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Discussion

Chairman: MR J. F. NEWCOMBE

NEWCOMBE (*Central Middlesex Hospital*): In relation to the origin of the immigrants, we heard that quite a number come from Asia or from Africa. I think we can assume that most of the people who are affected by this disease from Africa are the Indo-Asian; is that correct, rather than the negro population of Africa?

DR M. W. MCNICOL (*Central Middlesex Hospital*): We believe that recently the majority of our cases have come from the Asian population at the moment being displaced from East Africa.

NEWCOMBE: The second thing that I would like to ask you is in relation to the positive and negative tuberculin tests in your patients who attended the Chest Clinic. Have we got any information as to how long these people have been in the United Kingdom, depending on whether they are positive or negative? Is there any difference?

MCNICOL: From our information there does not seem to be any relationship with length of stay in the United Kingdom and a positive or negative test.

NEWCOMBE: Do you have any information on positives entering this country?

MCNICOL: None at all.

DR F. H. SCADDING (*Middlesex and Brompton Hospitals*): Could I ask Dr Mikhail whether he regards mediastinoscopy as safe in the presence of superior vena caval obstruction? Quite often one is faced with this problem in patients with carcinoma: is it safe to do this in the presence of mediastinal obstruction?

DR J. R. MIKHAIL (*Central Middlesex Hospital*): We have not performed mediastinoscopy in cases with mediastinal obstruction. I do not really feel that as a physician I am competent to say what the risks are, but we ourselves have not performed mediastinoscopy under these circumstances.

DR P. STRADLING (*Hammersmith Hospital*): We performed a mediastinoscopy recently on a patient who had mediastinal obstruction and there was considerable difficulty and a lot of bleeding; the surgeon got round this and the patient survived, but it was a very difficult operation. May I ask Dr Mikhail, please, what other investigations he does as a routine before he does a mediastinoscopy? Do they all have bronchoscopy first? It seemed that some of his cases might well have been diagnosed by bronchoscopy.

MIKHAIL: A large number of these cases have bronchoscopy at the same time as mediastinoscopy. We usually perform both together. If bronchoscopy is being performed, the bronchial biopsy is not taken until after the mediastinoscopy has been completed, because of the risk of haemorrhage.

PROF. J. CROFTON (*University of Edinburgh*): Could I ask Dr McNicol the tuberculin positivity rating of the Heaf test; was this true grade I, or was it grade II or more? Any positive would put the percentage fairly high. I was interested that he said that his Patels were 'tuberculous' and also had a high incidence of asthma. Dr Horne spent a year in Gujerat, where most of the Patels come from, and they did an analysis of all the respiratory cases coming into the general wards. Tuberculosis was much the highest, but the second highest was cor pulmonale due to chronic bronchitis. I would be interested to know whether you had the same experience, which one does not usually associate with India, but do they smoke a lot in that area? One other point I would like to make to Dr Scadding in his interesting view on tuberculin negativity—would he not agree that miliary tuberculosis is often tuberculin-negative, especially in elderly patients with anaemia or blood dyscrasia and slight pyrexia, whose miliary is very cryptic?

DR W. GRIFFEL (*Oxford*): I would like to ask two questions: firstly, whether the shift in non-pulmonary tuberculosis has been observed elsewhere and whether we really for the first time can see the first chapter in the history of infection with tuberculosis, and have first-hand opportunity to see that there are more cases of non-pulmonary tuberculosis when a population first comes in contact with tuberculosis; secondly, to Professor Scadding, whether, when he desensitizes under cover of steroids, the symptoms and signs are different than when he did not desensitize, because there are some exudative changes in these hypersensitive cases?

MCNICOL: As far as we can tell this is not an earlier stage. These are really different manifestations of an active disease. It is very difficult to believe that in any population this could be latent rather than an early form or stage. We are seeing also in these groups florid pulmonary tuberculosis, so it seems that these form a different spectrum of disease manifestations and not a matter of different staging. I think that would be our feeling locally, very strongly.

PROF. J. G. SCADDING (*Brompton Hospital*): I do not think I could answer the question very well. The studies were done in the relatively early days of chemotherapy, when we first became aware that you could control tuberculosis with fair certainty by long-term chemotherapy, and we were really exploring what happened when you desensitize people. The most interesting thing was that it was possible to do it, which rather astonished us! Not every patient could be desensitized, but the majority could be, and since the subsequent course of all patients treated with long-term chemotherapy was so good, there was very little chance of finding out whether the desensitized ones did any better. Some of them certainly retained their desensitization for a very long

period: we followed up some of them for a long time. I think that if Dr Citron is here, as he followed some of them he might have something further to add to that.

DR K. M. CITRON (*Wandsworth Chest Clinic*): I have very little more to add. Some of these patients retained their negative tuberculin test for a number of years. I think it raises a very interesting theoretical prospect, which might explain the patients with acute miliary tuberculosis, as Professor Crofton mentioned, who are tuberculin-negative. I wonder in fact whether they are not desensitizing themselves. That is to say, if you have enough antigen flooding the system, then you may, as it were, auto-desensitize yourself. I think this is a possibility which might be supported by the fact that by giving increasing doses of tuberculin to the very ill patients with extensive active disease, you can actually render them tuberculin-negative.

PROF. SCADDING: In addition to patients with miliary disease, in an anatomical sense, that is widespread discrete granulomas, two groups of these are apt to be tuberculin-negative. There are the ones in which the whole process is exceedingly indolent. The patients are not ill; they may be very slowly progressive; they are not febrile, yet some of these will be tuberculin-negative. At the other end of the scale, you have the hyperacute ones, who are desperately ill and fall into the general category of very ill people. Now in these latter ones, it may be that this sort of desensitization occurs by antigen flooding, as it were, but I do not know—and, of course, at the very extreme end of the scale is the so-called acute mycobacterial septicaemia. I think one of the best accounts of which came from this hospital, from Dr Horace Joules and Dr Keith Ball, in the early 1950s, where the patient was very acutely ill and had a blood dyscrasia with some sort of leukaemoid response. Pathologically it was probably not tuberculosis in the sense that they could find no tubercles but a lot of necrotic lesions and swarms of bacilli. Unfortunately, I have been unable to find enough of these cases reported with adequate tuberculin tests to be certain what proportion of them are negative, but I know some of them have been reported to be negative and I should rather expect them to be, but I have only once seen one of these cases. If you can give precise information about tuberculin sensitivity, I should be glad to hear about it.

DR K. H. LIM (*Barnet Chest Clinic*): Some patients with bronchial carcinoma may present with hilar adenopathy, the primary lesion being undetectable radiologically. The glands may show sarcoid changes, and it is possible that a wrong diagnosis may be made if it is based on histology of the gland alone. Has Dr Mikhail come across any such cases? I had such a case recently where there was a carcinoma and this was resected. The glands showed typical sarcoid changes. I showed this to Professor Scadding and he said that sarcoid changes can occur in the region of the glands draining a carcinoma, but that the patient had two conditions because the mucosa of the bronchus which was removed also showed sarcoid changes.

MIKHAIL: Sarcoid changes in glands draining malignant disease generally are a well-recognized entity. I have not seen a case of multi-system sarcoidosis and malignant disease but there is no reason why this should not occur.

PROF. SCADDING: I think they do occur but not more frequently that we can expect to see by chance. I know of quite a number of instances; certainly one, if not two, patients of my own that I have been following for years have developed a carcinoma, and why shouldn't they, seeing that bronchial carcinoma is now the commonest primary cancer? On the general problem of whether you should interpret a non-caseating granuloma found in a lymph node which has been removed and happens to be draining an area which has a carcinoma, as simply a local sarcoid reaction or part of systemic sarcoidosis, this as far as I can see is simply a matter of empirical study. If you look at these patients and find nothing, no evidence of anything except the granulomatous changes in the node, the presumption is that it is simply a granulomatous reaction, but if you find distant granulomas in areas not involved, where you could not conceive of anything produced by the carcinoma as stimulating the production of the granuloma, then you would have to regard it as a generalized non-caseating epithelioid cell granulomatosis —which is the characteristic of sarcoidosis.

STRADLING: May I ask Dr Lim, was this paratracheal gland obvious in the X-ray, or was this just a routine mediastinoscopy, because I have not seen confusion on an X-ray and I imagine I could get it on mediastinoscopy?

LIM: There was a lesion in the right lower zone, with prominence of the right hilum, and, to take up Dr Stradling's point, we did a bronchoscopy first and found the carcinoma. This was removed—I think he had a lobectomy. The histological examination afterwards showed carcinoma but the draining glands showed sarcoid changes. My point is that in this patient, for instance, or in another patient, the primary might not have been so obvious and therefore you would think here is a case of enlarged mediastinal glands and if you do the mediastinoscopy first you might make a mistake and label it as sarcoidosis and miss the primary. In your large series of cases has this happened?

QUESTION: Bronchial carcinoma is present less frequently in these immigrants because of their age and possibly because of their ethnic origin, than in the British-born population. Is that true?

MIKHAIL: Yes, I would think so, because most of the cases of sarcoidosis are more frequent in females rather than males and more common in the child-bearing age of the 20s to 40s, whereas this is not the real carcinoma age-group. Most of the cases of sarcoidosis are in Irish and West Indians. On the whole, the West Indians have not been smoking as long as the indigenous population and the incidence of carcinoma is probably not as high at the present time in this particular group.

DR A. B. WHITE (*Seaham Hall Hospital*): Could you give us your observations on the incidence of *kansasii* infection in North East England?

DR P. JENKINS (*Tuberculosis Reference Laboratory, Cardiff*): We wouldn't push urban air pollution too far, but there is a very striking relationship in Wales between miners with a history of dust exposure, men who worked as blast-furnace operatives, or arc-welders, and infection

by *M. kansasii* and also *intracellulare,* the organisms which are mainly the cause of pulmonary infections. The relationship is very striking indeed, but I presume that it will come out in the BTA survey of opportunist mycobacterial infections and industrial dust exposure which is continuing at present.

DR N. MACDONALD (*Clare Hall Hospital*): Professor Scadding's request earlier was about patients with acute tuberculosis. We had a couple at Clare Hall from the Indian sub-continent who were admitted originally to fever hospitals with suspected typhoid. They were tuberculin-negative to begin with and later with treatment became tuberculin-positive. The diagnosis, incidentally, was made in one by bone marrow biopsy and in the other by liver biopsy. This brings me to a point, with regard to Dr McNicol's paper, concerning the explanation for the very high incidence in Asians particularly; obviously one thinks naturally of housing conditions, stress and so on, but these apply more or less equally to all immigrant groups. In fact, I think we must think in terms of inherited immunity, or lack of it, perhaps. I think this is pretty obvious because so many of these lesions are very acute in character. The other point, of course, is that they very often have extremely strongly positive tuberculin reactions, particularly the middle-aged group.

DR P. I. LEGGAT (*Newcastle Chest Clinic*): One question to Dr McNicol. In the North, although we have our usual high rate among Asians compared with the indigenous population, it is particularly so in Pakistanis. Have you broken down your Asiatics into Pakistanis and Indians, and did you find the same sort of thing? The Pakistanis have this very high rate, mainly because they come over, as you know, by themselves, without their families, and multiple house occupancy, and I'm afraid to say, multiple bed occupancy is the reason. Did you find the same with your patients?

MCNICOL: We have not yet broken down our figures in detail. I would, like you, count a lot of the factors as purely social and somewhat disagree with Dr MacDonald. When we started out we felt the same things about the West Indian patients, the Caribbean group, who over the past 6 years have been showing a very low pattern, which in some ways is not dissimilar to the local population. It seems to us that these more florid manifestations are found in our most recent immigrants but at present we have no detailed breakdown of Indians and Pakistanis.

DR G. F. BARRAN (*West Norfolk and King's Lynn General Hospital*): I would ask Professor Scadding if he would comment on the patient I was recently asked to see? A child of 6 was operated on for a supposed strangulated hernia of the groin. The surgeon, to his surprise, found a tuberculous gland. Tubercle bacilli were seen on Ziehl-Neelson. Unfortunately the gland was not cultured; the child came from a household where tuberculosis had been known—I do not think there is any doubt that this child had a tuberculous gland in its groin. The tuberculin sensitivity was originally negative, down to 100 tuberculin units, but one month later it was positive. I would have thought that active tuberculosis in this child would have produced a positive reaction to tuberculin, but perhaps glandular tuberculosis is one of those groups that we have been considering when the tuberculous sensitivity is low. Perhaps Professor Scadding could comment on this patient?

SCADDING: I would like to know when this test was done. I mean, if it was done in close relationship to the operation, it is possible that some disturbance associated with the strain of the operation might have caused a temporary non-specific depression? I do not know.

BARRAN: It was done very shortly after.

SCADDING: Of course, I am afraid one is saving one's hypothesis by dragging in the concept of a non-specific depression after the operation, but I really rather suspect that that was the explanation in this case, paritcularly as it became positive so shortly afterwards, and with the established caseating lesion in a lymph node you would expect the patient to be tuberculin-positive. Another thing, of course, I think we must all be very careful about with these tuberculin tests is the potency of our tuberculin dilutions. Certainly in both the hospitals in which I work, I occasionally get the situation where I say I don't believe this—repeat it and make sure you get a nice fresh solution, then it is positive. So this is a point on which you have to be very careful. That is why one should only regard the test as really negative if one has repeated it with every precaution.

BARRAN: That actually was done.

DR A. MITHAL (*Cambridge Chest Clinic*): I should like to ask Dr Jenkins if he knows about the BCG vaccination status in any of those patients which he reported from Cardiff with the swimming bath infections? Is there any bearing on preventing the future possibility of infections with these opportunist mycobacteria?

JEKKINS: I cannot give you any details about the BCG status of the outbreak in Cardiff. I do not know if the BCG status was ever published. There was a short note in the *British Medical Journal* about the outbreak, but it is undoubtedly true that there would be a certain degree of cross-immunity in patients who are vaccinated with B.C.G. who may well have increased immunity to opportunist infections, but the number of cases is so small that no-one yet has been able to draw any sort of statistical correlation between the two things.

SCADDING: Of course there might be some relative information in the age distribution of the cases, because the probability is that those below the age of 12 or 13 would not be vaccinated, whereas those younger—depending when the year was, which year was it? The majority would be likely to be vaccinated or tuberculin-positive.

JENKINS: Yes, in fact seventy-three of them were children and only seven adults, but then more children would have used the swimming-pool. The probability is that seventy-three were below the age of 12 and had not been vaccinated, or the majority of them had not been.