Symposium on Chest Diseases in Children (continued)

PULMONARY TUBERCULOSIS IN CHILDREN

Panel Discussion

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Case 1: A Positive Tuberculin Reaction

DR. PHILIP ZORAB, M.D., M.R.C.P. (*Chief Medical Assistant, Brompton Hospital*): This is the X-ray of a child which I think is absolutely normal. If it isn't, we have misread it. He is a boy of 11 who has a strongly positive tuberculin test, the Heaf being 1 mm., grade 3. If this had been discovered, as many of them are, on routine testing at school I would like to ask the Panel how they would manage this case; how often would they see him, whether they would treat him and so on.

DR. DAVIES: Do we know whether this child ever had a tuberculin test before?

DR. ZORAB: No, we have no previous information.

DR. DAVIES: And it was recorded as a strongly positive Heaf?

DR. ZORAB: Yes, so that if you did it at 1/1,000 by another method you would have had a large weal.

DR. DAVIES: You think it would correspond to the M.R.C. classification (1956) of more than 15 mm. of induration to the three tuberculin units?

DR. ZORAB: Yes.

DR. DAVIES: So we have a strongly positive tuberculin reaction in a symptomless boy of 11. Dr. Kendig, what would you do with this boy?

DR. KENDIG: I think the general pattern in America is this—if we had a child under three who had a positive tuberculin reaction with no other evidence of tuberculous disease we would give isoniazid for a full year—probably between 10 and 20 mg./kg. per day. If the child were approaching puberty, as this one is, I would put it in the same category—provided we did not know when the last tuberculin test was done. If the

tuberculin test had been negative last year and was positive this year, no matter what the age of the child we would treat in the same fashion. If the age were between 5 and 10 and the same thing was true I think the child must be individualized, depending on its general condition, whether or not there is a diseased adult at home and so on. In our country there is more of a tendency to treat the child than not.

DR. DAVIES: There are two issues here—one, would we treat the child, the other, with what? Perhaps we can take the first—do we think we should treat it? Dr. Lynne Reid, have you any comments from your point of view?

DR. LYNNE REID: I would agree with everything that Dr. Kendig has said. I think we should call in Dr. Macpherson.

DR. DAVIES: That is what we have done and I shall ask her to speak later. What do you think Dr. Seal?

DR. SEAL: I would call this a difficult problem; certainly if I decided to treat, I think there is strong evidence that we should treat with two major drugs and I would be against INAH alone. I think one thing one should think of is: if this is a strong reaction the chances are that it is recent and there is evidence that disease is more likely to occur in this group. Just a plain film showing nothing I would regard as insufficient evidence that there is, in fact, nothing there, and I think this child should be looked at more carefully; perhaps a lateral tomograph may show something which the plain film doesn't because there are some silent areas in that plain film.

DR. DAVIES: Well, there isn't any doubt that the Medical Research Council showed that children of a comparable age-level, if they had strongly

positive tuberculin reactions, were four times as likely in the next three years to develop adult-type tuberculosis as those with less strongly positive reactions so that this is a select group. Dr. Macpherson, would you treat this child in the same way as a child whom you knew had converted recently or would you be prepared to observe? Do you think a strongly positive reaction gives some evidence of recent infection?

DR. MARGARET MACPHERSON, M.D., F.R.C.P. (*Physician, Child Contact Clinic, Brompton Hospital*): Yes, I think it is probably evidence of recent infection. Before starting treatment I would like to know what the actual Mantoux was, both 1/10,000 and 1/1,000, so that at least we would have a slightly more definite record before starting treatment. One does occasionally find difficult Heaf tests to read and one can be much more sure of the intradermal test. Another thing I think which would weigh in this case was whether there was a history of known contact, especially in the family.

DR. ZORAB: I will just give you briefly the family history. The father, aged 60, is well. His brother living with the family has active tuberculosis with a positive sputum. This is the record of the seven brothers and sisters, his nephews and nieces: all have strongly positive Heaf tests, three have active pulmonary tuberculosis and one, aged 4, with a positive Heaf test has also been put on treatment. So there are four other members of the family living in the same house who have been infected by the same man. Perhaps this might influence one as to whether we should treat this child or not.

DR. MACPHERSON: Without a doubt I would treat this child, and with PAS and isoniazid.

DR. DAVIES: Dr. Kendig, did the U.S. Public Health Service trial of 1957 cover this age-group?

DR. KENDIG: It covered all age-groups—they had no limit, but as the children grew older there was a smaller number involved, and the only thing we can say from that study and from a few other things done after that time is that isoniazid alone, in a very small dose (5 mg./kg.) is effective in children under 3 years old in reducing the incidence of tuberculous complications something like 15 times. Even when complications did occur the severity was much less than in those untreated. Now that applied to the ones in the young age-groups; over that age we are unable to draw any particular conclusions and it is planned at present that some of these children will be retreated at the time of puberty or early adolescence to determine whether or not retreatment will be effective in reducing the incidence of so-called reinfection type tuberculosis at that age. We did not use, in this study, any other drug than isoniazid and as

far as we could tell this was a reasonably effective approach. There is of course always the question of whether or not isoniazid-resistance will develop.

DR. DAVIES: That was one of the things that worried us—that although there was only a small number of patients who had been treated who developed overt tuberculous disease we don't know whether they developed it with resistant bacilli. Another point is whether, as in adult disease, using two drugs instead of one might make protection more complete in fact.

DR. KENDIG: Well, they are not on the same basis, but as some of the children did develop tuberculous disease, two groups—one is the Committee on Chest Diseases in Children of the American Academy of Pediatrics and the other is the Committee on Respiratory Diseases in Childhood of the American Thoracic Society—reached the same conclusion as the one I have just given you, except that we feel that the dosage should be greater, and we now feel that we should give between 10 and 20 mg. of isoniazid per kg. a day for a full year, but we do *not* feel, on the basis of what we have learned and the evidence in hand, that it is necessary to give these children PAS because there has been no tendency at all as far as we could tell to develop isoniazid-resistant organisms in this age-group.

DR. DAVIES: We will now go on to a case of Dr. Yudkin's.

Case 2—A Tuberculous Mediastinal Gland

DR. YUDKIN, Ph.D., M.R.C.P., D.C.H. (*Pædiatrician, Whittington Hospital*): This little girl, aged 2, was admitted in December 1960, with noisy breathing and a spasmodic cough; she was found to have tuberculosis and went on for a long time with a wheeze, obstructed breathing and a large mass of mediastinal glands (Fig. 1). She was treated with several drugs but ran a pyrexia for a long time, and the question was raised repeatedly: do we recommend surgical intervention in a situation like this?

DR. DAVIES: This is quite clear-cut: a child of 2 with enlarged mediastinal glands, presumably due to tuberculosis, because the child had a strongly positive tuberculin reaction; it has two special problems—one is the continuing pyrexia and the other is a wheeze confined to the right side of the chest—or was it generalized?

DR. YUDKIN: Yes, it was generalized.

DR. DAVIES: Before hearing anyone else I would like to ask Dr. Seal about this.

DR. SEAL: Well I'll give the party line on this: the next step would be to discover whether or not there was important obstruction to the airways, and I think in Sully Hospital certainly this child would have a bronchogram and if that wheeze

FIG. 1.—Case 2.

has the significance we think it has then there will be evidence of encroachment upon the airway, and obstructive emphysema is a distinct possibility in the near future. Also we may find that the trachea itself may be involved and I think there are certain sinister possibilities that haven't yet started to occur in this case. First there are cases that die of asphyxia due to caseous nodes obstructing the larynx. Secondly, perforation with aspiration of caseous material into part of the lung is a possibility, and however well that may eventually resolve we feel that in many cases permanent lung damage results, and therefore we would consider in this case there was a definite indication for a thoracotomy and incision of the enlarged caseous nodes, not their dissection and removal but incision and evacuation with a spoon. If a bronchial perforation were found, which would be quite possible in this case, it would be closed and we would therefore be placing an operation with no mortality, and with the morbidity only of the thoracotomy wound, in the place of the possibility, slight though it may be, of death from asphyxia and the development of a large segmental lesion with subsequent impairment of lung function. Therefore we would consider in this case it was a good swap, more rational in fact than incising lymph nodes in the neck to prevent the development of an unsightly scar.

DR. DAVIES: Could I ask you one or two questions? First of all, why did you choose a

bronchogram rather than, say, tomographs or bronchoscopy?

DR. SEAL: Well probably all three would be done, but a bronchogram would delineate very nicely the encroachment on the main bronchus or trachea.

DR. DAVIES: You think you can demonstrate the impending perforation, or whatever there is, in the trachea on the bronchogram?

DR. SEAL: Yes; tomography would do that equally well of course.

DR. YUDKIN: Would you do a bronchogram at the same time as you would do a bronchoscopy?

DR. SEAL: Not in children. I think you need an anaesthetic, and bronchograms after bronchoscopy have proved unsatisfactory.

DR. DAVIES: Do you think a bronchoscopy, though, should be done?

DR. SEAL: Well if you regard it as a therapeutic bronchoscopy I think that it is not a very certain way of dealing with the obstruction. I think that it has so proved in the main—some people are better at this than others—in some hands bronchoscopy would be done and a considerable amount of material would be removed. The child may do very well with that procedure alone. The opinion at Sully is that bronchoscopy is a very ineffective way of dealing with the perforating caseous nodes.

DR. DAVIES: Supposing this child hadn't got a wheeze—would you still take the same line?

DR. SEAL: Yes, I would.

DR. DAVIES: You mean you would investigate with a bronchogram: you wouldn't advocate thoracotomy without further investigation?

DR. SEAL: You would need to show that sinister complications were imminent.

DR. DAVIES: Well, the big mass of glands you would regard as needing full investigation with a possibility of thoracotomy? And the wheeze makes this virtually certain?

DR. SEAL: The wheeze makes it seem that your investigations will show you encroachment on bronchi. The purpose of investigation is to delineate this more precisely, so that the surgeon when he does his thoracotomy knows, for instance, that it is a lymph node in the region of the azygos vein that is involving both trachea and right upper lobe bronchus, so that he is furnished with information and is not doing a blind thoracotomy, and that's one of the reasons for investigating these people fully.

DR. LYNNE REID: Yes, there are two aspects of this. One thing is that though you have a wheeze you haven't any evidence of either collapse or emphysema, so you've got no evidence in this child that the presence of the wheeze is involved with upset of ventilation of any part of the lung.

I think that bronchoscopy certainly should be done because you may in fact get away with aspirating material and avoid quite a good deal of other investigation and treatment. However, one should ask Dr. Kerdig as a clinician whether he feels the wheeze *per se* means anything. From the pathologist's point of view I don't think we have any evidence of any upset functionally. The presence of caseous nodes may subside with chemotherapy. How long has the patient had the temperature?

DR. YUDKIN: She came in with it at the beginning of December and was still running it in April.

DR. LYNNE REID: Dr. Seal mentioned the sinister complications but this is a sick child who is going to be in hospital—I wonder whether these complications are as serious in a child who is going to be in hospital for some months, possibly years? I should say this is a case to watch.

DR. KENDIG: The main observation I would like to make is that if we have a child which has persistent fever and we don't have any more symptoms and signs than these—any child in fact with fever who apparently has primary tuberculosis—we'd better investigate it to be sure it hasn't got something else like tuberculous meningitis which sometimes drags a little bit in the partially treated state. Now as far as the actual impingement of the enlarged nodes on the bronchi—we in the U.S.A. are way behind you there, because we are much more conservative in our approach and I don't know anyone at home who is doing thoracotomies at the moment, apart from a few. Our tendency would be to give the child a good dose of isoniazid and PAS—20 mg./kg. a day of the first and 200 mg./kg. of the second—and then give corticosteroids in addition. There has been some suggestion that the use of steroids for a reasonable period of time in conjunction with the antimicrobial agents might be of some value in this particular instance, and at the present time we have a co-operative study under way in a number of institutions to determine whether or not this is of value. Certainly I would say: first we should investigate as to whether there is another cause of the fever, second, the child should have a bronchoscopic examination, and then the child should be treated with INAH and PAS for a full year, with corticosteroids for probably two or three months in a gradually decreasing dose until after it is apparently controlled. We get to surgery, if at all, if there is an involved lobe which is bronchiectatic or atelactatic over a period of time.

DR. SEAL: One thing I would like to point out—there is very little evidence that anti-tuberculous drugs will influence that lymph node one iota in the short term, and that in one year of effective chemotherapy that lymph node will be influenced

as would be a caseous lesion in the parenchyma. It will certainly influence it bacteriologically, so we might see tubercle bacilli but we won't grow them. But we know that giving effective anti-tuberculous drugs to that lymph node will not influence its inevitable natural history; it might even get bigger on anti-tuberculous drugs, and this phenomenon I am sure Dr. Macpherson has seen herself on many occasions. It certainly won't prevent it perforating the bronchus and it certainly won't prevent the development of a segmental lesion if it does perforate. Steroids might, but anti-tuberculous drugs won't.

DR. KENDIG: I quite agree with that. I don't think that the anti-tuberculous drugs do—we use them to control the infection and we use the steroids with the idea of trying to control the inflammatory reaction and probably to cause reduction in the size of the node. I quite agree that the anti-tuberculous drugs will not change the course of events in the node itself.

DR. DAVIES: Dr. Macpherson, we showed you this case and I think your views were roughly similar about the need for full investigation of the possibility of thoracotomy.

DR. MACPHERSON: Yes, I remember being told about this case and seeing the pictures. I think what influenced me was that the child had had its wheeze for a very long time and it hadn't really altered very much. In my experience you may get wheeze over a short period of time and then presumably the gland mass gets smaller and that child may get well under observation without having a thoracotomy, but if the wheeze persists over a period of months under supervision—and this child has had it for a very long time—not controlled by any treatment then I certainly think the child should have a bronchoscopy to see what the bronchi were like. If there is evidence of a main bronchus being eroded—or the trachea—then I think the child should have a thoracotomy. One should keep it under observation in hospital for a certain length of time, so avoiding any tragedy happening, but the time comes when you have got to face the question and take a decision.

DR. DAVIES: The only comment I have got to make is that whatever one feels about the need for surgery in children with segmental lesions, in those cases, to some extent, the damage is already done. Here one knows there is a big risk of a segmental lesion developing and I was in favour of Dr. Seal's approach—that is, preventive rather than curative.

DR. SEAL: If you are not sure, I think exactly the same comments would apply to a case of obstructive emphysema of, say, middle and lower lobes as would apply to this case.

DR. DAVIES: It seems possible to prevent

pulmonary involvement here and I must say I did advocate surgical intervention.

DR. YUDKIN: I have always been very difficult to persuade of the need for surgical intervention. Dr. Davies worked very hard and got Dr. Macpherson to help him. Finally we agreed to have the patient transferred, but there was an epidemic of measles in the ward so she stayed with us for three months because she couldn't go, and got better. For two months she went on having fever and wheezing and then the fever did stop for two and a half months, which is the present position now. Not only did the temperature come down and the wheeze stop but she herself got much better, and she began to put on weight. She eventually went home and is now under the care of the Chest Clinic.

DR. SEAL: I will say that what I think happened, and that is the lymph node *did* perforate—she is one of the fortunate ones who perforated at the junction of the upper-lobe bronchus and the trachea and she has coughed it up. This sort of case is a frequent problem and oddly enough one of our surgeons at Sully would like to demonstrate rather more than just a slight wheeze and he might be inclined to wait, while one of our physicians would be clamouring for a surgeon to do a thoracotomy: every now and again the opposite to what has happened here occurs when there has been some delay. So this sort of thing can happen either way.

DR. LYNNE REID: Can you tell us what happened at bronchoscopy?

DR. YUDKIN: It wasn't done. The idea was that she should be done where there was a thoracic surgeon experienced in the surgery of children available—we have seen one or two children whose respiration became obstructed during the performance of bronchoscopy and who needed thoracotomy, in one case even in the X-ray Department, to remove obstruction in the trachea.

QUESTIONER: Could I ask Dr. Seal if there has been any operative mortality in these children? Are you dealing with a risk which is one in a hundred, one in a thousand . . . ?

DR. SEAL: The position at the moment is that as you know this work was done at Sully against a certain amount of opposition and there was a mortality of two in the first hundred; now 150 have been done with much more rigid indications and there has been no mortality. I think the mortality was really a matter of surgical technique in the very early days when they did not appreciate that all that was required was incision of the node and scooping out within the capsule, making no attempt whatever to enucleate the node, which is extremely dangerous. The other death was an

FIG. 2.—Case 2.

anæsthetic one which was due to the disintegration of the endotracheal tube. Now one can say that if one appreciates the surgical techniques involved there is no mortality.

DR. LYNNE REID: Could we ask about morbidity?

DR. SEAL: It depends what you mean by morbidity—there is the morbidity of thoracotomy. It is done under anti-tuberculous drug cover and tuberculous empyemata are unknown, the secret being drugs plus expansion of the lung immediately in the post-operative period. Attention must be paid to that. I would say there is no morbidity other than that of a thoracotomy—no post-operative collapse, broncho-pleural fistulæ or empyemata.

DR. DAVIES: This child did in fact develop a segmental lesion of the middle lobe (Fig. 2).

DR. SEAL: The middle lobe is written off isn't it?

DR. DAVIES: This is a good moment to introduce Dr. Zorab's next case, illustrating the management of segmental lesions.

Case 3—A Segmental Lesion

DR. ZORAB: The interest in this case lies in the fact that it is similar to the last but takes the story a bit further. This is a child, V.C., age 3 months, who was examined because she was in contact with her mother who had tuberculosis with a positive

sputum. That was in July 1953. She was found to be strongly tuberculin positive and her chest X-ray showed large mediastinal glands with partial collapse of the right upper lobe and commencing obstructive emphysema of the right lower lobe (Fig. 3).

FIG. 3.—Case 3.

DR. DAVIES: Is that appearance due to the right lower lobe compressing the right upper lobe?

DR. ZORAB: Yes, I am sure that is right. The child was admitted under Dr. Macpherson. At that time she was not bronchoscoped but was managed conservatively on isoniazid and PAS. In November 1953, she was seen to have collapse of the right middle lobe and basal segments of the right lower lobe (Fig. 4).

DR. DAVIES: Can I stop you there? By what radiological criteria do you diagnose collapse? From where I am it is difficult to see any reduction of volume.

DR. ZORAB: The lateral film shows that the fissure is low.

DR. DAVIES: A stage of collapse—consolidation?

DR. ZORAB: In December 1953, the child was bronchoscoped; this showed an oedematous carina which was much widened, as from glands at the bifurcation. The right and left main bronchi were both seriously reduced in diameter by pressure from without, but there was no ulceration or granulation tissue seen, which is an interesting point. The next film taken two weeks later shows the position at its worst. There is marked obstructive emphysema of the right lower lobe—the mediastinum is across and the lateral film showed that the right middle lobe was almost completely collapsed (Fig. 5).

FIG. 4.—Case 3.

FIG. 5.—Case 3.

DR. DAVIES: I think we can agree on that.

DR. ZORAB: No other measures were taken. The child gradually improved and after a few months in the country in a medical institution had no further trouble. This is the bronchogram done in 1954, ten months later; it just shows the right middle lobe bronchus, which had been compressed to be patent but not absolutely normal; there is just slight crowding of the bronchi (Fig. 6).

DR. DAVIES: Do you think that the little notch in the bronchogram is the site of the perforation in the right main bronchus?

DR. ZORAB: Yes, I do.

FIG. 6.—Case 3.

DR. DAVIES: Dr. Kendig, do we understand that for practical purposes the management of these problems in the States is entirely conservative; that surgery is not really planned as a possibility; in other words that given a child with gross obstructive emphysema as here, you would not consider thoracotomy?

DR. KENDIG: No, as far as I know there is nobody in the States doing surgery to the extent that you are doing here and I think it would take a marked degree of involvement before anyone would consider it. I think this case, where there may be minimal involvement of the right middle lobe as a terminal result, is a reason for thinking that probably many of these children may be operated on when it isn't absolutely necessary.

DR. SEAL: In Sully, we would certainly have performed a thoracotomy at the time of obstructive emphysema; though your child belongs to the group that fare relatively well untreated, there is much residual lung damage. I could show a completely destroyed bronchiectatic lung from a child presenting with obstructive emphysema and treated conservatively. Even if you have strong objections to thoracotomy and evacuation of nodes in these children and prefer to end up with scarred pulmonary parenchyma rather than run the small risks of thoracotomy, I fail to understand why no attempt was made at therapeutic bronchoscopy—the bronchoscopist is sometimes able to suck out much of the caseous material. Another cause of obstructive emphysema is inhalation of a foreign

body and I dare say many children may eventually survive and end up apparently fit untreated, but in such circumstances I am sure you would rush to phone your surgical colleagues. Surely this child at one stage *had* a foreign body in the bronchus—a chunk of caseous material containing viable tubercle bacilli. I feel a bronchoscopy is the least that should have been done. We would have completely evacuated the offending nodes in the rational way—from within—while the pulmonary parenchyma was not irreversibly damaged. In this child there is now permanently damaged lung.

DR. ZORAB: This case is an example of the course obstructive emphysema may take without surgical intervention.

DR. SEAL: You have shown us one of the 50% that do well.

DR. LYNNE REID: Certain of the changes associated with these primary tuberculous nodes can perhaps be antecedent to permanent lung damage but what I would say is that even if the surgeon had gone in at the time when you had the obstructive emphysema and collapse you've already had much of the damage. We'll accept that on the one hand you may get a pure massive collapse which can re-expand and leave you with a normal lobe, because in spite of what some people have said a massively collapsed lobe is visible on an X-ray; any lobe has got enough substance in its bronchi, its blood vessels and compressed alveoli to show as a thin sliver of lung such as the thin middle lobe we have just seen. On the other hand some of the 'white' segments or lobes are in fact a mixture and in those cases, as Dr. Seal has said, you have aspirated caseous material; commonly when you get aspiration you also get a certain amount of consolidation so that those lobes tend to be not quite as small as the one we've seen in this case. The tubercle bacillus itself may cause caseation or it is quite possible for there to be an almost abacterial non-caseating pneumonia. Some of these may resolve but an important sequelæ of some of them is a patchy bronchiolitis obliterans or bronchiolitis deformans with patchy peribronchiolar fibrosis in the periphery.

So I think there is a possibility that even if the X-ray clears you are not in fact left with a perfectly normal lobe. How much you are going to prevent that by operating I don't think we know; another thing I would say is that after all the lung has got a 'space-occupying' function: I think that to leave lobes that even look fairly good radiologically is not a bad form of treatment at this stage of the proceedings, even if you do have to go in later on in a small percentage.

DR. DAVIES: Dr. Macpherson, would you like to

have the last word, to say what you feel about this?

DR. MACPHERSON: Dr. Seal has rather accused us of picking out the 50% who do well, but I wonder if he considers that the fact that this child on bronchoscopy had no evidence of a bronchial lesion, in the main bronchi at least, is significant. Mightn't it be that this child had a large carinal gland and no evidence of ulceration?

DR. SEAL: Yes. I think that I have seen examples of pressure by two lymph nodes on a middle-lobe bronchus without perforation causing compression of that bronchus with the subsequent development of ectasia of the distal bronchi, but I have had to search very hard to find an example to photograph. When we have seen these segmental lesions at the time when thoracotomies were performed we have found an enlarged node was associated with the segmental lesion. All we can say is that we never found, not once, simple airlessness of a lobe: we always found collapse-consolidation, and what's more we always found perforation of the expected bronchus—if it was a lobar lesion there was perforation of the lobar bronchus, if it was left-upper-lobe-less-lingula the perforation was distal to the origin of the lingular bronchi and similarly if we saw such a lesion in the middle-lobe bronchus there was always perforation. In cases of obstructive emphysema also, with a single exception, the offending node had perforated the bronchus. In this case I think the bronchoscopist has missed the perforation—either it wasn't done at the appropriate time or it was beyond endoscopic vision. I think the bronchograms show here that there has been perforation of the right main bronchus and similarly I think there is now some stenosis of the middle-lobe bronchus, and I think perforation must have occurred, but I don't think your bronchoscopist saw it.

DR. LYNNE REID: Not all of those nodes perforate through—I know that quite a percentage of them may—but I don't feel they all do.

DR. MACPHERSON: There may be sudden perforation and aspiration of caseous material and the child may die, but that's into a *main* bronchus, that's why I purposely said there's been no perforation of a main bronchus. One can't tell whether there's been a perforation further on in many cases—but the real risk is when you get the trachea or a main bronchus perforated.

DR. DAVIES: The child has been left without residual calcification, and I personally think that that's probably evidence of perforation: the caseous contents of the gland must have been coughed up. If caseous material had been left behind I can't conceive that calcification wouldn't be a residuum.

DR. SEAL: Can I ask Dr. Macpherson a question? If she knew, at the time of that first X-ray when there was obstructive emphysema, that a surgeon could do a thoracotomy and evacuate the caseous contents safely, whether it had perforated or not, leaving the child now fit, without a middle-lobe lesion, with nothing more than a thoracotomy scar, would she swap that for the present situation?

DR. MACPHERSON: I think I would. I certainly would have done in 1953, with glands at the carina.

DR. MOORE: I would say that this child is now seen regularly at Southampton and is very fit and very happy—I won't say pleased not to have the scar, but she's very happy as she is!

Case 4—Tuberculous Pericarditis

DR. DAVIES: I will now ask Dr. Yudkin to present the next case, Paul G.

DR. YUDKIN: Paul G. is 5½ years old. He was a contact of a patient who was already under the Chest Clinic and who had been living in the same house; in March he was found to have a slightly positive Heaf test, and in April he was seen again when he seemed well but had lost a few pounds in weight. In May he was seen again: he had not been taken to his doctor but when seen at the Clinic he was said not to have been well for the past two days and to have a morning cough; X-rays taken then (Fig. 7) show this enormous heart shadow and on careful examination we could hear some scrunching pericardial friction noises. He came into Hospital for treatment; this picture was taken three or four weeks later (Fig. 8) and as you see shows tremendous improvement. We've never met this problem before—tuberculous pericarditis was something I saw in the Pathology Department as a student—we've certainly never seen it as an active condition in a child who had apparently otherwise only primary tuberculosis; the primary lesion seems to be in the left upper lobe. The problem is how should we treat him?

DR. DAVIES: Do we know the sensitivity of the source-case's tubercle bacilli?

DR. YUDKIN: Yes, they were sensitive to all three drugs.

DR. DAVIES: Did we know that at the time the child came in?

DR. YUDKIN: No.

DR. DAVIES: So did you then treat the child with all three drugs?

DR. YUDKIN: We treated the child with all three drugs and with prednisone.

DR. DAVIES: Could we take you, Dr. Kendig, step by step from the beginning?

Given a boy of 5 who has a weakly positive

FIG. 7.—Case 4.

FIG. 8.—Case 4.

Mantoux reaction and who is otherwise well and has a normal chest X-ray, would you treat him?

DR. KENDIG: And nothing else? I think it would depend entirely on the family background, how much contact he has had, whether there was any tuberculosis in the family at the time, his general physical condition. In general I think our tendency has been *not* to treat these, but I am afraid what people write and what they are actually doing are probably something different—I am afraid more people are treating a child of 5 years old who has absolutely nothing apart from a positive tuberculin reaction.

DR. DAVIES: Then the situation of a child with a lesion, in this case pericarditis. Would you treat with all three drugs or with two?

DR. KENDIG: I would treat with all three temporarily and probably drop the streptomycin one month after a satisfactory clinical result.

DR. DAVIES: I think I can speak for Dr. Yudkin that he treated with all three drugs until the sensitivity tests of the source-case were available—until he knew, in other words, that the child had probably been infected by tubercle bacilli that were sensitive to all three drugs.

DR. KENDIG: That would certainly be logical.

DR. DAVIES: Would you use steroids—I don't say as a routine, that's the wrong word, but would you tend to use steroids for a child with tuberculous pericarditis?

DR. KENDIG: Yes.

DR. DAVIES: And for how long?

DR. KENDIG: For probably six to eight weeks with a gradual reduction in dosage, or if the pericarditis cleared before that discontinue it after a month perhaps.

DR. DAVIES: Dr. Yudkin, how long did you go on with steroids?

DR. YUDKIN: It was, in fact, four weeks.

DR. KENDIG: That would be logical: continue steroids only so long as you have the effusion and then a gradual reduction.

DR. SEAL: The pathogenesis of this disease is again associated with that primary complex and I think that what has happened here again is that the lymph node is the culprit, and in most of these cases that have been investigated it's the sub-carinal node that's so closely associated with the base of the pericardium. Here we have again the perforation mechanism, this time into the pericardium with, to some extent, an abacterial response. It would happen possibly as well if the caseous contents were sterile but also probably there *are* tubercle bacilli multiplying and therefore you have to treat. Steroids are rational because I think there is some evidence they will reduce fibrosis and since the danger here is the subsequent development of constrictive pericarditis that would be the indication for steroid therapy.

DR. LYNNE REID: I'm not very happy that one

can assume you've had a perforation again—I agree completely about the lymph node, but these do spread without it. I think once you've seen one of these punctate holes in a bronchus with the caseation coming through it's so dramatic one imagines it's what always happens. I suspect even with the pericardium that one can't deduce that you've had that perforation. I would like to know about his Mantoux—have you any evidence that he's more strongly positive now?

DR. YUDKIN: He became more strongly positive when he was in hospital.

DR. KENDIG: I should like to come back here to this problem of effusion. I don't see how we can say definitely that it will be the result of a node rupturing in this area because in the vast majority of instances when the fluid is withdrawn one is not going to be able to show the presence of tubercle bacilli. The same thing is probably true I think in tuberculous pleurisy with effusion—in the vast majority of instances it *isn't* the result of rupture of a node.

DR. DAVIES: Pericarditis is quite an uncommon complication of tuberculosis in children. I think I'm right in saying that in your series, Dr. Macpherson, at Brompton there was only one child in the 1,700 you had under observation?

DR. MACPHERSON: Yes, he was rather a peculiar case in that his general practitioner had suggested a course of sunlight treatment and it was after that that he developed a pericardial effusion.

DR. DAVIES: Well, I suppose they all get intensive sunlight in Richmond, Virginia. Is that associated with a lot of pericarditis?

DR. KENDIG: No, we've had very few of them following sunshine!

DR. SEAL: We have seen a patient reach this stage and then while under treatment with anti-tuberculous drugs develop a systolic murmur and a big mediastinal mass. The lymph node had perforated not only into the pericardium but into the ascending aorta, and there was a false aneurysm at the base of the heart walled off by pericardial adhesions.

Case 5—Tuberculous Meningitis

DR. YUDKIN: The next case was Philip B., who was only 5 months old when he was admitted on May 1 this year with a story of being fretful, listless, and anorectic for a week, and had vomited on and off. Two days before admission there had been twitching of the left arm and leg for a few minutes and thereafter his left arm hadn't moved so well. When he came in, and after the lumbar puncture, it was obvious he had tuberculous meningitis as he also had quite an extensive tuberculous lesion in his chest. For a few weeks after Philip was born his parents were living with the paternal grandfather

who had chronic bronchitis and emphysema. This grandfather was then found to have open tuberculosis.

DR. DAVIES: We might leave the problem of the pulmonary lesion and discuss the treatment of the tuberculous meningitis. One of the things we are proudest of at the Whittington is that we have a meningitis unit, Dr. Ashby looking after the adults and Dr. Yudkin the children, and I should probably think it's true to say that though the number now is very small, over the years since streptomycin became available the experience gained in this hospital must be just about as great as anywhere else in the country. What then would be your approach to the treatment of tuberculous meningitis in a boy of 5 months, Dr. Ashby?

DR. MICHAEL ASHBY, M.D., M.R.C.P. (*Physician, Whittington Hospital*): Well, it's Dr. Yudkin who deals with the children, but my attitude from a neurological point of view would be that the child presented with some epileptic phenomena and hemiparesis that were probably attributable to the vascular lesions of tuberculous meningitis, and that this was the sort of case where you would go straight to the steroids.

DR. DAVIES: You suggest that you select your cases for steroids? You don't use them regularly?

DR. ASHBY: I use them regularly but here's a brilliant example of how you can't get onto them too quickly—you shouldn't put steroids off until late. Here's something where, if the dice had fallen slightly differently and the child had got steroids a week before, it mightn't have happened—I don't say it wouldn't have done but our experience with adults is that we don't get these neurological lesions, which appear to be vascular in origin, anything like as frequently—they never occur—now that you get people on steroids on the first day.

DR. DAVIES: Dr. Kendig, would you like to comment on the use of steroids?

DR. KENDIG: I am in full agreement. I think they should be given right from the beginning. Two things are accomplished with steroids; one has been very definitely shown: the incidence of CSF block can be reduced; and the main thing of course as Dr. Ashby has just said is that the incidence of vascular phenomena is reduced. If you get thrombotic phenomena in the cerebral and meningeal vessels you're through—that child is going to be a cripple for the rest of his life if he survives at all, and therefore I think we should give him anything that will reduce the inflammatory process as quickly as possible in order to prevent the incidence of these complications.

DR. DAVIES: In what dose would you give isoniazid?

DR. KENDIG: We give 20 mg./kg. body weight per day.

DR. DAVIES: Do you use intrathecal treatment?

DR. KENDIG: We do not.

DR. DAVIES: What are your comments on that, Dr. Ashby?

DR. ASHBY: Well, I still use it in adults. I am sure you can treat people successfully without, but Honor Smith, Lorber and I who have some of the biggest units over here just feel that it's dangerous and you're going to make serious mistakes. There's no doubt about it, a very large number of people have been successfully treated without. I think Lorber's argument is that he's found, at least in one child, viable tubercle bacilli on lumbar puncture when it had already been on treatment for many weeks. He'll give perhaps 15 intrathecal injections and then stop and if the child relapses—of course he gets onto it very quickly—he will start again.

DR. DAVIES: Dr. Kendig, when you are treating without intrathecal treatment—do you do repeated lumbar punctures?

DR. KENDIG: Yes.

DR. DAVIES: How often do you do them?

DR. KENDIG: The first one after three or four days just to see how things are going and then probably every couple of weeks thereafter.

DR. DAVIES: Could we have your comments, Dr. Yudkin?

DR. YUDKIN: We went on using intrathecal treatment for quite a long while and then it became rather difficult to do what we wanted to do—a control study—because at the time we wanted to do that fortunately we stopped getting 40, 50 or 60 patients a year which we had been having until then. So on the basis of other people's evidence for six months we started children off without intrathecal treatment and if we didn't get an improvement within ten days to a fortnight we started them on it again. But in the last three years we haven't used intrathecal therapy at all and not only have we not used it but, having made the diagnosis by lumbar puncture, we don't do any more lumbar punctures either, our view being that these children are going to have two years of treatment, that the actual number of cells and the amount of sugar you find in the fluid are really no evidence of the child's health or welfare and we're not going to change our treatment whatever we find. So that basically now we treat a child with tuberculous meningitis in exactly the same way we treat one with miliary tuberculosis alone.

DR. DAVIES: Do you confidently say you are not going to develop spinal block at all?

DR. YUDKIN: Well, our experience of spinal block was that we got it much more in the days when we were using streptomycin intrathecally

than we ever have it now that we've stopped it. The fact is that we know that streptomycin is irritant when injected intrathecally and we haven't had any evidence of spinal block at all since we stopped using it. I qualify everything I've said by the fact that our experience in the last three years has been less than we had in one year when we first had the unit going.

DR. KENDIG: There are three comments I'd like to make on that—one is that since we've started isoniazid we've gradually discontinued intrathecal therapy and while we had a number of relapses prior to that time there's been no instance of relapse in any case since the advent of isoniazid even without intrathecal therapy. The second thing is that we do lumbar punctures at fairly frequent intervals during the early stage because we are particularly interested in whether or not the CSF protein is elevated, and to what extent, because that is going to determine to some extent how long we are going to continue the corticosteroid therapy which may be continued for six weeks or sometimes for longer. Now a few years ago when we started we had housing problems at the Medical College and economic problems for some of the patients, and we were drawing patients from all over the State of Virginia: sometimes they were 400 miles from Richmond. We had several patients who came in and after four to six months they made such rapid strides and seemed to be doing so well that we sent them home, off streptomycin but on PAS and isoniazid, and it was thought they could keep up this for at least a year and would be brought back into the Medical College. Well, they didn't come back and when we got round to realizing they were *not* coming back we reviewed the situation and found that we had a reasonable number of patients who had been treated less than a year—I think, for eight months or less, some as little as six months—in the States this was unheard of and not a single instance of relapse have we had. All these children got along perfectly all right once they were over the acute phase. Goodness knows, I don't recommend that—we still think in the States that they should have a minimum of a year—but as a result of this and some other studies those two committees I mentioned earlier which set the standard for what we do both say now that treatment should be carried out for a minimum of one year, but they don't say anything about treating it any longer.

I should like to show how we first started with corticosteroids—this was back in 1955 or 1956. Very little work had been done on steroids in tuberculosis meningitis. We had a child admitted to hospital at about 2 years of age, a Negro child, apparently making fair progress over a period of

about a month and then it didn't seem quite so well and a repeat lumbar puncture showed she had a CSF protein of 5.6 g./100 ml. At this time she had a temperature of about 101° and had vomited a couple of times. (On admission her CSF protein was about 200 mg.) Since we consider a CSF protein of 300 mg. is *prima facie* evidence of block we were pretty definite this child had that so after much discussion we decided to give the child steroids, and in about two weeks the protein came down to about 650 mg. Not knowing what we were doing and having no literature on the subject

we gradually discontinued the steroids—and as we did so the protein rose to 5.8 g. But by then it was perfectly obvious we could control it and so we put the child on steroids and in two weeks we had it down and that's the way we kept it for almost five months. The child went home with some Cushing's Syndrome but the tuberculous meningitis was completely controlled. It was a classic example of what could be accomplished with corticosteroids by those who really didn't know what they were doing and who were feeling their way along!

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