REFRESHER COURSE FOR GENERAL PRACTITIONERS

THE EARLY DIAGNOSIS OF TUBERCULOUS MENINGITIS

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An apparent cure, without sequelae, can be expected in 20 to 30% of cases of tuberculous meningitis treated by streptomycin. There is good reason to believe that those figures could be improved by earlier diagnosis. In 82 cases admitted to the Children's Hospital, Sheffield, in the last two and a half years, the average duration of symptoms before admission was 16 days. Only nine children were admitted within a week of the onset, and 33 within two weeks. Thirty-five children had symptoms for over three weeks before admission, and 17 for more than four weeks.

Early diagnosis can be achieved by consideration of the following factors.

History of Exposure to Tuberculosis

An efficient tuberculosis service should ensure that the family doctor is informed when any of his patients are found to have active tuberculosis, and the service should keep under constant supervision any child who is a contact of such a case. The family doctor, however, has the responsibility, with that contact history in mind, of remembering the possibility of tuberculous meningitis when untoward symptoms occur.

Whenever faced with an ailing child it is essential to take a careful history of possible exposure to tuberculosis. If there is a history of a case of tuberculosis, or of chronic cough in the family, one should determine whether the child has been in contact with that case. It is of great importance to ask whether a child visits or plays in a house in which there is a sufferer from tuberculosis, or whether an infected person, such as a relative, visits the home and so exposes the child to the risk of infection. It will be remembered that there is a special danger of tuberculous meningitis developing within six months of contact.

The source of infection is much more frequently human than bovine, but one should nevertheless ask about the milk supply. It is not enough to demand whether the milk is pasteurized or boiled. Careful questioning may reveal that up to a week ago the child was being given unboiled farm milk.

Known Previous Infection

The knowledge that a child has had a primary tuberculous lesion, particularly in recent months, is of great help in diagnosis. This history is often lacking, but it may be known that the child has a positive tuberculin reaction. Ideally, the family doctor should know the tuberculin reactions of all his child patients: the test is very easily carried out in general practice.* He should certainly know the reaction of any young patient who has subnormal health or who is a possible contact of a case of tuberculosis. A positive tuberculin reaction puts a completely different

complexion on symptoms which in a tuberculin-negative child are usually those of a trivial illness.

Age of Maximum Susceptibility

Tuberculous meningitis occurs at any age, but it is rare in the first six months of life. The greatest incidence is in the second and third years.

Symptoms

The commonest early symptoms are:

1. *Personality Changes.*—The mother notices that the child has become different. A previously good-tempered child becomes cross, peevish, and irritable. Nothing seems to please him. He does not want to speak or to be spoken to. He wants to be left to his own devices, sitting in a corner alone and resenting interference; alternatively he wants to be nursed, only to cry and fuss as soon as he reaches his mother's knee. He is sullen and moody, and never smiles. He loses interest in his toys and pushes them away or sits without playing with them. His sleep is often disturbed.

These symptoms are of gradual onset, irritability being the first: but they are steadily progressive, though an occasional case may show a deceptive remission. The insidious but persistent and progressive nature of the symptoms is of great importance in diagnosis, helping one to distinguish tuberculous meningitis from the common mild illnesses of childhood.

2. *Lassitude, Drowsiness, and Loss of Appetite.*—The child becomes easily tired and wants to lie down. A child who has recently begun to sit, stand, or walk ceases to do so. Lassitude and easy fatigability are usually very early symptoms which later gradually merge into drowsiness. The appetite usually fails early in the disease, but occasionally it remains unaffected in the first few days of the illness.

3. *Vomiting, Headache, and Constipation.*—This is an extremely important triad of early symptoms. It is a bad mistake, however, to think the triad is essential for the diagnosis. Vomiting occurred before admission in 80% of our 82 cases, but it was an initial symptom in only half of these. There was headache in 40% of cases before admission, and it was one of the initial symptoms in 29%. Constipation was one of the first symptoms in only 7% of the series. It is more common later in the illness, partly as a result of anorexia, vomiting, and restricted movement, but it is by no means invariable. In infancy diarrhoea may take the place of constipation, and this symptom occurred in 14% of our cases who were under 2 years of age.

4. *Fits.*—Fits are a common early symptom in infants, but are rare in later childhood. They occurred in 30% of our cases who were under 2 years of age, but in only 2.5% of those aged 2 or over.

Fits should always be regarded as of sufficient importance to necessitate further investigation in hospital. They should never be ascribed to teething. They are commonly febrile convulsions due to an upper respiratory tract

*The skin of the back is thoroughly cleaned with acetone, to remove grease, and allowed to dry. Tuberculin jelly, obtainable from Allen and Hanburys, is applied, sufficient to cover 2 or 3 mm. of skin: it is covered with zinc oxide strapping, which is left for 48 hours and then removed. The result is not read then, but 48 hours later. A positive reaction is shown by erythema and vesiculation. This indicates that at some time the child has been infected with tuberculosis, but it does not in itself mean that there is any active infection.

infection, but the final diagnosis should be left to the specialist in hospital, who is in a position to carry out the necessary investigations.

5. *Cough*.—This occurred in 40% of our cases in which there was no miliary spread.

6. *Loss of Weight*.—This is common, but is often found in the later stages only. It is a grave mistake to think that a diagnosis of tuberculous meningitis can be excluded because there is no evidence of loss of weight.

7. *Fever*.—Fever is by no means invariable, and is rarely marked. In the early stage the temperature is likely to be normal.

8. *Eye Symptoms*.—Ptosis, ocular palsies, and photophobia are rarely found in the early stage. The diagnosis should be established in the majority of cases long before a squint develops. Rolling and staring of the eyes are also late symptoms.

9. *Other Symptoms*.—Twitching, tremors, and neck stiffness are rarely found in the early stages.

The onset of tuberculous meningitis is frequently obscured by the pre-existing symptoms of miliary tuberculosis. The story in these cases is usually one of chronic progressive ill-health, followed by the personality changes, vomiting, and headache indicative of meningeal involvement.

Many of these symptoms are, trivial in themselves and occur in the majority of childhood illnesses. It is extremely common for a child to present irritability, headache, vomiting, and constipation for two or three days and then recover without it becoming possible to attach a name to the illness. The symptoms are often ascribed to teething, influenza, food-poisoning, or constipation. If the symptoms become persistent and progressive the suspicion of more serious disease should be aroused. The significance of the early, vague symptoms is particularly likely to be missed in a child who has recently had some acute infectious disease or a head injury and remains unwell subsequently. It is in these cases that a knowledge of contact with tuberculosis, or of a positive tuberculin reaction, is of such great help in diagnosis. As stated above, symptoms which are usually trivial in a tuberculin-negative child assume great significance in a child, especially a young one, with a positive tuberculin reaction.

Physical Signs

The symptoms are of far greater importance for early diagnosis than physical signs.

1. *The Choroidal Tubercles*.—This is the only physical sign which enables one to make a confident diagnosis of tuberculous meningitis before a lumbar puncture has been performed. The tubercles can be found only in those cases in which there is associated miliary tuberculosis. They are pale, yellowish areas about a quarter of the size of the disk, and are found commonly fairly near the disk. They have been fully described by Illingworth and Wright (1948). They are unlikely to be found without dilating the pupil with 1% homatropine, and in a young child they are unlikely to be seen without proper sedation—e.g., chloral by mouth, 2 gr. (0.13 g.) at 6 months, 4 gr. (0.25 g.) at the age of 2 years.

2. *Meningism*.—Neck stiffness and Kernig's sign are not usually found in infants with early tuberculous meningitis. Even in the older child they are not usually found in the earliest days of the disease. In older children minor degrees of meningism should always be looked for with the child in the sitting position. With one hand under the chin and the other behind the occiput the head is first fully extended, and then fully flexed so that the chin touches the chest. In

slight degrees of meningism the stiffness can be detected only in the last part of this manoeuvre, when the chin is almost touching the chest. The child nearly always feels pain in the back during the latter part of this movement, and in the mildest cases of meningism this pain may be the only sign of meningeal involvement. The test is fallacious if performed immediately after lumbar puncture.

3. *Signs of Increased Intracranial Pressure*.—An experienced finger may detect bulging of the fontanelle in an infant, but there may be no detectable bulging till late in the disease. Early papilloedema can sometimes be found on ophthalmoscopic examination.

4. *Temperature, Pulse, and Respiration*.—They do not help much in the diagnosis. The temperature is frequently normal in the early stage.

5. *Other Signs*.—Ptosis and ocular palsies are usually late signs. The *tache cérébrale*, or dermographism, and hollowing of the abdomen are of no value in diagnosis.

None of these findings, except the choroidal tubercles, are pathognomonic of tuberculous infection. Meningism and signs of increased intracranial pressure occur in many other conditions, and these physical signs can be evaluated only against the background of the symptoms and other features already mentioned.

Special Investigations

1. *Lumbar Puncture*.—In all cases the diagnosis is finally established by lumbar puncture. This procedure should not, I think, be performed by the general practitioner but should be done in hospital, where the fluid obtained can be cultured at once and where there are facilities for immediate microscopy of a stained specimen for tuberculosis and other organisms. A lumbar puncture must be done when meningitis is suspected. It is an extremely bad practice to give chemotherapeutic drugs in the home to a child with meningism. If it is due to tuberculosis, valuable time will be lost, because penicillin and sulphonamides will have no effect on the condition. If streptomycin became more generally available it would be disastrous to give it in the home for suspected tuberculous meningitis without proving the diagnosis. It is vital to make a definite diagnosis before treatment is begun, as therapy must be continued for at least four to six months and the drug may have serious toxic effects. The treatment requires expert specialist supervision and can be adequately given only in a hospital equipped for the purpose.

If tuberculous meningitis is suspected, therefore, the child should be sent to hospital without waste of time. If lumbar puncture disproves the diagnosis no damage has been done. Grave harm has been done, however, if a child with tuberculous meningitis is observed for a week or two in the home and sent to hospital for investigation and treatment only when he has lapsed into coma or developed other signs of the last stage of the disease.

2. *The Tuberculin Test*.—Reliance must not be placed on the tuberculin patch or jelly test performed during the course of meningitis, because the allergic response to tuberculin is commonly reduced in these cases so that a negative result is obtained. A properly performed Mantoux test, using fresh material and a 1 in 100 solution if the 1 in 1,000 is negative, is positive in over 90% of cases, but not all practitioners have the necessary equipment or experience to perform the test. A previous history of a positive tuberculin reaction is therefore of greater value.

3. *The Blood Sedimentation Rates and White Cell Counts*.—These do not help, because they may be normal in cases of tuberculous meningitis.

4. *X Ray of Chest*.—An x ray of the chest may be normal, or may show miliary tuberculosis or a primary focus. A diagnosis of tuberculous meningitis certainly cannot be excluded because of a recent negative x-ray report.

Illustrative Case Histories

The following case histories show how a case should be diagnosed and how avoidable delays occur in diagnosis.

Case 1.—An 11-months-old baby of a tuberculous father was seen at frequent intervals in a baby clinic because of the contact history. He was known to be tuberculin positive. At one visit he was found to have lost weight for the first time, but there had been no symptoms until the night before his visit, when he had vomited once. A lumbar puncture was done immediately and the tubercle bacillus was found in the cerebrospinal fluid. Streptomycin treatment was begun less than 24 hours after the first symptom, and now, several months later, he is very well and has every prospect of a complete cure.

Case 2.—A 13-months-old daughter of a tuberculous father with positive sputum became ill three weeks before admission to hospital. She went off her food, refused to stand up, and wanted to be nursed all day. The family doctor thought that she was teething. A week later she developed a cough and a squint, but the diagnosis of teething was maintained. Four days before admission she became unconscious and was finally sent to hospital as a case of bronchopneumonia. Tuberculous meningitis was diagnosed immediately, but she died eight days after admission in spite of streptomycin treatment.

Case 3.—A girl of 12 complained of headache for four weeks following a head injury. Ten days before admission to hospital the family doctor diagnosed meningitis and treated her with sulphonamides, without examination of the cerebrospinal fluid. She failed to improve and was sent to hospital. The cerebrospinal fluid was examined, but no organism was isolated, and sulphonamide treatment was continued. The girl continued to deteriorate, with the result that the diagnosis was reconsidered and she was transferred to a special centre as a case of tuberculous meningitis. Ten valuable days were therefore lost after the initial diagnosis of meningitis before streptomycin could be given.

Conclusion

The general practitioner cannot be expected to make a final diagnosis of tuberculous meningitis. What he can and should do is to bear the diagnosis constantly in mind when any child who is a known or possible contact of tuberculosis, or who is known to have a positive tuberculin reaction, develops untoward symptoms for which no other definite cause can be found: or when any child becomes irritable and difficult, develops a headache, and begins to vomit and these symptoms are persistent and progressive. The fully developed picture usually evolves slowly, so that in the early stage only a few of the characteristic symptoms are present. Perhaps the most important of these are irritability, lassitude, and loss of appetite in a previously good-tempered, well child. Vomiting, headaches, and constipation may not occur for a week or more after the onset. Meningism is not to be expected in the infant, and may not be found until later in the older child. Squint and other ocular signs are usually later manifestations. A careful evaluation of the symptoms and their persistence and progressiveness should enable one to avoid the common mistake of diagnosing teething, influenza, or food poisoning. The diagnosis can be finally established only by lumbar puncture. When the family doctor has good reason to suspect the diagnosis he should send the child to hospital for investigation without delay, so that if the diagnosis is confirmed the patient may have the great advantage of early treatment.

REFERENCE

Illingworth, R. S., and Wright T. (1948). *British Medical Journal*, 2, 365.

Nova et Vetera

GALEN ON THE CHRISTIAN AND JEWISH RELIGIONS

Galen on Jews and Christians. By R. Walzer. (Pp. 101. 10s. 6d. net.) London: Oxford University Press. 1949.

The name of Galen (A.D. 130–200)—“Prince of Physicians,” as he was known for fifteen centuries—was attached legitimately to an immense number of works and illegitimately to many others. Something of the order of a hundred works that were really by him have survived in his original Greek. Some, lost in that language, have come down in Arabic translations. Of others there are but fragments or references in the one language or the other. For long after his death “his works, like the monuments of Greek philosophy and science in general, had been read only in pagan schools and under pagan teachers. But when the teaching of philosophy and medicine was made part of a Christian syllabus of higher education the preservation of Galen, who had meanwhile become a minor classic, was assured. Since the Arabs of the ninth century adhered almost completely to this syllabus, it is not surprising that they knew medical and philosophical works of Galen which disappeared in the late Byzantine period.”

This very learned little work by Dr. Walzer presents Galen in an unusual aspect. It is well known that there are not many references to the Christian and Jewish religions by pagan Greek or Latin writers. By them the two religions are usually confused and both are commonly treated with scorn. Galen is an exception. Instead of treating Judaism and Christianity as idle superstitions he at least gives his reasons for rejecting their point of view. Armed with unusually recondite learning and with quite extraordinary skill and industry, Dr. Walzer, Lecturer in Mediaeval Philosophy at Oxford, has collected these passages in Galen's writings and placed them in their setting with their original background. In doing so he has shed new light on the position of these religions in the empire in the great age of the Antonine Emperors.

Galen regarded himself as a free philosopher, thinking at large and following reason wheresoever it should lead. In fact it led him to a fantastically dogmatic view of the nature of the human spirit and the structure of the human body which at times prevented him from recording accurately the evidence of his own senses. With these errors Dr. Walzer is, quite rightly, unconcerned. He seeks to expound Galen's viewpoint and is not occupied with either his great scientific achievements or his not inconsiderable scientific errors. But what will specially interest the medical reader is that of the six references to these religions in the works of Galen four occur in medical writings. Galen, as a “philosopher” who will swear by the word of no man, objects to the attitude that will bow automatically to the voice of authority—any authority. Writing about A.D. 165 in a work on anatomy he would “compare those who practise medicine without scientific knowledge to Moses, who framed laws for the Jews, since it is his method in his books to write without offering proofs: ‘God commanded,’ ‘God spake.’” Or again, about A.D. 180 in his work *On the Differences of Pulses*: “One might more easily teach novelties to the followers of Moses and of Christ than to the physicians and philosophers who cling fast to their schools.” How astonished the writer of such phrases would be at hearing that his anatomical and clinical findings, often demonstrably false even to the unaided senses, would remain for a millennium and a half as a rigid standard to which all observations must conform. Dr. Walzer's work illustrates a most unexpected by-way of medicine, and he deserves great credit for the admirable way in which he has shown that what may seem a very obscure issue is in fact not without bearing on our own ways of thinking.

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