

S T R E P T O M Y C I N C E N T R E

It is known that both the World Health Organisation and the UNICEF have established streptomycin centres in Europe; and that the WHO keeps the various centres in contact by sending experts to visit them.

Some of these centres are only just beginning to function, and have only a small number of beds; they represent, in fact, merely a beginning, calculated to encourage the countries concerned to go on with the work. Other centres, fewer in number, have been in existence already for two years; they have acquired wide experience, collected teams of medical officers and research workers, and elaborated methods of work.

Amongst these, mention may be made of Professor Cocchi's centre in Florence and Professor Robert Debre's centre in Paris.

France would be willing to place this latter centre at the disposal of the future International Children's Centre; already, as shown below, many students from both the WHO and the UNICEF have come to this centre for training. It might constitute a new link between the WHO and the International Centre; the purpose of the brief account given below is to demonstrate the advantages of such a link.

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The Streptomycin Centre of "Les Enfants Malades" like the B.C.G. Pilot Station, provides a remarkable pattern for the International Research and Instruction Centres we wish to see established.

Originally intended mainly as a welfare centre for Parisian children, it has now, in response to the requirements of our age, become an important research centre. Though Parisian in origin and purpose, it quickly assumed an international character, in view of:

the fact that children of various nationalities - British, Dutch, German - were treated there;

the fact that foreign workers and students come regularly to work there;

the fact that contact was rapidly established between this centre and other European centres of a similar nature, notably the very fine centre run by Professor C. Cocchi of Florence.

The need for a centre for research on the use of streptomycin amongst children is obvious in view of the fact that this antibiotic has been in use for three years only; and we may safely say that the period of therapeutic experiments is not yet completed.

That this centre can only exist in Europe is evident from examination of the facts.

Whereas it is in the United States that streptomycin is produced; and in the United States that the first very fine experiments showing the advantages of this new drug were made, yet it is in Europe that the use of the drug amongst children is most advanced.

The reason for this is very simple - merely that advanced tuberculosis is much more frequent in Europe than in North America.

The prevalence of tuberculosis in Europe increased still further as a result of the hardships of the war, occupation, under-nourishment, overcrowding and inadequate housing; moreover, there

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were insufficient sanatoriums to accommodate sick deportees on their return to their country, with the result that they infected the children in their entourage.

For all these reasons, tuberculosis has taken a heavy toll in the old Western countries, which suffered most from the war. Thus in France and Italy, hundreds of children suffering from advanced tuberculosis require treatment every year; whereas in the Scandinavian countries, for example, such cases are few and far between.

It is thus unfortunately only too natural that the Streptomycin Research Centre in Paris exercises a great influence. The Streptomycin Centre is housed in the Hôpital des Enfants Malades in Paris; and in the Brevannes Hospital. It is not necessary to give full details of the medical work of the Centre; the main points are as follows:

189 children suffering from tubercular meningitis were treated at the Hôpital des Enfants Malades, Paris, between January and September 1st, 1947.

100 of these children are still alive; 89 died.

The time-factor is fairly important. The earliest cases now date back two years.

Of these 100 children, treatment ceased in 61 cases after varying periods of time and in 22 cases of these, more than a year ago. It therefore seems to have proved that tubercular meningitis in children can be cured by streptomycin; and that the main point now is to discover the reason for the failures.

There are at least three factors which appear to be important:

(1) age is an important factor in the prognosis. Out of 9 infants of less than 1 year old, only two survived; among children of 2 - 16, 50% survived; whilst of those over 16, 2/3 survived.

(2) the second main factor is the condition of the child on being admitted to the hospital.

It appears that a distinction should be made between the cases of immediate death, which can almost invariably be foreseen right from the beginning of the treatment; and cases of death occurring later, after a marked initial improvement, and from the third month onwards. Of the 89 children who died, 49 died immediately, 40 in the later stages of the treatment.

Thus the greatest number of deaths were due to treatment being commenced too late, in the final stages of complete coma.

(3) finally, the way in which the treatment is administered is obviously of the greatest importance. The following figures give a sufficiently clear indication of the effect of initial error and of technical improvements.

Of a first set of 93 cases treated between January and September, 1947, 63 died, whilst 30 survived.

Of a second set of 96 cases treated between September, 1947 and September, 1948, 26 children died; these included 14 cases which died within 6 weeks, and twelve which died later after the fourth month; 70 cases survived.

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During the same period, 85 children were treated for miliary, pulmonary or generalised tuberculosis. Of these 85 cases, 81 were cured.

In view of the novelty of the treatment and its exceptional importance, the Chief of the service and his assistants were quickly joined by a group of research workers who made a study of the various questions raised by this new therapeutic method. The quality of the results obtained provide yet further proof, if such were required, of the value of team work. These results also show that this method is not confined to the Americans but that the old countries of Europe can also adopt it, when necessary, and with the same advantages as obtained by American research workers.

The composition of this team was as follows:

(1) Clinicians whose wide experience enabled them to expand and complete the classical descriptions of advanced tuberculosis; and to describe new aspects and new symptoms of the disease; some of these were of great importance, such as for instance, the modifications which take place in the base of the eye during meningitis; a new evolutive method; and the special complications which help in the understanding of the physiopathology of many other intracranial syndromes and necessitate close neuro-surgical cooperation.

(2) ORL specialists to study tubercular otitis and acoustic neuritis due to streptomycin; and to elaborate accurate audiometric methods for warding off this serious complication.

An ophtalmologist who was responsible for the rediscovery - the discovery was first made by Bouehart in the same hospital 80 years ago - of tubercular chloroidyls; this ophtalmologist is able, by studying the base of the eye, to supply information on intercranial circulation.

(3) Biologists who studied:

- a) the effect of streptomycin on rabbits experimentally infected with tuberculosis;
- b) the problem of the sensitivity of the germ to streptomycin; and the problem of the acquired or more probably natural immunity to streptomycin of certain germs;
- c) the problem of the difference between the bacterioidal and the bacteriostatic dose; this difference is always very marked, and this is a question which has never been fully explained;
- d) the variations of allergy in advanced tuberculosis under the influence of streptomycin.

(4) Anatomo-pathologists who make a systematic study of the lessons of the various tissues both in human beings suffering from tuberculosis and in rabbits experimentally infected.

(5) Chemists who have:

- a) defined the modifications of the cephalo-rachidian fluid, and in particular the sugar variations of their prognostic significance;
- b) studied the Nael variations in patients.

(6) Bio-chemists who have attempted to define the action of the following associated therapeutical substances:

- a) Sulphones
- b) as. salycilie para-amine

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(7) Neuro-surgeons who have elaborated methods of treatment for persistent and complicated types of faulty circulation of the cephalo-rachidian fluid.

(8) Specialists in electro-encephalography who study the graphs of these children.

The tasks enumerated above require widely varying technical qualifications, and the fact that they were completed is due to the collaboration of large numbers of assistants, many of them foreigners who came to spend several months at the Streptomycin Centre. During the course of two years, the following people have worked at the Centre:

Dr. ANDREN	(STOCKHOLM)
Dr. de FONSECA	(PORTUGUESE EAST INDIA)
Dr. GUINAUD DONIOL	(GENEVA)
Dr. HONAR-BAKHCH	(TEHERAN)
Dr. MALHERBE	(BRUSSELS)
Dr. VANDERCAM	(BRUSSELS)
Dr. DELCOUR	(BRUSSELS)
Dr. VAN GOIDSENHOVEN	(BELGIUM)
Dr. WISSLER	(SWITZERLAND)
Dr. WASR HOCKERT	(FINLAND)
Dr. Mrs. BACALOVA	(BULGARIA)
Dr. PATAR	(JUGOSLAVIA)
Dr. PANSINI	(JUGOSLAVIA)
Dr. STEVENS	(LOUVAIN)
Mrs. HINKOVA	(CZECHOSLOVAKIA)
Dr. VAN ZEBEN	(HOLLAND)
Mrs. MAXWELL	(ENGLAND)
Mrs. ROLI	(ITALY)

A few months ago the Streptomycin Centre was enlarged by an annexe at the Bravannes Hospital, where children are kept under observation after the first weeks of their treatment.

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Such, in brief, is the character and work of the Streptomycin Centre in Paris. It can be used with advantage by doctors of many countries for purposes of both practical work and research. We would be glad to place it at the disposal of the Children's International Centre if the big international organs interested in child welfare thought fit.

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