces, fumes in industry or severe climatic conditions; its association with dust inhalation, therefore, lacks recognition.

EMPLOYMENT IN DUSTY TRADES IN INDIA

The number of men exposed to dust hazard in various types of mining and factory industries working in metals and minerals may be said to be as follows :—

Mining	4,08,162
Factory industries	1,52,720

	5,60,882

The details of these are given in tables below :

TABLE 4

Number of men exposed to dust hazard in various types of mining working in metals and non-metals

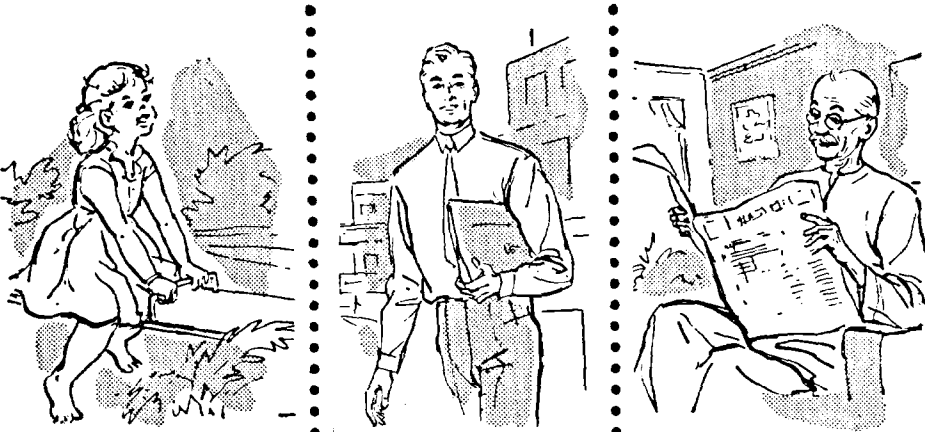
Year 1954		
Mines	No. of mines	Average daily No. of worker
Mines (all minerals)		
Underground (men)		221,956
Open workings (men & women)		186,206
Coal Mines	853	
Non-coal	2174	
Coal Mines (underground)		187,406
(Open working)		33,563
Gold (U. G.)		11,038
Iron Ore (Open working)		24,891
Copper (U. G.)		2,368
Manganese (U. G.)		1,930
(Open working)		73,185
Mica (U. G.)		16,925
(Open working)		6,403

TABLE 5

No. of men exposed to dust hazard in various types of industries working in metals and non-metals

Year 1954		
Industries	No. of factories	Average daily No. of workers
Bricks & Tiles	612	25,897
Glass	187	26,824
Pottery, China earthen-ware	63	12,399
Cement	24	21,651
Non-metallic minerals—		
Stone-dressing & crushing	153	6,075
Asbestos	7	2,409
Ferrous—		
Metal extracting & refinery	7	41,299
Metal founding	32	2,504
Non-ferrous—		
Metal extracting & refinery	18	4,273
Metal founding	38	1,576
Metal products		
Cutlery, Locks—	62	1,796
Mineral Fertilizers	58	7,037
	1261	1,53,740

WHY PROTINULES?



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Carbohydrates derived from cane and milk sugars	9 Gm.
Vitamin A	5000 I.U.
Vitamin D ₂ B.P.	500 I.U.
Vitamin B ₁ B.P.	2 mg.
Vitamin B ₂ (Riboflavin B.P.)	2 mg.
Vitamin B ₆ B.P.C.	1 mg.
Vitamin B ₁₂ B.P.	15 mcg.
Niacinamide B.P.	20 mg.
Calcium Pantothenate U.S.P.	1.5 mg.
Inositol N.F.	25 mg.
Biotin	10 mcg.

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The separate totals are significant in that they indicate occupational groupings in each industry. The degree of hazard in each varies, as well as variations are found in similar jobs in different industries. The above figures only indicate the possible numbers exposed to the dust hazard in the chief industries especially silica dust, and there may be another 100,000 in other industries and processes exposed to other harmful dusts mentioned above.

INCIDENCE OF TUBERCULOSIS IN CERTAIN DUSTY INDUSTRIES IN INDIA

Industrial statisticians assess the health of an industry from the tuberculosis death rate. This method is especially applicable to silica brick industries.

Tuberculosis is in fact the most common cause of death in silicosis; some 40 per cent to 70 per cent of fatal cases of silicosis die from tuberculosis of the lung.

Conjunction of a tuberculosis infection with silicotic lesion is very common and is due to a combined action of dust and infection (tuberculosis).

During the course of investigations in the problem of silicosis in various dusty industries, the author has reported the following figures elsewhere.

TABLE 7

Incidence (per 1000 employed) of Tuberculosis, Lobar Pneumonia and all respiratory diseases in underground and surface workers during the 5-year period 1941-1945

	Underground						Surface			
	Tuberculosis			Lobar Pneumonia	All respiratory diseases	Number Employed	Tuberculosis			All respiratory diseases
	Number Employed	Without Pneumococcosis	With Pneumococcosis				Number Employed	Tuberculosis	Lobar Pneumonia	
Mysore Mine	20,025	5.74	1.60	7.34	17.48	147.32	10,199	2.26	6.57	55.83
Champion Reef Mine	11,999	11.00	3.83	14.83	18.42	182.27	8,897	1.80	6.18	39.43
Ooregum Mine	10,546	6.07	2.56	8.63	17.35	133.42	6,308	1.59	8.56	53.42
Nundydroog Mine	24,617	4.83	1.99	6.82	11.01	101.03	10,532	1.52	7.03	55.17
Totals	67,187	6.40	2.29	8.69	15.26	134.42	35,936	1.81	6.96	51.17

(Incidence per 1,000 employed)

(Table taken from a paper —“Pneumoconiosis on Kolar Gold Field”—by Caplan and Burdon.)

TABLE 6
Incidence of Tuberculosis in various industries in India (based on surveys carried out by the Chief Adviser Factories Organisation)

Cases of Tuberculosis							
Pottery & Ceramics	Mica Mines	Silica Brick manufacture	Fire clay Brick manufacture	Metal Grinding	Supervisory staff	Hand drillers	
Below							
19	1						
20-29	8	5				1	
30-39	18	18			2	2	
40-49	16	15			5	1	
50-59	6	3			1		
60-69	1						
Total	50	41	8	16	4	8	4
No. of workers	808	329	112	215	44	42	52
% workers with							
T.B.	6.3	18.6	7.1	7.4	9.0	19.0	6.6

The data on incidence of tuberculosis in the miners as found in the underground workers in Kolar Gold Fields is very illuminating in this respect.

The increased susceptibility of underground workers to pulmonary tuberculosis is apparently due to an underground factor (siliceous dust) responsible for the increased incidence.

In a fluoroscopic examination of chest Bordia (17)

TABLE 8

The percentage of active disease and abnormalities of tuberculous nature in different occupational groups

Occupational Group	Total Examined	Abnormalities of Tuberculous nature	Active disease
Farmers	240	17 (7.08%)	16 (6.6%)
Hospital personnel	319	19 (5.9%)	4 (1.2%)
People in sedentary occupations	3,841	205 (5.3%)	122 (3.1%)
Labourers	2,448	113 (4.6%)	70 (2.8%)
Prisoners	269	12 (4.4%)	5 (1.8%)
Police personnel	457	10 (2.1%)	2 (0.44%)
Students	1,814	34 (1.8%)	9 (0.49%)
Miscellaneous	813	61 (7.5%)	34 (4.1%)
	10,201	471 (4.6%)	262 (2.5%)

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TABLE 9

The percentage of active disease and abnormalities of tuberculous nature in different age groups

Age group	Total Examined	Abnormalities of Tuberculous nature	Active disease
16 to 20 yrs.	2,781	109 (3.9%)	51 (1.8%)
21 to 25 yrs.	2,537	100 (3.9%)	51 (2.9%)
26 to 30 yrs.	1,838	85 (4.7%)	51 (2.8%)
31 to 35 yrs.	1,053	58 (5.5%)	33 (3.1%)
36 to 40 yrs.	857	59 (6.8%)	27 (3.2%)
41 onwards	1,135	88 (7.8%)	46 (4.0%)

Billimoria (18) has reported the following incidence of Tuberculosis in an Iron and Steel Industry :

TABLE 10

Department	Main physical factors	Total cases in 1946 1947 1948			Average rate per 1000
(1) Steel Melting Shops Blast Furnaces	Excessive Heat; Heat & Dust	10	13	12	2.4
(2) All Mills	Heat	20	17	29	4.2
(3) Brick Foundries	Silicosis contact	9	13	11	3.6
(4) Coke Oven Foundries	Fumes, Mist, Smoke & Dust	12	12	6	4.1
(5) Miscellaneous Departments inside the Works	General Works atmosphere	32	44	44	4.3
(6) General Offices & Town Dept.	Normal town life	13	24	18	4.7

He, however, has stated that “the physical factors (extreme heat, gases, fumes and mists and even the presence of silica) in steel making *per se* are not a potent cause of tuberculosis. The economic factor, he considers, is an important factor.

Krishna Row (19) working in a South Indian cotton mill has reported 3.29 per cent cases of clinical tuber-

culosis and 1.29 per cent cases of confirmed tuberculosis (X-ray and sputum examination). Col. C. K. Lakshmanan (20) reported incidence of active tuberculosis in the Jute Industry in Calcutta to be “6 times more than the incidence in the workers at their homes in their village from where the workers in Jute Industry are immigrating”.

CONCLUSION

Increasing industrialisation and urbanisation in India is giving rise to a complicated set-up in industries where temperature, humidity, fatigue and exposure to dust adversely affect the workers' resistance and aggravate the effects on the respiratory organs and increase their susceptibility to infection with tuberculosis.

Tuberculosis morbidity reports from the State Insurance dispensaries are obviously inadequate for evaluating the incidence of the disease in various dusty industries.

The pneumoconioses have received less attention of the chest clinicians than they deserve. But to the industrial physicians in factories and mines whose patients are exposed to dusty trades, to those responsible for the conduct of these trades and to the factory and mine inspector pneumoconiosis is of great importance.

No surveys as yet on an all-India basis have been taken on the incidence, types of tuberculosis and factors with causation in the factory or mining industries. The question of silicosis and dust hazard has been studied by Sen, Ukil and Sikand but the field covered has been very small.

It will not be presumptuous to state that of all methods of epidemiological investigations, biological methods, i.e., information on the state of tubercularisation of industrial populations by skin reactions by tuberculin test is the simplest and cheapest to secure.

The two other methods which may be made use of are tuberculosis mortality data and tuberculosis morbidity data collection from industries. Mass radiography is alone capable of establishing the extent of tuberculosis endemicity in the industrial and mining populations and the Employees State Insurance authorities should take up this subject as it is in their interest to cut down disablement costs and also in view of the fact that the insurance scheme is gradually being extended to the families of insured workers. Another fact is that still about 15 lakh workers have not been covered under the insurance scheme.

It is also necessary to know the anatomo-clinical forms of pulmonary tuberculosis in industrial populations as well as their pathogenesis in view of the peculiar social factors of large populations of tribal

people in various States in India migrating to industrial centres. In Orissa they form about 23% of the total population of the State, and are considered virgin soil especially for tuberculosis.

The challenge of the problem of tuberculosis in industry is one which those responsible for industrial health should not ignore. There is always a danger of overlooking diseases which chiefly affect the working classes. More facts are wanted—facts which must be derived by direct observations of appropriate industrial populations. Further studies of official mortality and morbidity figures in the industrial population can provide not only indications but proof. We need to study relationships between respiratory illnesses and symptoms in younger groups of men exposed to dust and other suspected environmental hazards, compared with suitable controls.

Morbidity surveys of tuberculosis in workers exposed to respiratory irritants could help to elucidate this important problem to industrial health.

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WORLD DISTRIBUTION OF ENDEMIC GOITRE

BY DR. KELLY & DR. SNEDDEN

Goitre . . . occurs with varying intensity in almost every country . . . The disease has been observed in the far north, in the tropics, and in the far south; it occurs independently of climate, season or weather. Moreover, in its incidence goitre makes no distinction of race, nationality, colour, creed or class; the North American, the European, the Chinese, the Himalayan Indian, the Turkoman, and the peoples of Central and South America all suffer from it under certain conditions—some severely, some moderately, some but mildly.

IODINE prophylaxis and rising standards of living have made possible the near eradication of endemic goitre in a number of countries that were formerly severely affected. Nevertheless, the world distribution of endemic goitre has not changed appreciably over the last hundred years, and in many countries the prevalence is still very high. From the incomplete statistics at present available, Kelly & Snedden estimate that the total number of goitrous people in the world must be not far short of 200 million. Statistics for 1952 showed that in eight states of Mexico alone there were more than 2 million goitrous people out of a total population of about 10 million; and in El Salvador, with a population of less than 2 million, 329,000 people were affected. It has been estimated that there are 9 million cases of goitre in India, 5 million in Italy, and 1.4 million in Yugoslavia. It should be noted that it indicates only where goitre has been found and gives no indication of its severity.

In general, the areas of endemic goitre tend to follow the mountain ranges—for example, the Alps, the Pyrenees, the Himalayas, and the Andes. On the other hand, there are also some low-lying areas, such as the basin of the Great Lakes between Canada and the USA, the plains of Lombardy, the Netherlands, and parts of Finland. It has been suggested that all these areas have one thing in common: a low iodine content in the soil. The iodine has either been leached out by flooding or swept away with the topsoil by the action of glaciers. The iodine content of post-glacial soils, generated by the grinding up of virgin rock, is only about one-tenth that of mature agricultural soils. Atmospheric iodine, derived from the sea and carried inland by winds, is brought down by rain and snow, gradually enriching the soil, but this is a slow process and hundreds of thousands of

years are required to restore the iodine content to pre-glacial values. It is claimed that the distribution of goitre in North America and a number of countries of Europe, Asia and Australasia shows a close correlation with the areas affected by the last glacial period.

In a survey based on more than 1300 references, Kelly & Snedden present a country-by-country analysis of the distribution of endemic goitre throughout the world, which bears impressive testimony to the continued public health importance of the disease in many countries. In addition to a wealth of statistics on prevalence, the survey includes much historical material, and the authors also discuss the possible local causes of many of the endemics, as well as the measures taken to combat them.

THE AMERICAS

The most notorious goitre areas in North America are around the Great Lakes and along the Appalachian range. Goitre is also prevalent in an area between the Rocky Mountains and the Pacific coast, extending from the Cariboo Mountains in the north to Arizona in the south. The goitre situation in the Middle West has greatly improved in recent years following the introduction of iodized salt, but there are still many places where the rates are disquietingly high. As recently as 1958, it was estimated that there are 1 million working men in the USA who have hypothyroidism of which neither they nor their physicians are aware.

A vast goitre zone begins in the upper basin of the Rio Grande del Norte in Mexico and extends down through the Central American republics into Colombia

and Venezuela and along the Andes through Ecuador and Peru as far as Chile and western Argentina. The mid-central states of Mexico are heavily affected, and in some localities in the province of Oaxaca, 80-90% of the population is goitrous. There is some evidence that goitre was present in parts of Central and South America hundreds, if not thousands, of years before these countries were conquered by the Spaniards, but this is contested by Greenwald and others. At all events, the disease is found today in almost every country of South America. Brazil is estimated to have 11,640,000 goitrous persons out of a population of roughly 62,000,000, and there are parts of Peru where the goitre rate is 90% and cretinism, mental deficiency and deaf-mutism are common. Goitre is also widely diffused throughout a 1500-mile strip of territory bordering the Cordillera in Argentina. On the other hand, Chile and Uruguay are relatively free from the disease. Most of the South American republics are now taking energetic action to introduce iodine prophylaxis.

EUROPE

Northern Europe has relatively few goitrous areas. In Finland there are four goitre belts extending northwards from the Gulf of Finland into the central part of the country. A high frequency of nodular goitre is a feature of the endemic, which is estimated to be responsible for 2000 operation cases annually. Animal goitre is also common. A clear correlation between goitre prevalence and iodine deficiency in the diet has been demonstrated in Finland. Goitre is also widespread throughout most of Sweden, affecting both man and animals. In Norway, there are only localized foci, but the rates are often very high; in some places in Telemark it is claimed that they even reach 100%. Iceland has always been completely free from goitre. This is attributed to the high consumption of fish, which is rich in iodine. Denmark is also relatively goitre-free and so are the former Baltic States, northern Poland and northern Germany. On the other hand, practically the whole of southern Poland is goitrous, and goitre is also endemic in central and eastern Poland. The highest rates are in the south, particularly in Lower Silesia. The severity has increased since the Second World War. This has been attributed to the use of synthetic fertilizers in place of Chilean nitrate of soda, which contains iodine.

In Germany, goitre is found mainly in Westphalia,

Wurttemberg, and southern Bavaria, and in a strip roughly parallel to the Czechoslovakian border. The introduction of iodized salt in Bavaria in 1924 was followed by a marked decline in the goitre rate in schools. The practice was abandoned in 1930, for fear of harmful effects and 4 years later rates of over 70% were reported. A vast goitre area covers the whole Alpine region, including practically all of Austria and Switzerland, northern Italy, and south-eastern France. This region has long been notorious for the severity of endemic goitre and frequency of cretinism. With rising standards of living, the goitre rates have gradually declined during the present century, and in Switzerland, especially, where iodized salt has been in general use for more than thirty years, the position is now greatly improved. This can be strikingly seen in the drop in the number of army recruits rejected on account of goitre, and the reduction is greatest in the cantons where most iodized salt is used.

Goitre is a very serious problem in Yugoslavia, practically the whole of which is goitrous, with the exception of the Adriatic coast and a small region in the north-east. Domestic animals are also affected. In 1954, the iodization of salt was made a legal requirement and production is gradually being increased. Severe foci of endemic goitre are found in the mountain regions of Romania and Bulgaria. In Romania, the disease is associated with extreme poverty. There has been considerable improvement, however, following the institution of an antigointr campaign in 1947—including mass prophylaxis with iodized salt—and similar measures are now planned in Bulgaria. Iodine prophylaxis has also been introduced with good results in Hungary and in Czechoslovakia, where a number of careful studies on goitre have been carried out. The worst affected area is in the extreme east of Czechoslovakia, where goitre prevalence has been correlated with a diet containing excessive quantities of cabbage.

The principal goitrous areas in western Europe, apart from those already mentioned, are in the north-east of France, near the Belgian and German frontiers; in southern France, in the region of the Massif Central; and in the northern Spain, extending from the Pyrenees through the Cordillera Cantabrica and the Asturias to Galicia. Goitre also occurs at a number of foci in southern and central Spain. The region of Las Hurdes, in the north of the Province of Caceres, is one of the most notorious goitre centres in the world;

not a single man from this district has been found fit for military service, either because of low stature or marked feeble-mindedness. Portugal has a number of scattered foci of endemic goitre, but none of exceptional severity. In Italy, apart from the main Alpine belt already referred to, high prevalence rates are found in the Apennines at several places, and there is a little-known centre in the extreme south in the province of Catanzaro. Goitre is also fairly common in the islands of Sicily and Sardinia. Of the remaining countries of western Europe, the Netherlands is of interest because it is the only country where goitre prophylaxis with iodized water has been successfully applied for any length of time on a large scale, the results being comparable with those achieved in other countries using iodized salt. Since the Second World War, when the Germans stopped this form of prophylaxis, the use of iodized salt in bread-making has been made compulsory in affected areas—chiefly the eastern, central and southern parts of the country. This has resulted in a steady decrease in the prevalence of thyroid enlargement. Belgium is comparatively free from goitre, although during the Second World War there was an increase in the prevalence of simple goitre accompanied by a decrease in thyrotoxicosis. This has been attributed to an increased consumption of cabbage and related vegetables. In the British Isles, goitre prevalence has considerably diminished over the past hundred years with the rising standards of living, but the most recent surveys show that it is still disquietingly high. The areas principally affected are the western half of England and Wales and a small area in south-east England. In 1944, the Goitre Subcommittee of the Medical Research Council of Great Britain estimated that there were 500 000 cases of thyroid enlargement in persons between 5 and 20 years of age, and they urged the general introduction of iodized salt. Unfortunately this recommendation has not been implemented.

USSR AND ASIA

In the USSR, as elsewhere, most of the highly goitrous areas follow the mountain ranges—in the European part of the USSR, the Urals, the Carpathian mountains and the Caucasus; in the Asian part, the Chatkal Mountains and the Pamir plateau, the Altai Mountains, as well as the mountainous areas to the west and east of Lake Baikal and in the Maritime Territory to the north of Vladivostok. In most of these areas, endemic goitre is severe, and in some

valleys of the Pamir plateau it is claimed that the entire population is goitrous. A vast amount of systematic research carried out throughout the USSR has given ample support to the iodine deficiency theory of the causation of endemic goitre and has also provided some evidence that a high content of manganese occasions a reduced content of iodine in the soil. Large-scale programmes of prophylaxis with iodized salt have been instituted in almost every part of the USSR where goitre occurs and goitre rates have fallen considerably.

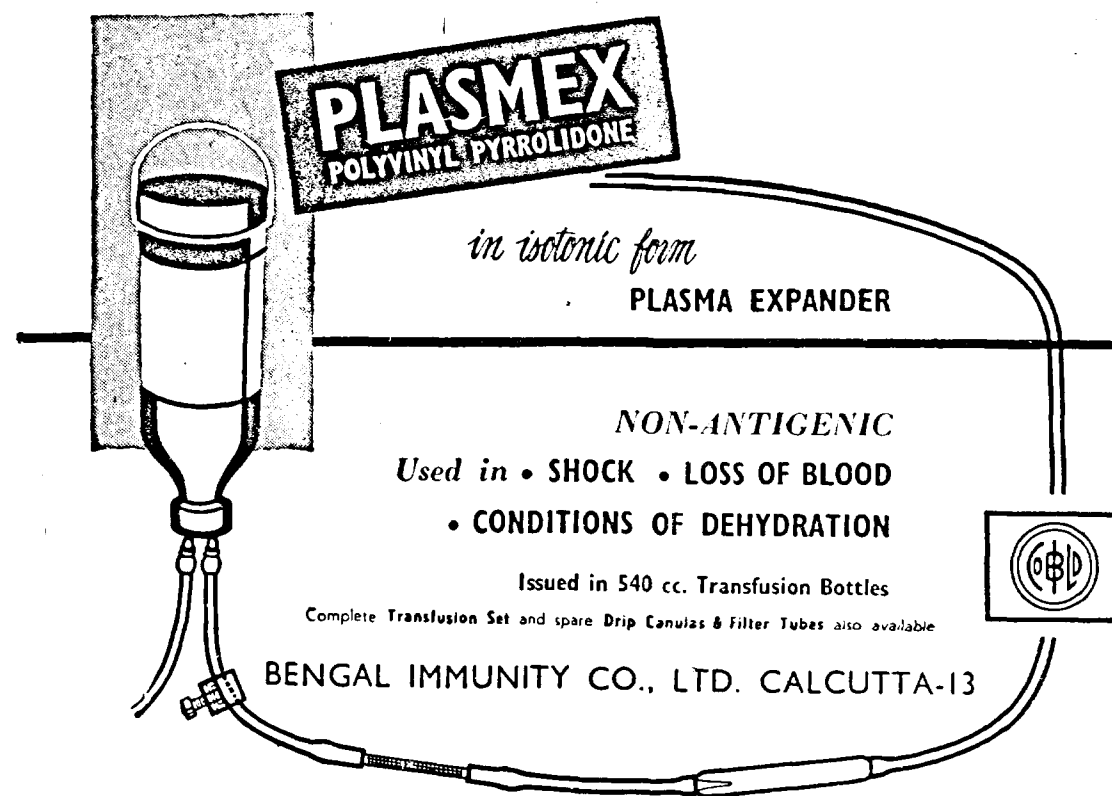
The endemic goitre area of the Pamir plateau referred to above merges into the classic goitre area of the Himalaya mountains, described by Kelly & Snedden as "the headquarters of goitre and cretinism on the continent of Asia". It extends through Kashmir, Nepal, and Burma into China and neighbouring countries, areas that have "a goitre reputation more formidable perhaps than that of any other part of the world". In comparison with this vast northern area of endemicity, which extends into northern Pakistan and the low-lying plains of Uttar Pradesh in northern India, goitre is not excessively acute elsewhere in India or Pakistan. The total number of goitrous persons in India was estimated at 5 million in 1917 (McCarrison) and at 9 million in 1959, with prevalence rates varying from around 10% in some places to 90% or more in others. Cretinism, deaf-mutism, and idiocy are very common. McCarrison produced experimental evidence that polluted drinking water is an important etiological factor, at least in some parts of the Himalayas and in Uttar Pradesh; a correlation has been found between the distribution of goitre and the calcium content of soils and drinking-water. Unbalanced diets associated with widespread poverty are thought to be an important contributory factor. Even though iodine deficiency may not be the primary cause of goitre in many parts of India, it is generally believed that the easiest and cheapest way of preventing the disease is by giving supplementary iodine. The iodization of salt presents some difficulties owing to the poor quality of the salt and the climatic conditions. Efforts are being made to improve the quality of the salt and also to find a satisfactory method of iodizing the present grade with potassium iodate.

The highest goitre rates in Burma are seen in the Kachin Hills in the north, and in the Shan States. The number of cretins and deaf-mutes is extremely high, rates of 10 per 1000 having been recorded among the

Kachins. These people drink water heavily impregnated with lime and eat powdered lime in large quantities—possibly important causative factors. The Shan States area extends southwards into northern Thailand and the north-west of Indo-China and links up with the vast endemic area of mainland China. This begins near the Manchurian border in the north-east of the country and follows as westward semi-circular route across the mountainous watershed north of Peking, afterwards continuing southwards into Yunnan, the most goitrous province of all China. The great plain of China and the coastal provinces are virtually free from simple goitre, although toxic goitre is common. Some of the earliest accounts of endemic goitre relate to China, and references have been cited showing that it was known there at least as early as the third century B. C. All travellers have been impressed by "the evidence of human misery and degradation due to goitre and cretinism". Iodine deficiency appears to be the principal cause of goitre in China, particularly in Yunnan province, but the hardness of the water may be an aggravating factor. An antigoitre campaign was organized in 1958 and prophylactic measures have been instituted in nearly all endemic

areas, mainly with iodized salt but also with traditional iodine-containing drugs, iodized oil and potassium iodide. The results so far appear promising.

Goitre is common in the inland mountainous parts of Malaya and foci are scattered throughout the Indonesian archipelago. Kelly & Snedden relate the interesting case of the two villages of Lampœ and Tjatoer, situated only a few hundred yards apart on the island of Bali. Tjatoer is inhabited by pure Balinese and goitre is common; Lampœ is a Chinese settlement and is free from goitre. The Balinese have a monotonous maize-and-rice diet and drink unboiled water from a goitre-genic spring, whereas the Chinese have a varied diet and boil their water before use. Prophylaxis with iodized salt was introduced in parts of Java in 1927 and extended to Sumatra in 1930. At that time an unusual method of iodization had to be used because salt was manufactured in block form: this involved pouring a solution of potassium iodide into a small hollow on the top of each brick and allowing it to spread throughout the brick by capillary action. Goitre is a serious problem in the jungle-clad



hilly country of North Borneo, where cretinism is common. Attempts to supply iodized salt to people of this area have not so far been very successful. In neighbouring Sarawak, many of the people are protected from goitre by consumption of an iodine-rich salt derived from natural salt springs; in inland areas however, where the people use imported salt, goitre is common.

Thyroid disease appears to have been on the increase in recent years in the Philippine Islands and also in Taiwan, and both areas exhibit severe endemic foci. On the other hand, Japan appears to be relatively free from goitre. This has been ascribed by some to the widespread and regular habit of eating seaweed; an amount equivalent to about 5 mg. of iodine is often consumed by one person at a meal. Quite high goitre rates have been recorded, however, in several mountainous inland localities, and some degree of thyroid enlargement was found in 61% of children at one school in the Japanese Alps.

Goitre is practically unknown in the countries of western Asia, with the exception of a few endemic areas in Turkey and the Lebanon. Two foci have also been described in Iran.

AFRICA

Goitre would appear to have been endemic in North Africa for at least four or five hundred years, since a number of accounts of the disease have been left by sixteenth century travellers to these parts. Greenwald maintains, however, that these earlier descriptions are unreliable and do not refer to goitre, which, in his view, did not appear on the African continent until the nineteenth or even the twentieth century.

At the present time, there are two principal goitre zones in the extreme north of Africa. One is in the neighbourhood of the Atlas Mountains, stretching across Morocco and northern Algeria, where the Department of Constantine is particularly affected; the other is along the Nile valley and in the region of the Dakhla Oasis in Egypt. Iodine deficiency appears to be the main cause of these endemics, although in Morocco it has been suggested that the cause is the high consumption of turnips. The Egyptian Nile valley foci have counterparts further south in the Sudan, the two most important being to the north of Khartoum and to the south-west of Malakal.

There is also a narrow goitrous strip, roughly 200 miles long and 60 miles wide, in the south-west of the Sudan, where it borders on the Central African Republic and the former Belgian Congo. A puzzling feature is that the endemic zone ceases abruptly outside the confines of this narrow strip, although the neighbouring territories have the same kind of terrain and climate and are inhabited by the same tribe subsisting on the same kind of diet. The strip is the watershed for innumerable small streams flowing northwards to the Nile, and it has been suggested that the virgin streams are deficient in iodine but gradually become enriched from rotting vegetation or other sources after flowing 50-60 miles through a leached-out sandy soil. It is hoped to make iodized salt generally available in the area.

There is an extensive area of endemic goitre covering the high plateau of Ethiopia, the prevalence being higher on the west side than on the east. The disease appears to be confined almost entirely to women, a circumstance that has been attributed to its mildness. From the data at present available, goitre does not seem to constitute an important problem in British Somaliland, Uganda or Tanganyika. Farther west, in the former Belgian Congo, however, there are 4 important goitre zones. The largest is a strip 600 miles in length stretching across the north of the territory. It is believed that goitre first appeared in this area only towards the close of the last century, and that the prevalence has since increased rapidly. A second endemic zone is found in the mountains around Lake Kivu and at the head of Lake Tanganyika in the north-east. In Ruanda-Urundi, high goitre rates seem to be correlated with heavy rainfall. At Lokandu, in the Maniema region, goitre occurs predominantly in women and is associated with sterility; it is thought that an excessive secretion of the sex hormone folliculin may act as a goitrogenic agent. The mountainous parts of Katanga are also goitrous and there is a small focus south-east of Leopoldville.

Two very interesting zones of endemic goitre have been studied by the French Colonial Service in former French Equatorial Africa. These are in Cameroun and in the neighbourhood of Koumra, Chad. The prevalence is high in both areas and very large goitres are often seen. In Cameroun, endemicity appears to be most severe on granite soils and at the boundary between savanna and forest. The origin of goitre in Koumra has been ascribed to a parasitic infection prevalent in the area, but other evidence

suggests that it is a question of water supply. Attempts to introduce iodized salt in this area have so far been unsuccessful. An extensive goitre survey has been carried out under government auspices in former French West Africa, and the goitrous zones have been carefully mapped out. Goitre is rare on the Atlantic seacoast and almost non-existent north of the 14th parallel. It has been suggested that the peoples living in the north of the territory are protected from goitre by the consumption of natural iodine-containing salt, whereas those south of the 14th parallel are dependent on a salt obtained by the incineration of local plant foods. Prophylactic trials with iodized salt have given highly promising results. The goitre belt in this part of Africa also extends into the territories of Gambia, Sierra Leone, Ghana and Nigeria, through former French Equatorial Africa into northern Angola. The goitrous areas are all associated with pre-Cambrian granitic rocks which have been subjected to intense weathering and have had their iodine leached out. Analyses of water supplies have shown a definite correlation between the goitre rate and the iodine content of the water.

Goitre is endemic in the Central Province of Northern Rhodesia and apparently at several places in Southern Rhodesia, though there is little published information. The Caprivi Strip, which lies between Angola and Bechuanaland and connects Northern Rhodesia with South-West Africa, forms part of a zone of high prevalence extending into South-West Africa and Bechuanaland. Goitre rates of up to 70% have been recorded in some places, and the disease is prevalent even among breast-fed infants. In the Union of South Africa, a narrow goitre belt stretches across the Transvaal from Zeerust to Nelspruit and then curves south to occupy almost the whole of Swaziland. Goitre is also common throughout the Drakensberg area, including the whole of Basutoland and neighbouring territories in the Orange Free State, Natal and Cape Province, with rates ranging from 30% to 50%. The region between Prince Albert and Port Elizabeth in the extreme south is a well-known goitre area, and there are also endemic foci in the south-east and north-west of Cape Province. Investigations by the South African Goitre Research Committee have amply confirmed that iodine deficiency is the primary cause of endemic goitre in the Union and neighbouring countries, but excessive quantities of fluorine in the drinking water in some areas and a high content of calcium in soils, waters and vegetation in others, appear to be contributory factors. The

introduction of iodized salt in all endemic areas except those where goitre is fluorine-induced has been strongly recommended.

AUSTRALIA AND NEW ZEALAND

As far as is known at present, goitre in Australia is confined to the south-east of the country. Foci are found all along the Great Dividing Range from the Queensland border in the north down to Gippsland in Victoria in the south, where the prevalence is comparatively high. Thyroid enlargement was found to be very common among school-children in the Canberra area in a survey conducted in 1947, and iodine prophylaxis with potassium iodide tablets was instituted with excellent results. There is also an endemic goitre area in the Adelaide Hills in the state of South Australia. Practically the whole of Tasmania is goitrous. Clements noted in 1949 that at least 20% of adult women had goitre and the death-rate from thyrotoxicosis is also higher than the Australian average. It was in Tasmania that the failure of iodine prophylaxis in school-children led to the discovery of the goitrogenic action of milk from cows fed on marrowstem kale. In New Zealand, goitre is believed to have been prevalent among the Maoris long before the arrival of British settlers; it is now common both in North and South Island. Surveys conducted in the 1920's showed high rates in school-children; in the Christchurch area more than 60% had goitre. Chemical analysis showed a deficiency of iodine in the recent alluvial soils of river valleys and in clayless sandy soils in the areas where the goitre rates were highest. Following the introduction of iodized salt, there has been a marked decline in the prevalence of thyroid enlargement in children. Iodine deficiency in sheep, which at one time caused serious losses of lambs, has been overcome by the use of iodized licks.

FACTS AND THEORIES ABOUT ENDEMIC GOITRE

In 1867, Saint-Lager listed 43 different views on the causes of endemic goitre, ranging from various properties of air and water to faulty nutrition, poverty, insanitary living conditions, and consanguinity in marriage. Although some of these views—such as, that goitre is caused by drinking certain kinds of water—had been widely held since ancient times, there

was little, if any, experimental evidence to support them. Towards the end of the nineteenth century, the first systematic studies were undertaken on the anatomy and physiology of the thyroid, and much has since been learned about the structure and function of the gland in health and disease. It is now accepted that pathological enlargement of the thyroid represents an attempt to compensate for its inability to produce sufficient hormone, but the primary causes of this metabolic defect—whether exogenous, endogenous, or both—still remain largely a matter of speculation.

FUNCTION OF THE THYROID

Vesalius, who gave one of the earliest descriptions of the thyroid, considered that its purpose was "to moisten the lumen of the trachea". Similar views persisted until the end of the 18th century, when Albrecht von Haller recognized the thyroid as a ductless gland, secreting a special substance into the bloodstream. Another hundred years elapsed, however, before the pioneer studies of Baumann

opened the way to a better understanding of thyroid function. In 1895, he isolated from the thyroid a substance which he called "thyroidine" because he found that it contained 10% of iodine. This could be shown experimentally to have exactly the same physiological action as whole-thyroid preparations. Following up these studies, Oswald isolated thyroglobulin in 1899. Research on the chemical composition of the active substances of the thyroid was intensified, and in 1919 Kendall isolated crystalline thyroxine (3,3', 5,5'-tetraiodothyronine), which Harington succeeded in synthesizing in 1926.

Meanwhile, recognition had been growing of the part played by the thyroid in regulating physical and mental development and metabolic activity. In 1836, Cooper performed thyroidectomy in puppies and noted that it resulted in dulling of the faculties. Twenty years later, Schiff carried out systematic thyroidectomies in various animals, most of which died, but in 1884 he found that death could be prevented by intra-abdominal transplants of thyroid gland. A year earlier, Kocher had described the condition of *cachexia strumipriva* resulting from total

extirpation of the thyroid in humans. He stressed the close relationship between this condition and cretinism, and noted that the symptoms were identical with those of the myxœdema described a few years earlier by English authors. Similar observations were made by the two cousins J. L. Reverdin and A. Reverdin.

Thyroid hyperfunction was recognized at about the same time. The combination of goitre, exophthalmos and cardiac disturbances was first described by Parry in 1786. Attention was again drawn to this syndrome by Graves in 1835 and by Carl von Basedow in 1840; in 1886, Mœbius attributed exophthalmic goitre to "an intoxication of the organism resulting from disturbed thyroid activity". That patients suffering from exophthalmic goitre have an increased metabolic rate was first demonstrated in 1895 by Magnus-Levy.

Thyroid hormones

Recent research has shown that, in addition to thyroxine, the thyroid contains a number of other iodinated thyronines, but, apart from 3,3', 5-triiodothyronine and possibly 3,3'-diiodothyronine, these do not appear to be secreted into the bloodstream under normal circumstances. When strongly stimulated, the thyroid may secrete newly formed hormones directly into the blood, but usually they are stored in the form of thyroglobulin, a compound of peptide structure which is broken down by the action of certain enzymes (cathepsins) to release hormones as needed. Monoiodotyrosine and diiodotyrosine, also formed in this process, are normally deiodinated by a specific enzyme and do not reach the peripheral blood, but large amounts of these substances have been found in the blood of patients with congenital goitre and hypothyroidism; diiodotyrosine has also been tentatively identified in the serum of two patients with endemic cretinism.

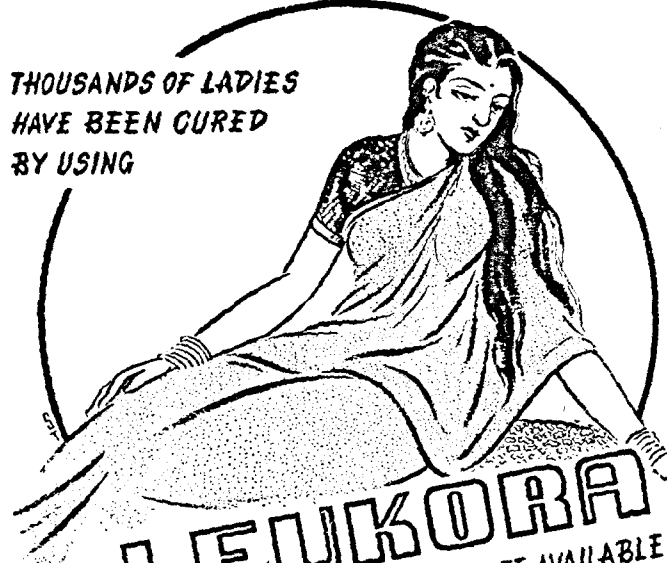
A normally functioning thyroid secretes 100-200 μ g of hormonal iodine daily. Part of this—the protein-bound iodine (PBI)—is precipitable with the serum proteins and therefore also known as "serum-precipitable iodine" (SPI). The SPI value of the serum—normally 3.5-8 μ g per 100 ml—provides a useful measure of thyroid function, concentrations lower than 3.5 μ g per 100 ml being indicative of hypothyroidism. The output of thyroid hormone is largely controlled by the thyrotropic or thyroid-

stimulating hormone (TSH) secreted by the anterior lobe of the pituitary gland, and the production of this hormone depends in turn upon the concentration of thyroid hormone in the blood. This self-regulatory or feed-back mechanism ensures that the thyroid is stimulated to increased activity as soon as the concentration of circulating hormone falls, and *vice versa*. Control of thyroid function is, however, a very complex matter and is still incompletely understood: there are a number of other regulatory influences, the relative contributions of which are not known, and it may be that they can affect to varying degrees one or more steps in the metabolic cycle in the gland. Another fundamental question that remains unanswered is: What is the nature of the reaction produced on cells by the thyroid hormone? Several theories have been proposed, but none has much evidence to support it. One suggestion is that it interferes with oxidative phosphorylation, causing oxidation to proceed without the liberation of a corresponding amount of phosphate bond energy. Stanbury considers that this is perhaps the most likely of the theories advanced so far.

The iodine cycle

The iodine used in the synthesis of the thyroid hormones is derived from two sources: iodine-containing substances in food and drinking water, and iodine split off from the circulating hormones by enzymes in the blood and returned to the plasma as iodide. Some of the iodide present in the blood is trapped by the thyroid gland, the remainder is excreted by the kidneys. The relative efficiency of these two processes is a measure of thyroid function and can be determined by administering radioactive iodine (iodine uptake test). The concentration of iodine in the resting thyroid is normally maintained at a level about twenty times that in the plasma, unless the latter is very high and the trapping capacity of the gland approaches saturation. The trapped iodide is used for the iodination of tyrosyl residues to give monoiodotyrosine and diiodotyrosine, but neither the mechanism of trapping nor that of iodination is well understood. It is known that trapping involves oxidative phosphorylation, depends upon cellular integrity and the presence of sulfhydryl groups, and is inhibited by thiocyanate and perchlorate ions, which even release trapped but uncombined iodine from the gland. It is also known that iodide is oxidized to iodine within the thyroid, but it is not

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certain that the gland contains a specific iodide oxidizing system, although there is some evidence that peroxidase may be concerned in the process. It seems probable, at all events, that the rate at which iodination proceeds in the gland is governed enzymatically and it may be that the iodide is first converted to an intermediate storage form of iodine which can only react with the tyrosyl residues in the presence of a transferring enzyme.

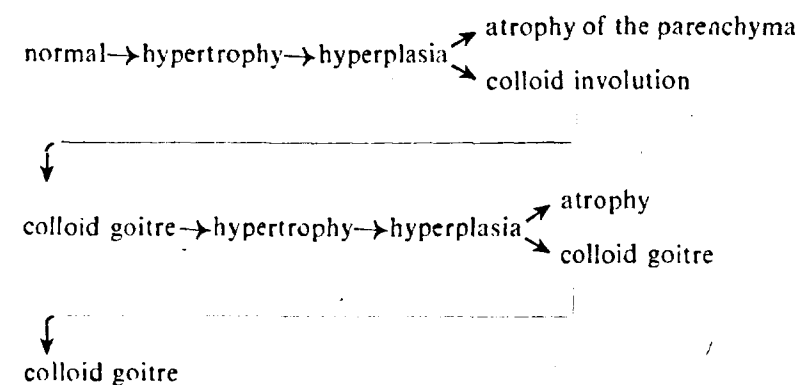
Thyroxine is formed by the condensation of two molecules of 3,5-diiodotyrosine, while the condensation of monoiodotyrosine with diiodotyrosine gives 3,3',5-triiodothyronine. Here again, the mechanism by which these reactions are brought about is unexplained, although it is generally assumed that one, or perhaps two, enzyme systems are involved. As already mentioned, the hormones are stored in the gland in the form of thyroglobulin, from which they are released as required into the bloodstream, where they are again broken down and the iodine returned to the plasma, thus completing the metabolic cycle.

DYSFUNCTION OF THE THYROID

If the thyroid is unable to trap sufficient iodine or fails to utilize the trapped iodine efficiently, the feedback mechanism breaks down, i.e., an increased output of TSH by the pituitary produces no corresponding increase in the production of thyroid hormone. Under the prolonged influence of the relatively high concentration of TSH, the thyroid gland undergoes hypertrophy and hyperplasia, apparently in an attempt to compensate for its deficient secretion of

hormone. This is known as the hyperplastic or parenchymatous phase of goitrogenesis, and is usually of short duration. If the enlarged gland is still unable to meet the physiological requirements for thyroid hormone, atrophy occurs, but this is a rare phenomenon. In the majority of cases, the increased amounts of iodine trapped by the enlarged gland suffice to restore the endocrine balance, and the gland enters the resting or colloid phase. Clinically, the gland presents as a uniform soft enlargement, indistinguishable from the hyperplastic goitre, but histologically the appearance is different. In the normal gland, the follicles are filled with a sticky fluid known as colloid and consisting mainly of thyroglobulin. During the hyperplastic phase, the colloid gradually disappears from the follicles which undergo various structural changes. The colloid phase is marked by a gradual return of the colloid to the follicles, which largely regain their normal appearance. The gland remains enlarged, however, and although the total iodide content is close to that of a normal thyroid, the concentration of iodide is much smaller.

While the colloid goitre may maintain the body in a state of euthyroidism, the balance is a precarious one, and any increase in the demand for hormone, or any reduction in the supplies of iodine, immediately precipitates a fresh burst of hyperplasia. The reaction is often localized, and it is common to find areas of hyperplasia and of colloid adjacent to one another. In regions where goitre is endemic, phases of hyperplasia and involution alternate at frequent intervals, leading to progressive enlargement of the gland. This process—the classical Marine cycle—may be depicted as follows:



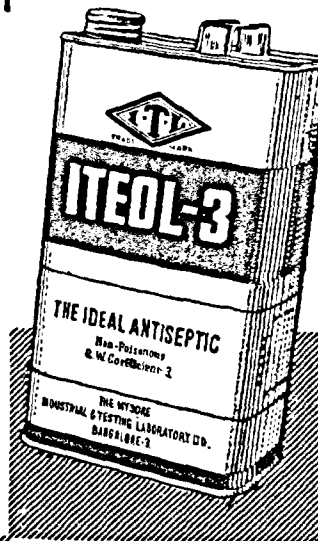
With repetition of the cycle, the hyperplastic reaction tends to become more localized. There is

much evidence that it is this process that leads to the formation of the nodules characteristic of long-

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standing goitres, although some authors are of a contrary opinion. Using the technique of autoradiography, Taylor has distinguished five stages in the development of the thyroid nodule. At first, the nodule is very active, producing most of the hormone secreted by the gland, but in the later stages hæmorrhage and necrosis occur; the nodule then becomes cystic and fills up with inactive colloid. Such cysts may lead to complications, either through pressure on neighbouring tissues or because they may be the site of hæmorrhage or infection, with formation of goitrous abscesses. The whole question of the pathogenesis and pathology of the thyroid nodule is very complex and still incompletely understood.

SEQUELÆ OF ENDEMIC GOITRE

According to Clements, the usual sequel of endemic goitre in adults, at least up to the fourth decade of life, is the persistence of a colloid or nodular goitre with euthyroidism, the only disadvantage being the æsthetic one. Matovinovic & Ramalingaswami, on the other hand, claim that the compensatory mechanism is not completely efficient, so that there is always some degree of hypothyroidism. Clements concedes that myxœdema often develops during the fifth or sixth decade, being much more common in women than in men. This is because the cycle of hyperplasia and involution, leading to the progressive destruction of functional tissue, is repeated more frequently in women. Pregnancy, for example, makes increased demands on the thyroid and is usually associated with a fresh outburst of hyperplasia; and sometimes an increase in the size of the thyroid is observed with each menstrual period, especially in girls up to the age of 18 years.

Studies on the prevalence of thyrotoxicosis in relation to that of endemic goitre have, in many cases, shown a distinct correlation, toxic goitre being much more common in areas with a high prevalence of endemic goitre than in those where it is low. This is particularly true of North America, the British Isles, parts of continental Europe, and Australia. On the other hand, no consistent relationship has been found in certain other parts of the world, and some countries where the prevalence of endemic goitre has always been high appear to be relatively free from toxic goitre. Clements therefore asks whether the condition has been overlooked in the localities where it has not been reported; or whether the sequelæ of endemic goitre differ in different localities.

Some authors believe that nodular goitres predispose to cancer of the thyroid, but the evidence is inconclusive. From a review of American literature, Sokal concluded that cancer of the thyroid was twenty times more common among persons with hyperthyroidism than among those with euthyroidism. In Finland, no difference could be found in mortality rates from cancer of the thyroid between areas with a low prevalence of endemic goitre and those with a high prevalence. On the other hand, Spencer has found a correlation between the prevalence of endemic goitre and the death rate from malignant disease in general. He suggests that the lowered metabolic rate of hypothyroidism may possibly be associated with premature senility of tissue cells, leading to increased susceptibility to cancer.

It is well known that cretinism tends to be of frequent occurrence in areas where the prevalence of endemic goitre is high, and it is commonly assumed that there is a casual relationship between these two conditions. This has been questioned, however, by Clements, whose views on the subject are summarized in a separate article.

FACTORS INFLUENCING GOITROGENESIS

Any factor that prevents the thyroid gland from responding normally to the stimulation of TSH may initiate the development of a goitre. Sporadic goitres may be due to congenital thyroid insufficiency, but in areas where goitre is endemic, exogenous factors must operate. It is generally agreed today that the most important of these is a deficiency of iodine in the diet. Other dietary factors include substances that interfere with the trapping of iodide by the thyroid or with one of the stages in the synthesis of thyroid hormone. The possibility must also be considered of pituitary dysfunction leading to an excessive production of TSH and of the possible effects on the thyroid of prolonged disturbances of other endocrine functions. So far, however, only dietary factors have received much attention.

Water supplies

It is interesting that, although goitre has at different times been attributed to a great variety of causes, the belief that it is associated with some quality of the drinking water has persisted since very early times.

At the beginning of the nineteenth century, the goitrogenic action was generally attributed to a high mineral content of the water, particularly to the presence of calcium salts. In 1831, Boussingault suggested that the high prevalence of endemic goitre in the Cordilleras of New Grenada (now Colombia) was connected with the lime stone soil. Further studies in other countries pointed to the magnesium content of limestone as the significant factor. Thus, in 1835, McClelland published a study showing that the distribution of goitre in India coincided with that of magnesium limestone formations. Nearly a hundred years later, Stott and his colleagues drew attention to a direct correspondence between the distribution of goitre in the United Provinces of India and a high content of calcium in the soils and drinking water. Kelly & Snedden, in their review of the prevalence and geographical distribution of endemic goitre, quote numerous instances in which a high prevalence of goitre has been associated with hardness of the drinking water or with soils rich in calcium. It has been shown experimentally that calcium can exert a goitrogenic action, or at least enhance the goitrogenic action of an iodine-poor diet, but it seems that rather large amounts of calcium are needed to produce significant results. It is believed that the action of calcium is an indirect one, in that it inhibits the metabolic effects of thyroxine and thus increases iodine requirements. However, the etiological significance of calcium and magnesium in endemic goitre is still open to discussion.

There is good reason to believe that drinking water may sometimes contain more powerful goitrogens than these minerals, particularly when polluted by human or animal excreta. While studying the prevalence of endemic goitre in the Himalayas, McCarrison (1906) noted that in 8 villages situated one below the other down the mountain side the prevalence steadily increased from 11.8% in the highest village to 45.6% in the lowest. These villages were all served by the same water-supply which ran through open channels and became increasingly polluted on its way down. A ninth village situated some distance away with an independent, unpolluted water-supply was free from goitre. McCarrison showed that suspended matter filtered from the grossly polluted water of the village with the highest goitre rate caused goitre in volunteers; the goitrogenic action could be destroyed by boiling. This work has been followed up by Hettche, who believes the goitrogenic action to be due to substances of the urochrome type which bind copper in

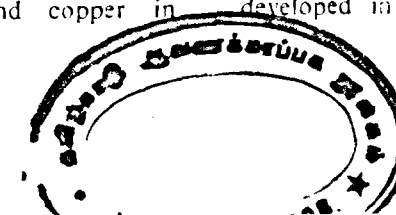
the serum. This problem, too, needs much further investigation.

Infection

Some authors consider that goitre is due to an infection of the thyroid, the chief proponent of this view being Greenwald. Painstaking historical studies have convinced him that endemic goitre is of recent origin in many countries and that the pattern often resembles that seen in infectious diseases. He asserts that many of the earlier accounts of swellings of the neck are either unreliable or else refer to sporadic goitres, tuberculous glands or parotitis. In his view, the infectious agent responsible for endemic goitre was at first confined to the Alps, where it was present some 2000 years ago. From there it spread slowly to the rest of Western Europe and was then carried to other parts of the world by Europeans. While the possibility that goitre is due to an infectious agent cannot be excluded, there is so far no experimental evidence in support of this hypothesis.

Iodine deficiency

By contrast, the theory that a deficient intake of iodine is the principal cause of endemic goitre has a sound scientific basis. As early as 1850, the French chemist Chatin carried out systematic iodine determinations on air, water, soils, and animal and vegetable foods from various parts of France. His results indicated that the prevalence of goitre in the various regions was inversely proportional to the content of iodine in the environment. The analytical methods available at the time, however, were not sufficiently refined to enable the small quantities of iodine present in natural products to be accurately determined; other workers were unable to repeat Chatin's results, which were therefore discredited. Fifty years later came the chemical investigations on the thyroid (see above) which showed iodine to be an essential component of thyroglobulin and thyroxine. This made it clear that if the quantity of iodine available to the thyroid fell below a certain minimum a metabolic disturbance was bound to follow. Attempts to produce goitres in animals by feeding them on iodine-deficient diets at first gave inconclusive results, as the diets were not sufficiently standardized; recently (1956) it has been observed, however, that marked thyroid hypertrophy developed in mice given an iodine-deficient diet of



well-defined composition, even when each constituent of the diet was stopped in turn. Careful analyses of soil and drinking water in many parts of the world have, in general, revealed a close correlation between iodine content and the prevalence of goitre. The occasional discrepancies that have been noted may be taken to indicate that in these cases other goitrogenic factors were operating.

Further support for an association between iodine deficiency and goitre comes from studies on iodine uptake and excretion. In areas free from endemic goitre, the mean daily excretion rate of iodine often exceeds 100 ug/day, whereas in endemic areas it is usually between 15 and 40 ug/day, and values of less than 10 ug/day may be common. Correspondingly, uptake tests with radioactive iodine reveal a high avidity of the thyroid for iodine in persons with a low excretion rate. Moreover, the radioactivity of the gland increases more rapidly in goitre patients, reaching a maximum 6 hours after administration of radio-

active iodine, as compared with 24 hours in normal subjects. If supplementary iodine is administered to goitre patients, a positive iodine balance is gradually established, and the excretion and uptake values approximate to those found in persons from non-endemic regions. This seems to be clear evidence that these patients suffer from iodine deficiency. Surprisingly, however, similar evidence of iodine deficiency can be obtained in persons living in endemic goitre areas but not showing thyroid enlargement. This must indicate either an exceptional adaptation to hypothyroidism in these subjects or that iodine deficiency is not the sole factor concerned in the development of goitre. It has been amply demonstrated that the administration of iodine exerts an adequate preventive effect in all but a very few instances, but, as Roche & Lissitzky point out, the problem that arises is "to what extent the action of iodides does not merely reflect the maintenance of the thyroid in its normal state or the restitution of a thyroid function possibly impaired by other endemic factors".

Goitrogens in the diet

In 1928, Chesney et al. observed that large goitres developed in rabbits fed almost exclusively on a cabbage diet. This observation has since been confirmed by many other workers and it has also been found that other vegetables of the genus *Brassica*, such as cauliflower, turnips and Brussels sprouts, possess similar goitrogenic properties. Perhaps the most striking example of such an action in man is that reported by Clements in Tasmania. Here the failure of iodine prophylaxis in school children was traced to a powerful goitrogen present in milk issued to the children under a free-milk scheme started at the same time as the programme of goitre prophylaxis. It was found that the cows supplying the milk had been fed on chou-moellier, or marrowstem kale. Both the milk and the kale caused thyroid hyperplasia when fed to experimental animals, and the milk was shown to interfere with the uptake of radioactive iodine in humans as well as in animals. Finally, Wright demonstrated in 1958 that the thiocyanate content of the milk is about six times that of milk from grazing cows. As already mentioned thiocyanates inhibit the trapping of iodine. The actual goitrogen present in chou-moellier has not so far been identified, however, but the thiocyanate derivative L-5-vinyl-2-thiooxazolidone (goitrin) has been isolated from a number of *Brassica* vegetables, as well as from the seeds of

numerous other cruciferous plants. This substance, which is a powerful goitrogen, appears to be present in the plant in the form of a precursor, progoitrin. The conversion of progoitrin—a glucoside—to goitrin is thought to be brought about by enzymatic action. Cooking diminishes the goitrogenic action of the food-stuffs, possibly by destroying the enzyme. The action of goitrin seems to resemble that of thiouracil and its derivatives rather than that of the thiocyanates, since it inhibits thyroxine synthesis and its effect is only partially reversed by iodides. This would explain the failure of iodine prophylaxis in Tasmania. Kelly & Snedden cite a number of other instances in which vegetables of the *Brassica* genus have been thought to be responsible for a high prevalence of endemic goitre. In Belgium, for example, the increase in simple goitre noted during the war may have been associated with the increased consumption of cabbage and related vegetables. This hypothesis is supported by the fact that there was a parallel decrease in toxic goitre, as would be expected if the diet contained an antithyroid substance. The reverse phenomenon—an increase in thyrotoxicosis and a decrease in endemic goitre—was observed in Denmark, and it has been suggested that this was due to the cessation of imports of soya-bean oil, which was shown by McCarrison to contain an antithyroid factor and which was used in Denmark on a large scale before the war for feeding cattle. The importance of dietary goitrogens in the etiology of endemic goitre still remains to be assessed, but it is highly probable that they are at least a contributory factor in some areas.

It has been suggested at various times that an unbalanced diet predisposes to endemic goitre, e.g., a diet over-rich in fat or in protein, or an excess or deficiency of certain vitamins. There is little evidence in favour of any of these views, however. It is true that a high prevalence of endemic goitre is often associated with poverty and malnutrition, but this might be explained by the fact that a poor diet is also deficient in iodine, or that insanitary living conditions lead to pollution of the drinking water. It also has to be remembered that poverty and malnutrition are often found in small, closed communities, where a high rate of consanguineous marriages will tend to bring out any hereditary defect in thyroid function.

EXPERIMENTAL GOITRE

Whatever exogenous factors are ultimately found to

be concerned in the etiology of endemic goitre, it seems certain that the explanation of the wide variations in the size of the thyroid found among different individuals living in the same endemic area will have to be sought in endogenous influences. In an attempt to elucidate the nature of some of these influences, Milcu has carried out a series of experiments on the production of goitre in animals under a variety of conditions. He claims that stimulation of the central nervous system accelerates goitrogenesis in rats given methylthiouracil or fed on a diet rich in cabbage. Inhibition of the central nervous system has the opposite effect, as shown, for example, by the fact that chlorpromazine diminished the uptake of radioactive iodine by the thyroid and inhibited the action of thyroxine on the tissues. Sympathectomy and parasympathectomy both reduced iodine uptake, and after parasympathectomy the ratio of the weight of the thyroid to the weight of the body increased by 18.6%. On the other hand, cervical sympathectomy tended to decrease the goitrogenic effect of methylthiouracil, with the production of a smaller goitre showing less marked histological changes. Milcu suggests, therefore, that susceptibility to goitre may be influenced by variations in autonomic tone.

Intrathyroid injections of procaine were followed by a reduction in iodine uptake, and a fall in the blood-iodide level and basal metabolic rate. Similar, though much less marked, effects could also be produced by injecting physiological saline or by simply inserting a needle into the thyroid. From the results of these and other experiments, Milcu concludes that irritation of the nerve endings within the thyroid leads to reflex inhibition of the secretion of TSH by the pituitary.

It appears that goitrogenesis may also be influenced by other hormones. Milcu found that, in rats on an iodine-deficient diet, the change from a parenchymatous to a colloid goitre was accelerated by administering oestradiol, testosterone, the hormones of the adrenal cortex, or extracts of the thymus and pineal glands. Under the influence of these hormones, the weight of the gland fell by 50–65%. The effect may be dependent on the dose, however, for small doses of oestradiol increased the uptake of iodine by the thyroid, whereas larger doses inhibited it.

There have been indications from recent research that immunological reactions may also play a part in goitrogenesis. To investigate this, Milcu subjected rabbits to repeated isoimmunization by giving 4 injec-

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tions of a suspension of normal thyroid tissue at intervals of 15—20 days. Twelve days after the last injection, complement-fixing and precipitating antibodies were found in the blood, and the thyroid showed changes characteristic of immunity thyroiditis. In animals killed 90 days after the last injection, the thyroid showed marked hyperplasia and weighed nearly 4 times as much as normal. In rats, thyroid tissue from animals kept on an iodine-deficient diet or given methylthiouracil appeared to have a less powerful antigenic effect than thyroid from normal animals. The immunological response was exacerbated by TSH but reduced by cortisone. The interpretation of these results is at present uncertain, but Milcu postulates that immuno-pathological factors may be concerned in the transition from a parenchymatous goitre to a colloid goitre and in the development of the late degenerative changes.

Although these experimental studies do not provide definite answers to any of the problems of goitrogenesis, they give a number of pointers to future

research. But, as Roche & Lissitzky point out, extrapolations of experimental results must be made with caution, particularly as experimental thyroid hypertrophy is not strictly comparable with human goitre. Experimental procedures generally bring about rapid hypertrophy of the gland, whereas in endemic goitre the pathological changes develop slowly, giving the body time to become adapted to the progressive disturbance in hormone secretion. There is no doubt that these pathological changes can be influenced by a great variety of factors whose relative importance remains to be assessed. The problem of the etiology of endemic goitre is thus far from being solved, but it still remains true, as stated by Greer in 1950, that very few cases of thyroid hypertrophy not due to iodine deficiency have been explained so far. Roche & Lissitzky therefore ask whether different etiological agents might not produce the same effects through the essential intermediary of a faulty supply of iodine to the thyroid, which could then be accepted as the immediate cause of endemic goitre without prejudice to the wider question of the primary cause.

Endocrine therapy in gynecologic disorders. Kupperman, H. S. and Studdiford, W. E.,
Postgraduate Medicine, U. S. A., 14: 410-424, November, 1953.

The use of two common steroids, progesterone and testosterone, has made possible effective control of functional menorrhagia. Testosterone, in a dose of 25 mg. per day for 5 days, is used chiefly for its hemostatic effect. Progesterone is used for its therapeutic effect in bringing about a changed endometrial pattern. It seems best to use these two agents in oil solution rather than in aqueous suspension. This type of solution gives a faster action and makes the active material more readily available. When progesterone therapy is terminated withdrawal bleeding takes place and full desquamation of the endometrium follows. The term "medical curettage" has been used to describe this effect of progesterone. Besides the therapeutic effect this procedure may lead to physiologic changes resulting in regular menstrual periods. The steroids may be used intramuscularly or orally. If given intramuscularly, 25 mg. of each agent (progesterone and testosterone propionate) is administered daily for 4 or 5 days. Bleeding will cease on the first or second day, and there will be withdrawal bleeding and desquamation some time after the last injection. Progesterone is then given alone starting exactly four weeks after the combined hormone therapy. It is administered in three monthly courses as a single injection or as 4 daily injections of 25 mg. each. Oral therapy may be used: tablets containing 50 mg. of

progesterone and 50 mg. of methyltestosterone may be given 4 times a day for a period of 5 days. For the "progesterone-only" periods anhydroxyprogesterone may be given parenterally as described, or orally in 10 to 20 mg. doses, 3 times a day for 7 days during 3 consecutive months. Advantages of hormone therapy include the following: functional uterine bleeding is physiologically controlled; the procedure is wholly without trauma; the combined treatment is likely to lead to permanent correction; the procedure may be carried out in the office; and it has economic advantages, medication being less costly than surgery. In treating functional dysmenorrhea, preovulatory use of methyltestosterone and methylandrostenediol offers five advantages: it is frequently effective, even where other therapy has failed; ovulation is not inhibited; there is limited masculinizing effect; there is no decrease in effectiveness on repeated usage; and it may be used with little concern in cases where sterility is a problem. To control symptoms of the usually severe climacteric, pellets of estradiol and testosterone have proved effective. There are some cases where patients show an allergy to hormonal materials and required desensitization. Progesterone, and sometimes estrogen, may be used in amenorrhea; anhydroxyprogesterone will markedly relieve premenstrual tension.

EXPERIENCES IN IMMUNIZATION AGAINST TUBERCULOSIS WITH BCG VACCINE IN JAPAN

By Brigadier General CRAWFORD F. SAMS, M. C., F. A. P. H. A.

Brigadier General Sams is a surgeon, Headquarters First Army, Governors Island, New York, N.Y. The author was formerly chief, Public Health and Welfare, Supreme Commander Allied Powers for Japan, and Chief Public Health and Welfare, United Nations Command for Korea. This paper was presented before a joint session of the Epidemiology and Laboratory Sections of the American Public Health Association at the Eighty-first Annual Meeting in New York, N.Y.—EDITOR.

THE disease that kills or disables the greatest number of people and which in the present state of our knowledge we can do something about—should be the primary objective on which the greatest effort is expended by those charged with preventive medicine and medical care programmes. In Japan tuberculosis was the leading cause of death between 1932 and 1951, and therefore this was the disease upon which we focussed much of our effort. It dropped to second place in 1951 as a result of these efforts. I might point out that more people died in Japan from tuberculosis in 1945 than were killed by two atomic bombs and all our air raids on all of those of the major cities that were practically levelled to the ground.

A study of the death rates from tuberculosis shows that in 1918 the death rate in Japan was only slightly higher than that of various western nations, such as the United States, Germany, Sweden, Italy, Denmark, England, and New Zealand. During the period 1918 until 1955 these countries had progressively reduced their death rates approximately 60 per cent through various control programmes. This was accomplished through the standard procedures of health education, case finding, contact tracing leading to early diagnosis, and to extensive hospitalization and treatment programmes. On the other hand, the Japanese death rate had a slight drop between 1918 and 1932 and then began a steady climb to reach a peak of 282.2 deaths per 100,000 population in 1945.

Much study was given to the causes behind the great divergence in tuberculosis death rates in that

27 year period. In an effort to find an answer to the question, we must consider the patient not only as an individual but must also study his environment and living habits. I cannot go into all of the detailed studies that have been made on this particular aspect of the problem, but they can be summarized briefly by saying that in comparing the group of other nations mentioned preciously to Japan, we find that the opportunity for acquiring the disease in Japan is many times greater. As an illustration is the fact that the population density per square mile in Japan is the highest in the world. Second, that in Japan under such crowded conditions we find people living not in pairs in single rooms but from eight to 12 people sleeping in one room, as contrasted to the custom in most of the other countries of two, sometimes three individuals in one room. The Japanese habitually sleep on their backs with head rests which is ideal for the dissemination of droplet infections. Likewise, instead of providing ventilation for these crowded rooms at night, they are sealed tight since there is no heating in Japanese homes in the winter. It is obvious that a single open case of tuberculosis under such conditions will have a greater opportunity to spread tubercle-bacilli-laden droplets when he coughs than in the average European or American home.

Another factor is nutrition. In recent years research has shown the importance of the essential amino acids in protein of animal origin in developing body resistance to infection and the healing of body wounds. The nutrition surveys which we conducted for six years in Japan, examining 150,000 people every three months and actually weighing food

consumed and analyzing its components, showed that the Japanese diet is deficient in the essential amino acids. The normal Japanese consumer, that fictitious individual who is a composite of all age groups and all economic groups, would require a minimum of 20 gm of protein of animal origin, if he were to have normal growth and normal resistance to infection. Our surveys showed that he consumed in certain areas as low as 4 gm. per day. Another element in resistance to the tubercle bacillus is blood calcium. We found that the blood calcium level of Japanese children was approximately 40 per cent of that of occidental children on a normal diet.

There were only 25,000 beds for tuberculosis in Japan in 1945 and they were mostly empty as the active cases had left these hospitals because of shortage of food.

Contrast the environmental picture I have described in Japan with the picture in the United States and I think the high tuberculosis death rate in Japan prior to 1945 can be logically explained.

We do not ordinarily think of epidemics of tuberculosis comparable to smallpox, typhus, etc. However, under the circumstances outlined, I think we might well consider that we were faced with an epidemic of tuberculosis in Japan. After taking measures to control the 'wild fire' type of epidemic, such as smallpox, typhus, and typhoid, which were occurring in Japan, we began our control programme for tuberculosis. This programme involved many facets.

We had to begin an extensive health education programme to overcome the Japanese feeling that tuberculosis was a shameful disease to be concealed at all costs.

In organising a nation-wide health center system of 800 centers during the Occupation, the Tuberculosis Control Division of each health center was established as a major function.

A tuberculosis control law was placed in effect which now requires that all individuals from infancy to 30 years must be tuberculin tested. If the tuberculin test is positive, a 35 mm. film is made in an effort to determine whether the case is active. Since most of the tuberculosis in Japan is pulmonary, a suspicious first picture requires a re-x-ray on larger

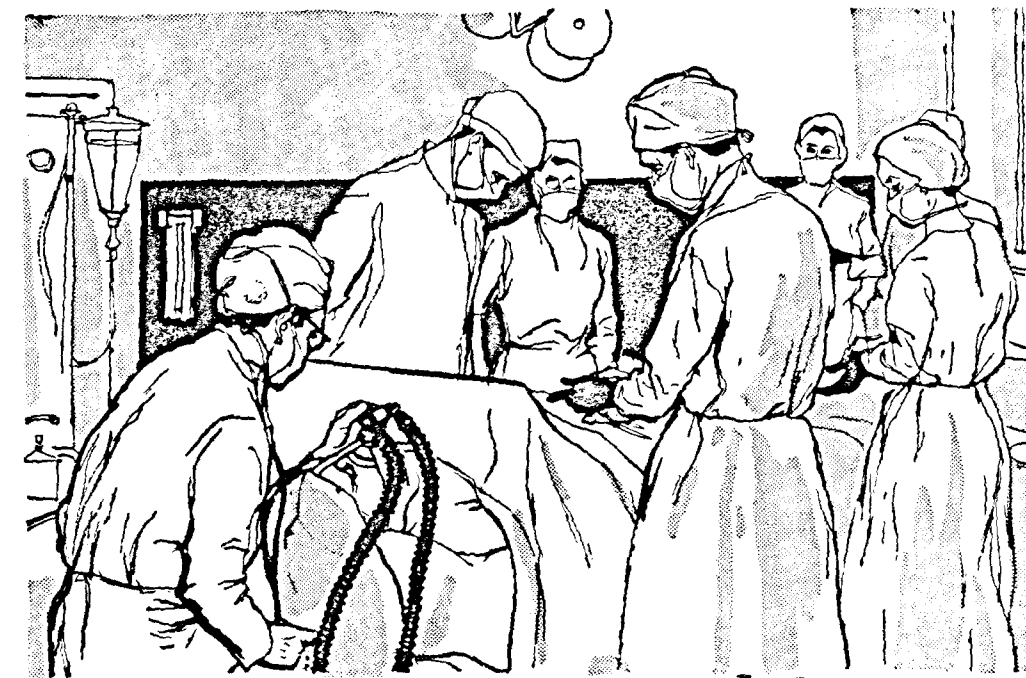
film, a physical examination, blood sedimentation rate, and repeated sputum tests. Under this programme in the first year 380,000 new cases were diagnosed. In the second year, with improvement in the health education and the mass survey programme, over 400,000 active cases were uncovered; in 1950 over 528,000 active cases were brought to light; and in 1951 590,000 were reported. This apparent increase in morbidity of tuberculosis did not mean that actually the incidence of tuberculosis was increasing. It simply was a measure of improvement in our efforts to uncover the active cases which were spreading the infection to others because, at the same time this increase was occurring, our death rate was dropping rapidly.

To overcome the dietary deficiency and increase the resistance of individuals when they did acquire a tubercle bacillus, a school lunch programme was inaugurated with powdered skim milk, a cheap source of protein of animal origin and of calcium, as the principle item in the school lunch. This eventually encompassed over 7,000,000 children and should pay in benefits as the years go on. The ultimate goal is 18,000,000 children.

Positive tuberculin tests, if we may assume that this is an indication of the presence of tubercle bacilli, showed that the Japanese acquire such bacilli early in life. If we take five-year age groups, we find the following:

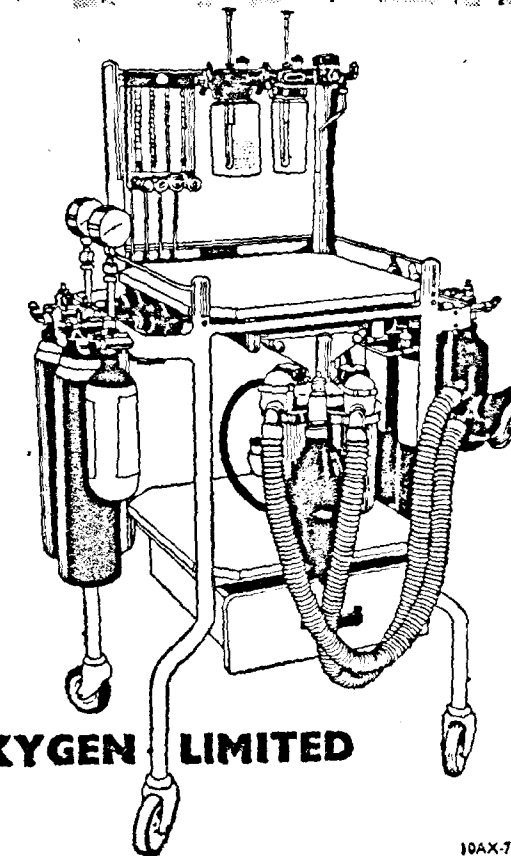
Year Age Group	Per cent. Tuberculin-Positive
0.0—1	2.0
1—4	11.5
5—9	26.2
10—14	44.9
15—19	54.7
20—24	65.9
25—29	76.6
30—34	77.7

There are 54,800,000 people in Japan who are under 30 years of age. A study of this group indicated that 25,500,000 or 46.6% of these people have acquired a natural infection which leaves approximately 30,000,000 who could be protected if they could be immunized against tuberculosis with BCG. They have now been immunized.



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The Japanese carried out numerous studies on BCG between 1927 and 1943 which cannot be discussed in detail. I can only summarize these studies by saying that on the whole mortality was reduced in the immunized groups by 88% as contrasted to the control groups over three and one half year observation periods. In 1943 the Japanese Research Council had evaluated the work done and recommended the extensive use of BCG. This programme was initiated, but due to the war it collapsed. We began to push this programme again at the beginning of the Occupation in 1945, immunizing that age group first which had the highest death rate—the 19 to 24 year age group. In 1945, 3,098,000 and in 1946, 6,729,833 tuberculin-negative young people were immunized with BCG. This programme was continued with 7,000,000 immunizations or reimmunizations for 1947, 8,000,000 for 1948 and then the programme was stopped from December, 1948, to October, 1949, because I was not satisfied with the results of our analysis of the reconversions of tuberculin reactions.

There were 11 laboratories making BCH vaccine. This was necessary because the life of liquid BCG vaccine is only about seven days and to attempt to distribute this vaccine from a single production source within the time limits was impossible under the transportation difficulties which exist in Japan. With the limited number of qualified Americans I had on my staff, it was likewise impossible to exercise that strict control required over the production of BCG in the 11 widely dispersed laboratories. Tests of the product of these laboratories indicated a wide variation in potency. Carefully controlled studies on tuberculin reaction conversion and reversion confirmed the wide variation in potency of the BCG vaccine production in these various laboratories. I therefore decided to convert to a dry vaccine which could be produced in one laboratory in which we could control the potency very carefully. The immunization programme using dry vaccine was reinstituted in October, 1949, and is being continued to date. In 1950, 13,900,000 and in 1951, 14,214,785 immunizations or reimmunizations were given.

A brief description of the procedure used in the BCG immunization programme is in order. First, as mentioned above, all individuals 30 years or under are given a tuberculin test (Mantoux test). Five T. U. of old tuberculin are injected intracutaneously. As you know, this consists of 0.1 ml. of a 1:2,000

dilution of old tuberculin. Our standard for reading the allergic reaction was as follows:

The non-specific reaction curve, which may be plotted by measuring the area of redness each hour as it develops, reaches its peak within 24 hours. The peak is indicated by an area of redness 3 to 5 mm. in diameter. The specific reaction curve is indicated by an area of redness 7-8 mm. in diameter in 48 hours, reaching a peak of 10-20 mm. in 72 hours. Our procedure was to read the test in 48 hours. An area of redness which measured in two directions and averaged 9 mm or more was considered a strongly positive-tuberculin reaction. An area 5-9 mm. in diameter was questionably positive. Any reaction of less than 4 mm was negative.

All the individuals who were less than strongly positive received BCG. The 0.1 ml. of BCG vaccine used by us contained a 0.4 mg. of BCG culture. This must be given intracutaneously to avoid abscess formation and local lymphadenitis. If given subcutaneously, no increase in immunization measured by subsequent tuberculin tests occurs, but an appreciable number of abscesses and in some cases lymphadenitis develops. With carefully controlled intracutaneous injections it is an exceedingly rare case which develops a local abscess.

Follow-ups on conversions from tuberculin-negative to tuberculin positive following BCG inoculation indicates that the highest percentage of conversions occurs in about three months.

We do not know the duration of immunity given by BCG. Danish workers such as Dr. Home and American workers such as Drs. Rosenthal, Aronson, and others with whom we maintained constant contact, have assumed immunity varying from six months to five years. We have found if we can use tuberculin as a measure of immunity, that we will obtain reconversions to tuberculin-negative in BCG immunized children in as high as 30 per cent within one year. Hence, our policy of reimmunizing all reconverted cases annually.

A word about production of BCG vaccine. We had an annual capacity of 30,000,000 doses in Japan in 1951. As those of you who have done laboratory work on tubercle bacilli know, the potency of the BCG culture is difficult to control and our procedure in order to maintain a uniform potency was to transfer

from glycerin-bile-potato medium to Sauton's medium with no more than five serial passages on each medium. The pellicle from Sauton's medium was cultured and filtered, the weighed mass was ground with glass balls in a container revolving 100 rpm. To dilute 80 mg. of BCG culture per ml. of diluent per cent sucrose was added. It is difficult to maintain a suspension, therefore, was immediately placed in ampules which varied from 20 to 100 ml. in capacity and were instantly frozen at -20°C . This temperature was maintained for one hour and then the vaccine was dried under vacuum for six hours at -40°C . The ampoules were then sealed and retained at freezing temperature until used. Our assay standard required less than 2 per cent moisture, as we have found that if we go above that moisture content less than 60% of the organisms will survive. Comparative tests with the dried vaccine as contrasted with the liquid vaccine showed that dried vaccine refrigerated for four months will maintain 82% tuberculin conversions for one year. On the other hand, after four months' refrigeration, if we use vaccine which has subsequently been permitted to stand at room temperature, our conversion rate drops within one year to 43%.

What have been the results of this, the largest BCG immunization programme in the world?

An analysis of the death rates from tuberculosis by five-year age groups shows that we have reduced the death rate from tuberculosis for the entire population, which includes both immunized and non-immunized groups, from a peak in 1945 of 282.2 per 100,000 per annum down to 82.1 in 1952. This startling drop of 70% in seven years which exceeded that which occurred in other countries in 30 years requires analysis. Practically all of this drop occurred in the immunized age group 0-29 years of age, inclusive. It must be borne in mind that this entire age group was not immunized for the entire period of five years, since it takes some time to accomplish these millions of immunizations and that only 53.3% of that entire age group was immunized with BCG in the first place, since the others were already tuberculin-positive from natural infection. Within this 53.3% only a fraction has been immunized for the entire five-year period. In the 30 and over age group, practically no drop occurred until the year 1950, and the improvement in this group is the result of our medical care programmes using streptomycin and para-amino-salicylic acid in combination which began in 1949. Based on studies made in the United States, we could anticipate

approximately a 70% reduction in death rate among those selected cases which have already acquired a clinical case of tuberculosis and the results in treating these cases in this age group plus the 46% of the 0-29 year age group who already have acquired a human tubercle bacillus should further contribute to the rapid drop in death rate in Japan.

We could, of course, have done nothing in the medical care field for those who already had acquired a clinical case of tuberculosis by simply letting them go on untreated and die. In about 30 years by continuing our BCG immunization programme, beginning with infancy when only 2% have already acquired a human tubercle bacillus, we could have produced a relatively completely immune population. However, we chose not to ignore that phase of the programme but by increasing tuberculosis beds from 25,000 in 1945 to 101,000 in 1951 and by pushing our streptomycin and para-amino-salicylic acid therapy programme, we will not only reduce deaths in that non-immunizable group, but will also reduce the reservoir of active cases which serve to spread the disease to others. This treatment programme is being applied to the 1,300,000 active cases of tuberculosis which have been uncovered in the 25,500,000 tuberculin-positive people less than 30 years of age.

SUMMARY

Very briefly this is a bird's-eye view of the most extensive and what we believe to be a successful tuberculosis control programme. The World Health Organisation, as you know, is now carrying out on a lesser scale in Europe and south-eastern Asia a BCG programme using similar techniques. The fact that this programme has so drastically reduced tuberculosis deaths in Japan when all the environmental factors, including overcrowding, malnutrition and collapse of normal living, caused by destruction of war, should have caused an increase in deaths as it did cause an increase in European countries, emphasizes the importance of BCG in the control of tuberculosis even under the worst environmental conditions.

A continued rapid drop in deaths from tuberculosis will occur in the future in Japan as a result of the programme instituted during the Occupation. Great credit is due to the comparatively small group of American personnel and the large group of Japanese who whole-heartedly co-operated in the initiation and maintenance of this programme.

Certain features of Biological Immunity in the Blood Serum of Patients with tumours of the Brain

BY DR. A. SHAPIRO AND DR. E. TERPUGOV
(Leningrad)

1. WE know that normal antibodies (alexin, hæmolysins, etc.) are part of the a specific apparatus protecting the organism from noxious influences.

2. The authors have studied the titre of antibodies in patients with tumours of the brain. The quantity of normal antibodies in the blood serum characterizes, to a certain extent, the general reactive capacity of the organism.

3. In cases of brain tumours lying in the interstitial part of the brain, the quantity of normal antibodies in the blood serum is sharply reduced. In cases of tumours situated in the area of the hypophysis, or in the frontal and temporal lobes, the quantity of normal antibodies is slightly diminished. In the absence of tumours it is close to normal.

4. A sharp fall in the quantity of normal antibodies is not a specific, characteristic symptom, pertaining

solely to tumours of the brain. It is founded, in all cases, on the presence of pathological factors, accompanied by intoxication or disbalance of the regulating mechanisms of the large hemispheres of the brain.

5. Sharp changes have been noted in the blood and serum of patients with tumours of the brain. They are connected with changes of the albumin fractions, detected by establishing the phenomenon of morphological blood dissociation, the phenomenon of separation of regular elements from the clot, and the index of the retraction.

6. The method of establishing the titre of normal antibodies, the phenomenon of morphological blood dissociation, the phenomenon of separation from the clot and the index of retraction is to be recommended in the neurosurgical clinic, as a supplementary factor in the chain of research connected with differentiated diagnosis.

The Method of functional Electroencephalography as a means of estimation of Neurodynamic conditions in cases of acute concealed injuries of the cranium and brain

BY DR. N. BEKHTEREVA
(Leningrad)

1. TWENTY five cases of concealed injuries of the cranium and brain were studied (4 concussions and 21 contusions of the brain). Fractures of the base and dome of the cranium were discovered in 13 cases. Neurodynamic conditions were estimated by electroencephalographic (EEG) registration, reflexes being incited by simple and complex conditioning signals and rhythmic sound irritants. The patients were regularly examined during their treatment in the Leningrad Neurosurgical Institute and in some cases in the out-patients' clinic.

2. Acute disorders of the bioelectric activity were observed in the first days after grave concealed injuries of the brain.

The amplitude of beat was usually found to be somewhat diminished and the rhythm sharply altered, slow beats were also indistinct and diffused. In a number of cases the predominant form of EEG activity at this stage were very short period beats, with an amplitude of about 10 to 25 Mv. At this period the EEG reactions to irritants may be indistinct, or, given the usual methods of registration, practically absent. Reactions of the normal type may be detected in some cases.

3. Elements of alpha-rhythm (different in the case

of individual patients) appear after some time in the EEG, but its pathological symptoms become, at the same time, more distinct. They are located in the area of gravest injury of the cerebral substance and usually increased by the use of irritants. Slow rhythmical beats can be detected in the EEG by applying conditioning signals. The reactions of that period are determined by weaker external check, weak internal check and liability of the irritating process, with a comparative predominance of the latter.

4. The normalization of EEG and of its reactions takes more or less time, depending on individual cases. There have been cases when neither sufficient restoration of the EEG background, nor normalization of reactions to irritants were observed by the time when a clinical cure was achieved. The registered neurodynamic condition of these patients was evidently a reflection of weak nervous processes. In cases when the alpha-rhythm is restored it remains for a long time unstable, easily checked and absent in the presence of irritants.

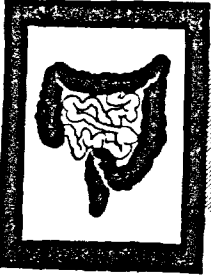
5. The methods of treatment applied in the clinic were taken into account in this research. The usage of some pharmacological substances caused alterations in the dynamics of the process.

Monograph on Prevention and Cure of a Serious Nervous Disease

New prospects in the treatment and, what is most important, the prevention of a grave and mysterious disease of the nervous system—hepato-cerebra dystrophy—are outlined in a fundamental monograph by Soviet Professor N. Konovalov presented in competition for a Lenin prize. This disease has been known to science for about 80 years. However, Konovalov's work is the first in world medicine which not only sums up everything done in this field so far, but on the basis of the author's personal observations, considerably widens and deepens the concept on this

form of dystrophy. Professor Konovalov refutes old, erroneous conceptions still current in medical science. He identifies new symptoms important for diagnosing and early identification of the disease. The author does not confine himself to a mere description of the symptoms but proceeding from the teaching of Ivan Pavlov, reveals the underlying mechanisms of the disease. The system of the treatment of the disease with unitol—a Soviet preparation developed by Konovalov—proved to be highly effective in many cases.

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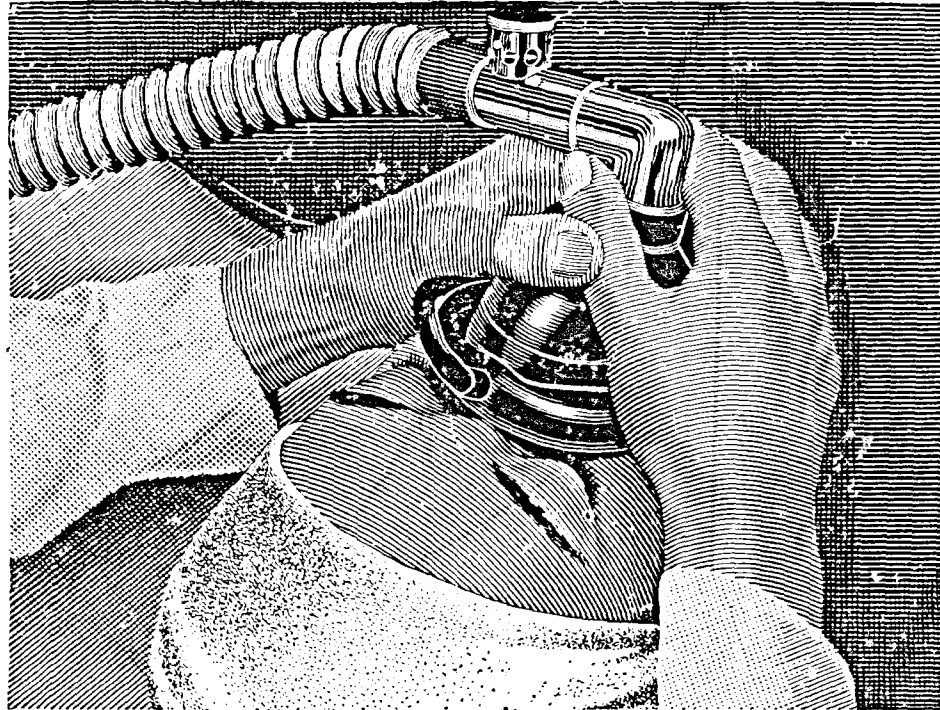
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By Dr. L. MOSONYI

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IT may be justly asked whether the two attributes in the title do not constitute a pleonasm. Is it at all possible to brand any phase of a therapeutic method not more than fifteen years old as "un-modern"? The answer is, however, in the affirmative, for during these very fifteen years, antibiotic research has grown into an independent science. Research work in this field has successfully solved new chemical, pharmacological, microbiological problems, it has developed enormous industrial bases of its own, it has its own history and legends, and in view of the benefit derived from the use of antibiotics by millions of people, it is not too exaggerated to call the antibiotic era the "atomic era" of medicine. The epithet "modern" simply means that the early empirical period abounding in errors due to inexperience has given way to the era of expedient research, economy, and prevalence of the ancient medical principle "primum nil nocere". In the course of this era, most of the methods and procedures employed to-day throughout the world have taken shape. We are far from regarding the results of this era as final. Antibiotic research and therapy still have many aspects that need elucidation, therefore the present paper cannot claim to be anything else than a brief outline of the present trends in antibiotic research.

I

If we put the trends in antibiotic research to the test of expediency, we must answer the question whether antibiotic science has attained its ultimate aim, i.e. complete destruction of pathogens, on the one hand, and full prevention of unforeseen complications, on the other. The question involves such problems as mode of action, bacterial spectrum, antibiogram, the organism's own defensive power, development of resistance, the consequences of a shift in the balance of the bacterial flora, the emergence of new diseases and altered course of old ones. We intend to deal with the problems in this order, before discussing the other trends in research.

In spite of certain differences, the mode of action of the various antibiotics is fundamentally similar. Ettlinger has classified antibiotics into two groups: those of group one collect on the cell surface of bacteria, destroy the semipermeable membrane, causing thereby the substances essential for life to diffuse out of the cell. To this group belong in the first place the antibiotics of local action, as Polymyxin, Tyrocidine. The prototype of the antibiotics in group two is penicillin. By the use of penicillin prepared in isotope medium and thus rendered radioactive, it has been shown that antibiotics are taken up differently by the cells that are susceptible and those that are not susceptible to them. Susceptible cells will absorb invariably the same amount of the antibiotic, irrespective of its concentration in the surrounding medium, they retain it irreversibly, i.e. they will not lose or exchange it when eluted or when further doses are added. In addition, every bacterium, susceptible or resistant, takes up an amount, depending on concentration in the environment, that can be eluted. The antibiotic which has entered the bacterium interferes with the usual chain of metabolic processes, as indicated by increase in the amount of certain products of intermediary metabolism, such as glutamic acid and free nucleotides, and by the absence of certain characteristic end products. One of the most characteristic compounds thus not formed is an enzyme which breaks down ribonucleic acid. These phenomena suggest that penicillin interferes with protein synthesis. The staphylococcus model experiments of Gale seem to confirm this view. To build up its own proteins, staphylococcus requires fourteen amino acids. If only one of them is absent from the medium, or if, in the presence of all of them, antibiotics are added to the medium, this essential protein synthesis will not take place. Synthesis itself, enzyme action, proceeds after fictive patterns on the bacterial surface, and the antibiotic interferes, as it were, mechanically with the synthesis and breakdown of polypeptide chains. Most of the antibiotics are believed to act fundamentally in this way, though in different phases; for instance the tetracyclines and chloramphenicol inhibit the transi-

tion from preproteins into proteins. Streptomycin, itself a carbohydrate-like substance, inhibits the assimilation of carbohydrate end products, apparently by interference. Our recent experiments have proved that streptomycin interferes with the enzymatic processes controlling the formation of adrenocortical glycocorticoids. Hopps, Wiseman, and Hahn have studied the action of chloramphenicol on various enzymes and found that the antibiotic does not interfere with polysaccharide synthesis, but inhibits the ammonia assimilation and protein synthesis of *E. coli*. Of course, antibiotic action requires certain environmental conditions, for example the presence of certain ions. Friedman et al. have shown that cation exchange resins inactivate streptomycin and the tetracyclines, but not penicillin and chloromycetin. According to Mazzeo and Tamburino, certain organ extracts influence antibiotic action, for example liver homogenates strongly inhibit the bacteriostatic action of tetracyclines. Various antibiotics are known to act at more than one level; for example, streptomycin inhibits the oxalacetic acid-pyruvic acid cycle. Tyrothricin blocks the synthesis of adenylylphosphoric acid, while certain antibiotics act on respiratory surfaces (Savelsberg and Stroder), as shown in the Warburg apparatus, etc. These factors should also be considered when selecting the antibiotic in scientifically planned antibiotic therapy.

Determination of the bacterial spectrum stems from the early phase of antibiotic research. However great the blessing to have powerful antibiotics at our command against most bacteria, gram-positive or gram-negative, it is none the less true that certain bacteria, and even whole species, are still unvanquished. Of the more than one hundred various antibiotics only 14—16 are fit for use in human therapy; one of the chief aims of research is, therefore, the production of new ones that will act on as yet inaccessible micro-organisms. Some—rather slow—advance in this field is undeniable; although most of the new antibiotics have more or less identical spectra with the old ones, antibiotics active against viruses, rickettsiae, and fungi have been prepared recently. Ley and Smadel have reported on the therapeutic results obtained in 588 cases of rickettsial disease. In all of these cases recovery resulted from the use of so-called broad-spectrum antibiotics, in doses of 50 to 60 mg./kg. of body weight. In

viral and rickettsial infections it is advisable to resume dosage for a few days one week after the complete disappearance of clinical symptoms, because the pathogens seem to grow in six to eight-day cycles.

Recently, tetracycline, the basic compound of chlor—and oxytetracycline, has been added to the series of broad-spectrum antibiotics. Its preparation has contributed to our knowledge of the mode of action of antibiotics and has brought also practical advantages owing to the paucity of side effects. Removing a methyl group from the tetracycline molecule yields demethylchlortetracycline. This antibiotic has a high stability, sustains long, high blood levels, and acts against a wide range of bacteria (B. M. J., editorial).

Mycostain or Nystatin prepared from *Streptomyces noursei*, has been found to be eminently suited for the treatment of fungal diseases. Standardized on the basis of its activity on *Saccharomyces cerevisiae*, its units is 1 microgram, its dose is 20 to 30 mg./kg. body weight intravenously, or 0.3 to 1.0 g. orally, at 4 hours' intervals. Its toxicity is low; large doses cause rhinorrhea and gastrointestinal complaints (Ravina and Eloy). When administered parenterally, it causes pain or even severe phlebitis. Though it is poorly absorbed from the intestines, it has proved to be of value in the treatment of systemic mycoses (pulmonary mycoses) as well.

Griseofulvin was isolated by Oxford some twenty years ago. Its efficiency in curing dermatophyte ringworm infections has been established recently (Gentles).

The cytostatics are an important addition to antibiotic therapy. Sanamycin, a drug prepared from the fungi *Streptomyces chrysomallus* and *antibioticus* is used in the treatment of leucæmia and lymphogranulomatosis, owing to its elective action on lymphoid tissues. In a course, daily doses of 100 to 300 micrograms are given intravenously, up to a total dose of 5000 to 10,000 micrograms. Our experiences with Sanamycin in lymphoid leucæmia with hypersplenic symptoms and in Hodgkin's disease are favourable. The other new broad-spectrum antibiotic will be discussed elsewhere.

The sensitivity of bacteria to different antibiotics is reflected by the antibiogram which is performed when the culture of the pathogens has been obtained. The common technique is to place discs of paper steeped in a certain amount of the antibiotic under investigation on the bacterial colonies grown in solid medium, determining thereby the sensitivity of the strain to the different antibiotics. Confusion in evaluation may result from the practice that different amounts are used of the different antibiotics. The recent trend is to develop procedures the results of which would be easier to compare, and it has been suggested that even the traditional units of penicillin should be abandoned in favour of grams. One unit of penicillin is equivalent to 0.6 microgram. Instead of 1,000,000 units one could write 0.60 g., making comparison with the broad-spectrum antibiotics easier. Penicillin V, phenoxymethylpenicillin, is given exclusively by gravimetric dosage. Comparative analysis shows that penicillin is still the most effective antibiotic available.

The antibiogram provides information about the in vitro resistance of the tested bacterium

and is helpful in choosing the antibiotic, but, of course, cannot answer the question how and when the patient will be cured, because in vivo the organism's own defensive forces are also at play. In vitro effectiveness is often liable to be misleading, especially when we calculate with theoretical data, i. e. with the sensitivity not of the strain actually responsible for the disease, because such calculations are merely averages, statistical data, which are not fully valid in the pathogen-patient relation. In addition to these theoretical considerations, Hinglais and Langlade have explained the difference between in vitro and in vivo effectiveness. In their investigations they have shown that by the addition of sublethal doses of antibiotic to staphylococcus cultures (i. e. such doses as do not inhibit the growth of the population), certain properties of the pathogen may be abolished, for example, at various stages, fermentation of mannitol, production of coagulase or hæmolysin, development of the yellow enzyme may not come about, depending on the antibiotic added. Thus it is possible that the enhanced effect found in vitro

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is merely apparent, because bacterial growth has been unaffected; nevertheless, the micro-organism may have lost its ability to produce symptoms. The micro-organism, having thus become saprophytic, will fall easily victim to natural immunity, first of all to phagocytosis. Subsequently, it has been demonstrated that such avirulent strains really exist, reminding us of the case of the planet Neptune which had been known to exist theoretically before it could be detected by telescope. Scadding showed the presence of tubercle bacilli claimed to be completely apathogenic in the sputum of patients who had been treated with Isonicid. There is no need to dwell upon the importance of this fact.

In addition to this apparent disparity there, is also some very real discrepancy between in vivo and in vitro effects, as illustrated perhaps in the most convincing manner by the role of hormones in the affected organism. Experience has shown that cortisone therapy leads to a dramatic spread of latent infections (tuberculosis, sepsis). Foley infected mice with streptococci and gave them simultaneously penicillin and cortisone. Penicillin protected the animals, but when it was replaced by tetracycline, every animal succumbed. There was no difference in protective action between the two antibiotics in mice previously immunized against streptococci. These experiments indicate that the defensive forces of the organism are essential for the effect of tetracycline. In non-immune animals, cortisone suspends the action of natural immune bodies, but not that of the antibodies formed in immunized animals. Cortisone promotes the spread of mycoses as well, obviously by the same mechanism (Mankowski and Littleton). Oestradiol likewise enhances susceptibility; this may explain the increased liability of females to infection in certain phases of the menstrual cycle. Testosterone, on the other hand, offers some measure of protection against infections (Mankowski). An other effect of cortisone may be used in making therapy more effective; as cortisone promotes the resorption of fibrotic processes, daily 100 mg. of cortisone with sufficient doses of antibiotics administered for a few days, help the antibiotic to gain access to bacteria in tuberculous meningitis. This method has been employed successfully by ourselves in the treatment of persistent and recurrent basilar meningitis. However, cortisone may enhance the effect of streptomycin not only by lysing fibrotic granulation tissue; in

the pre-allergic state of tuberculosis, tubercle bacilli often reside within the cells where poorly diffusible antibiotics cannot reach them, so that they may continue to grow. Cortisone abolishes allergy and thus deprives bacteria of their protecting coat (D'Arcy Hart).

Although our own experience suggests that antibiotics act against phagocytosis (Mosonyi, Szoke, and Vajda) through interference with the vitamin household, in certain respects they may enhance the activity of certain defensive systems. Bottiger has shown that in their cycle between liver and intestine, the tetracyclines are present for a long time and at high concentrations in the cells of the reticuloendothelial system.

The development of resistance has grown into a problem harder to deal with in the case of antibiotics than in the case of sulfonamides. A chemotherapeutic drug is a synthetic substance whose structure may be altered with relative ease, so as to preserve its activity without provoking the resistance shown to the original compound. The antibiotics, on the other hand, have complicated structures difficult to synthesize; so far only chloramphenicol has been synthesized on an industrial scale (Threomycin, Chlorocid). Thus we know that even minute changes in structure may substantially reduced activity, therefore the methods followed in the case of sulfonamides do not apply to antibiotics. Oxamycin, a new antibiotic produced from *Streptomyces garyphalus* (Harris et al.), may prove to be an exception to this rule, having a very simple structure (D-4-amino-3-isoxazolidone). Similarly, Cycloserin, which is a double molecule of the former and chemically related to oxamycin, seems to be a simple compound.

Both antibiotics are absorbed rapidly, pass readily through the blood-CSF barrier and are distributed evenly in the body. The CSF level is about 50 per cent of the blood level.

Modifications like complexes, as in procaine-penicillin, or those of the side-chain, as in penicillin V, or lately in phenoxyethylpenicillin, cannot be interpreted as structural changes.

As changes in the chemical structure hardly involve any protection against the development of resistance—the theoretical aspects of which shall not be dealt with in this paper—new antibiotics are being produced

almost continuously with considerable advantage to the possibilities of modern antibiotic therapy. Resistance of staphylococci is an especially acute problem, though also coli organisms causing infections of the urinary tract often become resistant. Against penicillin resistant strains tetracyclines, as well as the newer Erythromycin, Carbomycin, and Novobiocin are particularly effective. Erythromycin, a highly active product of *Streptomyces erythreus*, can be taken by mouth. Apart from being suitable for the substitution of penicillin, it does not modify the physiological intestinal flora, being inactive on coli bacilli. Carbomycin, prepared from *Streptomyces halstedii*, has similar advantages; it can also be taken by mouth (Field and Taylor). Also Novobiocin, a product from *Streptomyces niveus* (Smith), has a growing popularity.

Oleandomycin and Rovamycin (spiramycin), new representatives of the Erythromycin group, are recent products of research. This group is the "reserve force" in antibiotic therapy, because its members have about the same antibacterial spectrum as penicillin or the tetracyclines. Their use is indicated when bacteriological tests show the pathogen to be resistant to penicillin or the tetracyclines.

Kanamycin, isolated from *Streptomyces kanamyceticus* by Umezawa (Yow), and Ristocetin, a product gained from *Nocardia luria*, are mainly employed in cases of infections with resistant staphylococci (Romansky).

Polymyxin B, an antibiotic of polypeptide nature, which can be injected in a watery solution intramuscularly and intrathecally, may be considered as almost the only agent active against *pyocyaneus*, which is becoming more and more common as pathogen. Unfortunately, there is a very slight margin between therapeutic and toxic doses; the recommended daily single dose is 1.5 to 2 mg./kg. of body weight.

Colimycin, produced by Koyama, has greatly broadened the spectrum of antibiotic therapy, being active against *Pseudomonas aeruginosa* and *pyocyaneus* both orally and parenterally. Its side effects are but insignificant.

Sulfamides may be used to advantage against coli strains which have become resistant. It must be noted that these drugs, though of great value, especi-

ally in urogenital or biliary diseases, are not used as widely as they should be, either because too much weight is attached to the gastrointestinal complaints they may involve or because the use of antibiotics seems to be more convenient.

The advantage of long-acting sulfonamides (Madribon, Orisul) is obvious, both from the economical point of view and owing to the practically complete absence of side-effects.

Viomycin, a product of *Streptomyces puniceus* (Wanner and Kaufmann), can be employed against tubercle bacilli grown resistant to streptomycin and Isonicid. Resistance to Viomycin has not been described so far and it may therefore gain wider acceptance. The dose is twice 1 g. intramuscularly every three days. The use of the pantothenic salt (Keller) seems to be more advantageous.

An other way to prevent the development of resistance is the combined use of antibiotics. The combinations streptomycin+Isonicid, and streptomycin+PAS are generally known, therefore we need not discuss them in detail. We should only like to refer to the more and more prevailing tendency in the medicamentous therapy of tuberculosis, i. e. to lengthen the intervals between the courses of streptomycin (twice 1 g. a week) and to administer larger doses of Isonicid. If PAS causes gastric complaints, it may be replaced by oxytetracycline (Tetran). As to the methods for preventing the development of resistance to other antibiotics, it is too early to say whether they are really efficient, nor can we, for the present, determine clinically whether the combinations are effective owing to synergism or owing to inhibition of resistance, although bacteriologic study should be likely to clarify this issue.

Combined therapy is furthermore advantageous because frequently the bacterial flora is apt to change due to a destruction or suppression of susceptible micro-organisms. According to Jackson and Axelroad, this process may theoretically involve various factors; antibiotics may increase the growth rate of certain, formerly suppressed bacteria (this view seems to be confirmed especially by the results of studies on the growth of the fungus *Candida albicans*). The biological resistance of the organism may be diminished by the destruction of bacteria ensuring balance, or due to a weakening of the defensive mechanisms,

such as fever, phagocytosis, antibody formation; finally, as a result of creating more favourable conditions for bacterial growth by the damage caused to tissues. The latter possibility is emphasized in the case of aureomycin by Lepper et al.; Mosonyi, Laszlo, Zulik, and Pero have reported on the impairment of liver cells by therapeutic doses of streptomycin. The size of the dose is certain to play a role in such lesions. According to Simon and Krupe, large doses of streptomycin decrease the glycogen content of the liver, while small doses enhance the apposition of glycogen.

The upset of balance in the bacterial flora may give rise to further pathologic conditions. The increase in the incidence of mycoses is well-known. These usually appear in the form of generalized sepsis or as affections localized to certain viscera: pneumonia, intestinal mycoses, anorectal syndrome. The significance of these diseases is increased by the fact that they join other diseases in an already weakened organism. Moreover, it may be difficult to interpret certain changes in the course of an established syndrome. Finally, the complications are extremely persistent, for example an anorectal syndrome may cause itching and vague abdominal complaints for months. More recently, methyl- and propylparabenzoic acids have been recommended against fungus infections (Manet), and it has also been suggested that these drugs be added in advance to broad-spectrum antibiotics, so as to prevent the development of mycoses.

Choleric form pseudomembranaceous gastritis caused by a foudroyant growth of resistant staphylococci is a more serious and often fatal complication. Erythromycin appears to be the drug of choice against this complication.

Brodie, Jannieson, and Sommerville have called attention to a new syndrome. On the administration of tetracyclines, a disease resembling scarlet fever develops, with sore throat, typical rash, and ending with typical desquamation. Diagnosis is further complicated by the fact that sore throat without rash also occurs. The syndrome is not a rarity; the above authors encountered it in 48 patients out of 378 cases treated with tetracycline. This number includes also the infrequent cases of gastritis and balanitis that occurred. In every case resistant staphylococcus was responsible for the complications.

The shift of the bacterial flora in response to antibiotics may lead not only to an emergence of uncommon pathological conditions or even to the appearance of new diseases, but also to such changes in the physiologic condition as may be advantageous for the organism. Elevation of the blood sugar level and the gain in weight in response to tetracyclines and penicillin (due to changes in absorption according to Völker et al.) are exploited in veterinary medicine in the first place. In experiments on Hindu university students, Satoskar and Lewis found that in response to daily doses of 0.05 g. of terramycin over a period of two months the serum albumin level increased and both the absolute and relative quantity of globulins decreased. Alteration of the intestinal flora has been suggested as the responsible factor.

Changes in the course of known diseases should also be dealt with. The classic, six-week phases of typhoid disappear, pneumonic crises remain absent, and terminal septic conditions, a common feature in haematological diseases, do not develop. This statement is in fact of general validity, because antibiotics have been spread at an almost even rate all over the world. A re-appearance of earlier entities need not be reckoned with even if resistant strains, similarly to those of staphylococci, should emerge, because new antibiotics becoming available in the meantime, would certainly take care of them.

Even of greater importance than the form of appearance of diseases are the problems how antibiotics alter the usual cycles of infectious disease, whether they interfere with the development of immunity, and whether they induce a so-called negative phase during which susceptibility to the invading pathogen increases. The answers to these questions are not yet final, though it is true that for example in scarlet fever secondary complications (infections, reinfections) have been found to be more common and protective antibody formation to proceed more slowly since the introduction of penicillin therapy. Similarly, the incidence of tuberculous meningitis seems to have been on the increase owing to the use of streptomycin. Our recent investigations (Mosonyi, Csiky, Lengyel, etc.) support the view that susceptibility to viral infection increases following antibiotic therapy. More experiments should be carried out in any case to obtain evidence deciding these problems. At any rate, it is absolutely certain that the use of antibiotics has proved to be

highly advantageous in the overwhelming majority of cases.

II

An other important trend is to make the use of antibiotics more economical. The development of methods with a view to prolonging the duration of action or to attaining higher concentrations at the desired sites, utilization of synergistic action and avoidance of antagonism are the main features of this work.

The methods for prolonging penicillin activity have been steadily improving, even since the introduction of solutions (suspensions) in oil, combination with procaine, and the use of caronamide-probenecid. More recently, a single dose of dibenzyl-ethylendiamine, Bicillin, has proved to maintain an effective bactericidal level for a week, and a dose of 6,000,000 units for one month. We are by no means enthusiastic about prolonging the action of penicillin to such a degree, which may come to rely on the implantation of crystals, lest we should lose control over the drug introduced into the body and be unable to prevent possible complications. For example, Mulligan reported on a case where ten days after the administration of 600,000 U of Bicillin an enormous rash developed, which could be cured only in three months by several courses of cortisone. It is undoubtedly more convenient for the patient to receive as few injections as possible, but not at the price of the drug remaining in the body for more than 24 hours.

Of the new preparations intended to produce higher topical activity, the most important is the diethylamino-ethyl ester of penicillin which, according to Dulfano, Irmer, et al., is secreted selectively in the lung and is therefore highly effective in the treatment of chronic infection and abscess of the lung. Local action is further enhanced by the oral, rectal routes of administration, as well as by inhalation, whose significance it is unnecessary to stress. All we want to point out is that it is more economical (by 100 per cent according to Young) to take the drug by mouth before meals.

In the present paper the author does not apply the term synergism to express a pharmacological notion merely implying combined action, direct or indirect, on the pathogen in question; it is

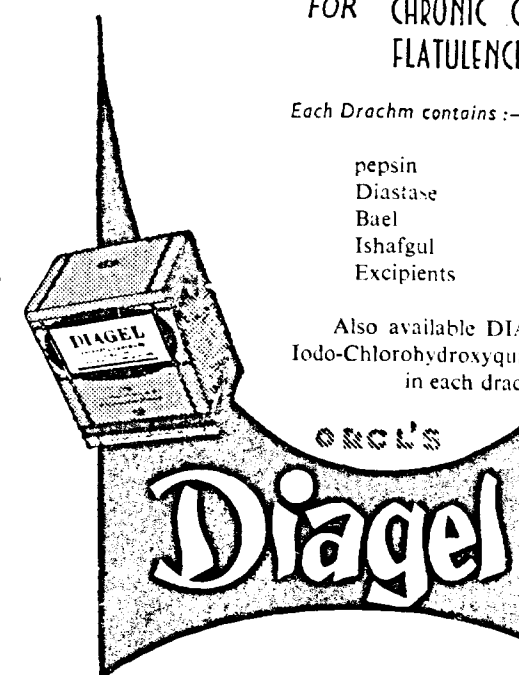
meant to imply also the final cure of interrelated diseases caused by different microorganisms. Having formulated such a broad definition, we do not intend to discuss theoretical problems. We emphasize, however, that in possession of the data concerning pharmacological synergism, economy of treatment should be increased not by reducing the doses of the synergistic drugs, but by ensuring faster success through the use of fully effective doses, thus shortening the duration of illness. Theoretical considerations have not always proved right in practice. For example, Garrod has shown that sulfathiazole reduces the action of penicillin on staphylococci, without abolishing it completely. Consequently the effect of sulfathiazole is enhanced later, owing to a reduction by penicillin in the bacterial population. Pharmacological synergism is proved by the investigations of Reynolds and Rowley, who showed that in the presence of streptomycin, bacteria take up more of radioactive penicillin. Of the new antibiotics, oxamycin is a synergist of

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penicillin, tetracyclines, chloramphenicol, and Bacitracin alike.

An example of clinical synergism is the effect of chlortetracycline on the healing of tuberculous fistulae (Rossler); this is obviously an action on secondary infection. Another example is that of Neomycin: in doses of 0.5 g. every six hours, this antibiotic acts excellently on secondary pneumococcal, pyocyanus, and proteus infections of tuberculous cavities. The earlier mentioned effects of cortisone and antibiotics are also illustrative of clinical synergism.

There are discrepancies between theory and practice also in the case of antagonism. It is known from the work of Jawetz that the tetracyclines antagonize penicillin and streptomycin. However, due to interference by the growth cycles of bacteria and the time at which antibiotics are administered, this antagonism rarely takes effect in practice. Sedallian et al. have found that in Dubos medium oxytetracycline suspended the action of Isonicid (INH). Although the results of in vitro studies may not apply fully to the conditions prevailing in the human body, it is advisable not to use the above mentioned agents in combinations with one another, so as to avoid possible antagonistic effects.

The problems presented by economical large-scale production of antibiotics are beyond the scope of our paper. It is, nevertheless, pertinent to mention the evidence published by Armstrong, Wilmot, and Elsdon-Dew as to the therapeutic value of the residue left after fermentation. Though it soon became clear that the obtained effect was due to small amounts of the antibiotic, these experiments proved useful, because they reminded us once again that even small doses of antibiotics may have full therapeutic activity, as in the earlier era of penicillin, when 150,000 to 200,000 units were the usual daily dose.

We do not approve of the use of combinations prepared in advance, in order to produce a synergistic effect. In exceptional cases the effect of such combinations may be spectacular, but, as a rule, the combination has no advantage whatever over the drug, which is active by itself on the pathogen. Combinations may in addition cause the development of hypersensitivity to more than one antibiotic or drug.

III

The third principle, that of the "*primum nil nocere*", will be discussed but briefly, not because we fail to appreciate its significance; on the contrary, we think it so important that in our view the various aspects it involves deserve to be considered separately. We merely wish to point to the essential practical principles of the question, first of all that an antibiotic, just like any other material, may have direct toxic action, the organism may prove intolerant to it, and finally may become hypersensitive to it.

The antibiotics most likely to have direct toxic effects are those of polypeptide structure; Polymyxin, Bacitracin, Tyrothricin may affect the liver and/or the kidneys. The toxicity of these antibiotics is well-known and they are therefore seldom used parenterally. The attempts at abolishing the noxious effect of streptomycin on the vestibular apparatus by modifying its molecular structure (dihydrostreptomycin) have failed, the latter having proved to be more toxic.

Chloramphenicol is believed to be toxic to the haematopoietic apparatus, although some workers ascribe this complication to allergy. Fear from harmful effects should, however, not detain us from its use, only the leucocyte count should be checked at regular intervals.

Symptoms of intolerance appear mostly after the oral use of broad-spectrum antibiotics, in the form of more or less marked gastrointestinal manifestations, such as eructation, loose stools, colics and nausea, without, however, interfering with the therapeutic activity.

Hypersensitivity is the commonest complication due to the use of antibiotics. Almost every material may elicit hypersensitivity, and it is now certain that the symptoms are caused by the biologically valuable antibiotic itself, and not by the vehicle or some contamination. Rentch-nick published a detailed list of hypersensitivity phenomena: various kinds of dermal eruptions, including those resembling rashes associated with infectious diseases, exfoliative dermatitis, symptoms of photosensitivity, ulcerous and vesicular mucosal changes, anaphylactoid reactions and manifestations similar to those caused by generalized serum sickness, changes

in the nervous system and haematopoietic organs. In his opinion, most of these complications are, in the long run, harmless, since they usually disappear when the responsible antibiotic is discontinued. Of special significance are the changes resembling those seen in periarteritis nodosa found by Waugh after long-continued

penicillin treatment. Also Walsh and Zimmermann have found evidence to show that treatment carried on over prolonged periods of time may cause hypersensitivity: in 3 cases the L. E. factor characteristic of collagen diseases occurred in the plasma and L. E. cells were found in the bone marrow.

Foreign Diplomats Acquainted with Soviet Health System

A lecture for the Diplomatic Corps was recently arranged by the Protocol Department of the Ministry of Foreign Affairs of the USSR, in the Vyshnevsky Institute of Surgery under the Academy of Sciences of the USSR. The lecture was given by S. V. Kurashov, the USSR Minister of Health. The subject of the lecture was "Public Health in the USSR".

S. V. Kurashov dwelt in detail on the system of public medical services in the USSR, in the course of which, he quoted many interesting comparative facts and figures about the number of doctors in the USSR, medical institutions, development of drugs and so on. In answer to the questions of further information was supplied about the participation of the USSR in the international health organisations and Soviet aid made available in this field to the countries of Africa and Asia.

The director of the Surgical Institute Prof. Vishnevsky spoke of the work of the Institute, specially in relation to the heart surgery. He also demonstrated some of the apparatuses (artificial heart, blood vessel stitching devices, etc.)

The report on the subject, simultaneously translated into English and French, was heard with great attention. The diplomats were later invited to see two films, one showing experiments on separating a dog's hind leg and its subsequent grafting, and the other, a colour film depicting surgery being performed on heart.

After this the diplomats saw on the screen of the colour television an operation being performed on the heart of a seven-year-old girl by Professor Vyshnevsky.

At the end the diplomats were shown calculating electronic machine "Ural-2" used for the diagnosis of disease and were also told about the use of cybernetics in Soviet medicine.

Most of the diplomats accredited in Moscow, were present at the lecture. The members of the staff of the foreign Embassies also attended it.

* * *

SUPPRESSION OF KOCH BACILLI

Soviet doctors are affirmative on the possibility of suppressing Koch bacilli and tuberculosis caused by it.

Particularly important in tuberculosis treatment are the preventive inoculations with the BCG (Bacillus Calmette-Guerin) vaccine. Soviet doctors were the first to start obligatory vaccination of all children (including new-born babies right at the maternity homes). The vaccination is free and is repeated after a definite period.

According to the Ministry of Public Health the incidence of TB among vaccinated children ranges from one-seventh to one-tenth of that among the non-vaccinated. In those cases when a child falls sick despite vaccination the disease is much milder and is quickly cured. Grave cases are very rare amongst those who have been vaccinated.

For early diagnosis of tuberculosis mass examinations of the population are held regularly. There are obligatory examinations for children who go to kindergartens and creches, school-children, students, and workers in certain trades. Thus tens of millions of people are examined annually for TB.

Whenever a TB case is detected in a mass examination the patient is immediately sent to a TB clinic where another thorough examination is held and appropriate treatment is prescribed. All this is free of charge.

Soviet doctors are successfully using a series of drugs for TB treatment, including streptomycin, phtyvasid, thybon, PASK. The administering of these drugs is always combined with methods of general therapy: blood transfusion, diet, physiotherapy and surgical treatment, if need be. Ordinarily, the TB patients are treated at specialized sanatoriums. The treatment at these establishments continues for not less than two months and is free as a rule.

Simple Palpation to Detect Valvular Incompetence in Patients with Varicose Veins

By. DR. ROBERT A. NABATOFF, M.D.
New York

DURING recent years, practically every report concerning the treatment of varicose veins has emphasized the importance of a proper high ligation of the long saphenous vein. This implies that the long saphenous vein is ligated flush with the femoral vein after all of its adjacent branches are ligated and divided. Unfortunately, in a significant number of cases, the dissection is not carried high enough. Unless the femoral vein is visualized, branches of the saphenous vein near the saphenofemoral junction may be overlooked, and it is these vessels that usually cause recurrent varicosities. The predominant venous insufficiency is usually at the saphenofemoral junction, but there may be incompetent valves in other communicating vessels of the thigh or leg or the short saphenous vein—popliteal vein junction. The success of operation depends upon the ability of the surgeon to detect and eliminate all sites of valvular incompetence.

Many diagnostic tests have been devised to aid the physician in the detection and localisation of "blow-outs". The tests most commonly used are: (1) Brodie-Trendelenburg, (2) comparative tourniquet (Ochsner-Mahorner), (3) Perthes' (4) Compression, and (5) Schwartz (percussion) test. Performing and interpreting these tests is a rather formidable and time consuming job for the average student or practitioner. According to Steiner and Palmer's findings, the Perthes', compression, and Schwartz tests have little to offer, are unreliable, and reveal no information that cannot be obtained by more accurate methods. "It would seem that the Brodie-Trendelenburg test, with the additional feature of the tourniquet placed just above the level of the knee... will actually afford all of the information required for one to treat any uncomplicated case of varicose veins." Luke also believes that valvular incompetence can be determined by the Brodie-Trendelenburg test and that the other modifications of this test are unnecessary in the evaluation of any case of primary varicose veins. He states: "The modifications of the Trendelenburg test were designed to indicate the competence of communicating

veins. In theory this would appear to be quite worthwhile; however, in practice, one cannot rely on such findings. In addition, when the operation of stripping of the great and small saphenous veins is carried out, most incompetent communicating veins are automatically interrupted. Thus, the modifications of the Trendelenburg test, such as the comparative tourniquet or multiple tourniquet tests, become unnecessary."

As the result of examining many patients with varicose veins, it has become apparent that in practically all cases of saphenofemoral insufficiency, a definite "bulge" can be palpated in the region of the fossa ovalis. This has been true in obese patients. If the tip of the index finger is placed just below the inguinal ligament, just mesial to the femoral artery, the "bulge" is easily palpated. In order to detect any valvular incompetence below this level, the tip of the index finger is run slowly down the thigh and leg along the course of the saphenous vein. If other "blow-outs" exist, a sudden increase of the pressure within the saphenous vein will occur immediately below the site of each incompetent valve. It has been my experience that the vast majority of patients with varicose veins have their predominant insufficiency at the saphenofemoral junction.

In order to detect valvular incompetence along the short saphenous system, the popliteal space is palpated. If short saphenous-popliteal vein insufficiency exists, a "bulge" can usually be palpated in the centre of this space. The finger is then run downward along the course of the short saphenous vein in order to detect any further "blow-outs". As a rule, the incompetence in the short saphenous system has its origin at the saphenopopliteal vein junction. Therefore, at the time of surgery it is important to ligate the short saphenous vein flush with the popliteal after all adjacent branches have been divided.

In the vast majority of patients with varicose veins, all venous incompetence originates along the long or

(Continued on page 47)

TB: Successful Mass Treatment at Home may be Possible

Report by Research Group in India

RESULTS of a carefully organized study in tuberculosis control in Madras point to the possibility of successful mass treatment of the disease without sending cases to hospital.

This is a matter of world importance, since many countries have a shortage of tuberculosis beds. India, for example, is estimated to have more than 2,500,000 cases of active tuberculosis and only 23,000 beds to serve them—roughly one bed for every 108 cases.

Although the investigation was carried out among a comparatively small number of patients, it was made under conditions of control as nearly ideal as possible and by highly experienced research workers.

The possibility of the successful application of the findings on a national scale in the countries of South East Asia will depend on discovering how to apply this new knowledge to mass campaigns.

Further investigations, therefore, using methods which would more nearly approach those practicable in mass campaigns are likely to be undertaken.

What follows is a summary of the methods of the Madras project and the results. It is given, as nearly as possible, in the words of the official report just published by the World Health Organization. As many technicalities as possible have been omitted: nevertheless the report cannot be brief (the reign of tuberculosis in this world has not been brief, either).

THE PROJECT AND THE PROBLEM

The project was carried out by the Tuberculosis Chemotherapy Centre, Madras, under the joint auspices of the Indian Council of Medical Research, the Madras State Government, the World Health Organization and the British Medical Research Council.

The Centre was set up in 1956 to investigate problems concerning the planning of mass home treatment of tuberculosis cases by means of drugs.

From among the many problems, it was decided, as a first step, to investigate the relative merits of 12 months of home and sanatorium treatment in

(Continued from page 46)

short saphenous vein. Occasionally there will be an atypical "blow-out". This can be easily detected by simple inspection and palpation of the thigh and leg. It has been our practice to have the patient stand for several minutes so that the veins may assume their greatest prominence. The tip of the index finger is then run along the course of the long and short saphenous veins. Each site of valvular insufficiency is localized and accurately mapped out. It has been my experience that accurate localization of all perforators can be carried out without the addition of any further diagnostic tests.

CONCLUSIONS

The use of simple palpation has been found to be accurate in the detection of sites of valvular incompe-

tence. It has not been necessary to use tourniquet tests or other complicated manoeuvres. The palpation technique is simple to master and takes only a few minutes to carry out. It greatly facilitates diagnostic study in patients with varicose veins. (The Journal of the American Medical Association)

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patients who came for help to routine tuberculosis clinics in Madras City.

The investigators asked themselves how would patients—drawn from a poor section of the community, living in overcrowded conditions on a poor diet, and in whom no special effort had been made to diagnose the disease early—respond when treated at home in comparison with treatment in sanatorium, where the accommodation, diet, rest and nursing care were all much more favourable.

It was decided to use a well-trying and standard form of treatment with a combination of drugs which could be taken by mouth.

In all, 96 patients were given treatment at home and 97 treatment in a sanatorium. Among these patients 82 at home and 81 in sanatorium had had organisms sensitive to both the drugs used, claimed that they had had no previous chemotherapy (despite questioning on several occasions during treatment), and followed the prescribed course of treatment for the full 12 months. These patients form the basis of the main analysis in this report although the entire 193 were followed up at the end of the period.

THE FINDINGS

The most important finding is that, even though the 49 males who took home treatment were rather more sick when the treatment started than the 50 males in the sanatorium, there was little to choose between the progress of both groups over the 12-month period. At the end of the period, the patients in each series who had bacteriologically active disease numbered 10 per cent.

Of the women, the 33 treated at home, who were on average definitely more ill at the start of treatment, made less favourable progress than the 31 in sanatorium but the difference was slight.

It should be noted that the satisfactory findings in the home patients were obtained even though the majority had major lesions, and that a high proportion had unfavourable clinical features when treatment began.

It seems very likely that if it were possible, either as a result of mass radiography, or of propaganda directed at the general public and the medical

profession, to diagnose the disease in its earlier stages, the results of home treatment might be even better than those reported here.

It has generally been considered that a good diet, satisfactory accommodation, adequate rest and nursing care, together make an important contribution to the treatment of tuberculosis and that they represent advantages of sanatorium treatment.

In the present study, the patients treated at home were at a major disadvantage in all these respects but, despite this, they fared remarkably well.

These factors seem to have little influence on the results of home treatment.

DIET SURPRISE

The diet of the patients in the sanatorium was balanced and was shown to be clearly superior to that of the patients having home treatment. Yet, although certain data have still to be analysed in detail, it is already clear that—despite diets which were deficient in important factors, notably the protein content—the patients at home, as a group, made good progress.

On the other hand, the control group in sanatorium, despite having a balanced diet, with an adequate protein content, and making substantial weight gains, derived surprisingly little additional benefit. The role of diet in the attainment of final cure, however, has still to be investigated.

The accommodation of the majority of the home patients, not only before but during treatment, was very unsatisfactory, a high proportion living in conditions of overcrowding. In addition, the home patients, especially the females, had less rest and returned to active work earlier.

These further differences, which are usually regarded as predisposing to an unfavourable response to treatment, also do not appear to have affected the results to any noteworthy extent.

An advantage of treatment in sanatorium is that the administration of medicines can be supervised, and no difficulty in this regard was encouraged in the present study. However, an unexpected problem arose in persuading the home patients to take the medicine regularly, especially once they felt well.

Many checks, notably during surprise visits to the home, were made to counter this difficulty.

Good evidence was obtained that a number of the patients were irregular in taking their medicine and it is concluded that, in any scheme for home treatment depending on the self-administration of medicines, particular emphasis should be laid on the importance of regularity in taking them. Moreover, the present study has shown that mere regularity in attendance at a clinic does not necessarily mean that the patient is co-operating by taking his medicine.

DOMESTIC TROUBLES

In contrast to these disadvantages of treatment at home, two unexpected advantages became apparent during the study.

The first advantage of treatment at home was sociological. Whereas major domestic problems were encountered in eight of the 96 home families, they arose in 20 of the 97 sanatorium families.

Moreover, the difficulties in the families of sanatorium patients were usually more serious than those in the families of patients treated at home.

There is little doubt that the long-term sanatorium treatment of patients in this study proved more disruptive to family life than treatment at home, and this must be considered a big disadvantage of sanatorium treatment in this group.

The second advantage of home treatment concerns the co-operation of the patients. When this study was being planned, the general consensus of expert opinion, both in Europe and India, had been that it would be very difficult to obtain the co-operation of a high proportion of any group of patients in treatment at home, even for as long as three months, but that patients would welcome treatment in sanatorium.

It turned out, however, that only one of the 96 patients given treatment at home, compared with seven of the 97 patients admitted to sanatorium, was lost from treatment during the 12 months.

In four more sanatorium patients there were interruptions in the sanatorium stay, although these did not necessitate their exclusion from the main analysis. It proved much more difficult to persuade

male patients to remain in sanatorium than female patients despite a very active welfare service for patients and their families. This may be considered another disadvantage of sanatorium treatment in this group.

Nevertheless, without the highly-organized domiciliary service which concentrated on persuading patients to attend, especially when there were signs that they were becoming inattentive to treatment, it is certain that in this study a considerable proportion of the home patients would also have stopped treatment.

In view of the poverty of the patients and their families, and the need to keep their co-operation, a limited amount of financial assistance was given to more than half the families since the main earner in the family often had to remain off work for several months, or in sanatorium for a full 12 months.

It seems likely that this assistance contributed to the good co-operation of both series of patients, although it did not succeed in preventing the losses from the sanatorium.

THE CONCLUSIONS

The results of home treatment by drugs, as carried out in this study, approach sufficiently closely to the results of sanatorium treatment to suggest that it is appropriate to treat the majority of patients at home.

Provided that it can be shown that relapse is infrequent and that there is no special risk to contacts if patients are treated at home, and provided that the results of this study would apply in other communities, there may be little to gain from admitting the general run of patients to sanatorium.

There would still remain, of course, a need to admit selected cases for in-patient care. The management of the more seriously ill patients who were treated at home in this study would certainly have been easier in sanatorium, since this would have given greater control over the patient and his treatment.

If home treatment is undertaken on a large scale, it seems essential also to have access to a small number of hospital beds for non-tuberculous conditions. (In the present study it became necessary to admit thirteen (16%) of the home patients to hospital, mostly for short periods only, for the investigation or treatment of such conditions.)

ESSENTIAL NEEDS

It cannot be assumed that any routine tuberculosis clinic would automatically obtain results approaching those reported here. The experience of the Centre suggests that certain minimum facilities are necessary for the satisfactory organization of an efficient home service based on a tuberculosis clinic.

Among these facilities are:

An adequate supply of medication, and alternative medicaments for patients who are not responding satisfactorily.

Enough staff, including a social worker and a public health nurse, to supervise the patients.

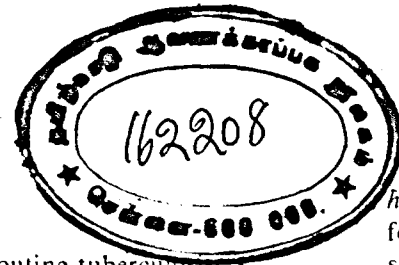
An efficient appointment system, so that it is known when patients have failed to attend.

Adequate transport for the senior clinical staff to visit ill patients, or patients whose co-operation is flagging.

An ambulance for ill patients.

A small number of hospital beds for special or emergency cases.

An organized system of surprise visits to the



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home, to collect specimens of urine of test for the presence of the drug and to check the stocks of medicine.

A laboratory capable of performing, as a minimum requirement, large numbers of reliable smear examinations of sputums for tubercle bacilli.

Financial resources sufficient to give at least limited assistance in cases of particular need since a proportion of patients will be in a destitute condition.

Without adequate facilities and close supervision of the patients, the results of home treatment might well fall far below those reported here.

There was a group of sixteen patients (10%) who remained infective in the later stages of the 12 months' treatment. These should be regarded as a potential public health risk.

It must be kept in mind that the results reported here relate only to a period of one year. A second year of treatment is being given in order to study relapse and its prevention, and these results will be reported later. It is hoped that this, and other studies also in progress, will help in the planning of mass campaigns against tuberculosis.

(Courtesy: W.H.O.)

SOVIET MEDICINE FOR JAPAN

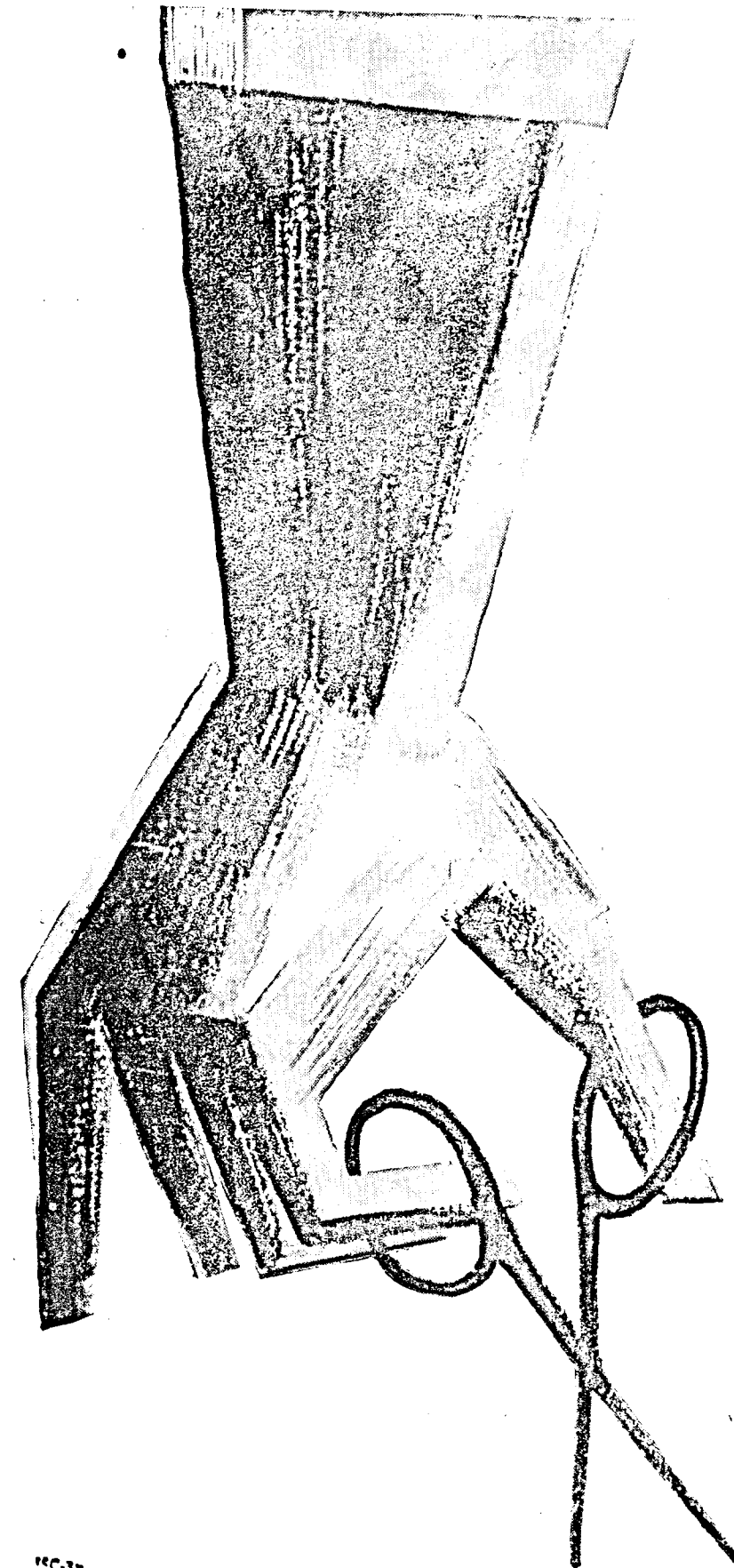
Owing to the fact that the epidemic of infantile paralysis, poliomyelitis, is gaining ground in Japan, the General Council of Japanese Trade Unions, the All-Japan Council for the Protection of Children from Poliomyelitis, and other public organisations in the country, are conducting a campaign of struggle against this severe ailment.

The Soviet trade unions, true to the principle of international proletarian solidarity, warmly responded to the request of the General Council of Japanese Trade Unions, and sent several consignments of Galantamine—a new Soviet medicine against poliomyelitis. The Soviet trade unions

recently sent live vaccine—a prophylactic remedy against poliomyelitis—sufficient for inoculating 100,000 children.

Japanese doctors and the public highly appraise this Soviet remedy against poliomyelitis.

As from July 15 a campaign of inoculation against infantile paralysis will be launched in Japan. In connection with this, Japanese firms have purchased in the USSR through the Ministry of Foreign trade, 10 million doses of the prophylactic vaccine. This large consignment of vaccine was sent to Japan by a specially chartered plane.



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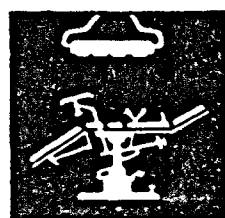
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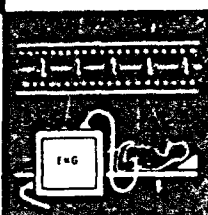
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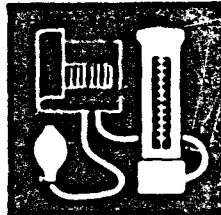
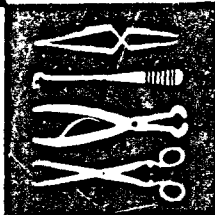
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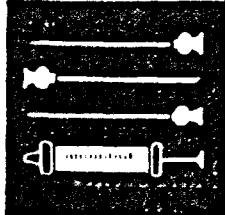
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