Review Article

Ethnic differences in respiratory diseases

D. Honeybourne

Dudley Road Hospital, Birmingham B18 7QH, and Department of Medicine, University of Birmingham, Birmingham, UK.

Introduction

In many parts of the United Kingdom, particularly in the larger cities, there are substantial ethnic minorities many of whom live in conditions of relative deprivation. These social conditions alone predispose to illnesses but in addition extra susceptibility to certain respiratory diseases because of ethnic origin is becoming increasingly apparent. These differences are of both academic interest in understanding the pathogenesis of diseases and also of practical importance to enable resources and specific treatment to be tailored to the needs of particular groups of patients. Studies of ethnic differences in the prevalence of a disease or the clinical features are far more likely to be reliable if carried out within a defined population than if international comparisons are made between different populations studied by different investigators who may for instance have a different definition of asthma. There are many diverse diseases which show pronounced ethnic differences in prevalence and clinical features but this review focuses on respiratory diseases. Particular reference is made to work published from UK studies, but also to some other articles from many parts of the world, and especially to studies of tuberculosis, asthma and sarcoidosis. Some possible explanations are offered for observed differences.

Tuberculosis

In the last century, there has been an astounding reduction in the incidence of tuberculosis (TB). During the reign of Queen Victoria one in five people died of TB whereas now it causes less than 0.1% of all deaths in the UK. The incidence of TB in England and Wales has continued to decline over the last 20 years but the proportion of cases occurring in immigrants of certain ethnic groups has increased. The yearly rate of

notifications in the period 1978–9 was found to be 16.4 per 10⁵ population in England which fell to 12.2 in 1983.¹ The highest rates amongst immigrants are in those of Indian origin (178 in 1983) followed closely by those of Pakistani and Bangladeshi origin (169 in 1983). West Indian immigrants had a rate of 30 in the same year, although Rastafarians are a higher risk group.² However, even in these ethnic minorities, the incidence of TB was lower in 1983 than in 1978–9. Similar high incidence rates have been found in the USA amongst immigrants of Asian or Latin American origin.³ In the UK, and other countries, the incidence of TB amongst the Vietnamese ‘boat people’ has been particularly high.⁴

The trends in adults of the non-white ethnic groups born in the UK have not yet been established but will become of increasing importance over the next decade. Children born in the UK of immigrant parents have been found to have an incidence of TB intermediate between children of the indigenous white ethnic group and children born abroad.⁴ Interesting differences have been reported in the decline of notification rates between ethnic groups from 1971 to 1978/9.⁵ The West Indian group showed a decline of 10% per year in both sexes, and rates in Pakistani/Bangladeshi males also declined by 10% per year. However, the Pakistani/Bangladeshi females’ rates declined by 6.5% per year, the white group by 5.1% per year but the Indian ethnic group had an annual decline in rate of less than 0.5% in both sexes. The reasons for this wide variation in the rates of decline are unknown.

In the 1983¹ survey of TB notifications, it was found that the white patients were, on average, older than their Asian counterparts and were much more likely to have respiratory than non-respiratory TB (82% of the whites compared to 66% of the Asians). The rate of non-respiratory TB in those from the Indian subcontinent is a staggering 80 times greater than in whites.⁶ In the UK today, the typical white patient with TB is an elderly male with respiratory TB. Ethnic differences are apparent in the extent of respiratory tuberculosis.

Correspondence: D. Honeybourne M.D., M.R.C.P. Dudley Road Hospital, Birmingham, B18 7QH, UK.
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Large cavitating pulmonary lesions are commoner in whites who are also more likely to be sputum or culture positive than Asians. This may be partly related to the older mean age of the white group. Whites are therefore more likely to be infectious than Asians. The chest X-rays of Asians are more likely to show mediastinal lymph node enlargement rather than shadowing within lung tissue compared to whites,⁶ and there seems to be a predilection for involvement of the right paratracheal glands.

In those patients who have non-respiratory tuberculosis, Asians are much more likely than whites to have lymph node involvement, especially in the cervical area, but are less likely to have genitourinary involvement. The proportion of whites with non-respiratory tuberculosis who have bone involvement is similar to the Asians, although bone and joint tuberculosis is about 85 times more likely to occur in Asians from the general population than whites.⁷ Tuberculous meningitis is more likely in Asians and mortality may be 30%⁸ so a high level of suspicion should be used in Asians with non-specific neurological symptoms and signs and a raised cerebrospinal fluid protein level, and treatment begun very early.⁹ Gastrointestinal tuberculosis is seen predominantly in Asian immigrants,¹⁰ but may occur sporadically in whites. Crohn's disease is very rare in Asians so here there is considerable clinical value in understanding ethnic differences in diseases.

Resistance to one or more antituberculosis drugs (isoniazid, rifampicin or streptomycin) was found in only 1.6% of *Mycobacterium* strains from white patients but occurred in 7.5% of those from the Indian subcontinent.⁵ Another survey has found an even higher rate of primary drug resistance (11%) in this latter group.¹¹ The incidence of side effects to antituberculosis therapy was found to be 7% in whites and 4% in Asians in one study¹² but this was not statistically significant. The same study found no difference in the proportion of patients with TB being admitted to hospital (79% of whites, 76% of Asians). Death before completion of a full course of therapy occurred in 13% of white patients and only 2% of Asians, TB being the cause of death in half of these patients. Whites therefore seem to be at higher risk of death from notified TB than Asians, perhaps at least partially due to age difference.¹³

There are four sources of TB amongst immigrants¹⁴: (1) They may have active TB when they arrive in the UK. This seems to be present in about 0.6% of Asian immigrants examined at Heathrow. (2) They may already be infected on arrival and show a positive Heaf or Mantoux test but only later develop clinical evidence of disease. (3) They may become infected and develop TB after arrival in the UK. (4) They may arrive with inactive disease which later becomes reactivated. This seems to be the main source of TB

amongst Asian immigrants particularly after recent superinfection.

The spread of TB amongst immigrants is enhanced by frequent overcrowding and poor socio-economic conditions. However the different clinical spectrum of TB in immigrants is probably due to other factors. In any infectious disease the clinical manifestations are related to the virulence of the organism and the resistance of the host. It has long been known that there are many strains of *Mycobacterium tuberculosis* and that many strains isolated in India are of low virulence in the guinea-pig, and it was later confirmed¹⁵ that Southern Indian strains are less virulent than British ones. Most Asian immigrants in the UK are infected with these Asian strains of low virulence.¹⁶ Patients with a good cell-mediated immune response and low antibody response to purified protein derivative (PPD) may have localized disease with smaller amounts of tubercle bacilli, whereas those with poorly developed cell-mediated immunity and a pronounced antibody response to PPD tend to have extensive disease and a poor response to therapy.¹⁷ This may broadly apply to whites and Asians respectively in the UK at the present time. It is known that the immune response is genetically controlled¹⁸ but is also influenced by environmental factors, such as malnutrition which reduces cell-mediated immunity.¹⁹ It has been suggested that vitamin D deficiency amongst Asian immigrants may impair cell-mediated immunity and thereby increase the risk of developing TB,²⁰ although an alternative explanation is that poor socio-economic factors may be responsible for both the increased risk of infection and the poor vitamin D status. The water supplies in India can contain large numbers of non-pathogenic mycobacteria which may stimulate the suppression of T-cell immunity¹⁸ or enhance antibody production with consequent tissue-damaging hypersensitivity.²¹ When the subject is exposed later to the pathogenic mycobacteria then the infection may become widely disseminated.

Prevention of TB may be achieved in several ways.

Firstly, improved socio-economic conditions should reduce overcrowding and lead to better nutrition. Secondly, efficient contact-tracing will enable subjects who have been infected with TB to be detected earlier and treatment should be more effective and prevent further spread. In Birmingham, for instance, a computerized contact-tracing procedure based at the central Chest Clinic is in use. Thirdly, chemoprophylaxis may be useful. This involves giving a drug, usually isoniazid, for 6 to 12 months to a subject who has a positive Heaf test (grades 2–4) but no evidence of active disease or previous BCG vaccination. It is indicated in children under the age of 16 years and may be useful in Asian immigrants up to the age of 40.²² Fourthly, BCG vaccination is of crucial importance.

The protective efficacy of BCG used in studies

around the world has varied from 84% (in UK school children) to 0% (in a general population study in Southern India).²³ The reasons for this difference include variation in quality of vaccines, variations in local strains of mycobacteria compared to the single strain used for BCG vaccination, and previous exposure to non-pathogenic mycobacteria may negate any subsequent benefit from BCG vaccination. Neonatal BCG in the UK has been shown to be effective in reducing the incidence of TB amongst children of Asian origin.²⁴ It is now known that BCG in Asian neonates is highly effective in producing a positive Heaf test,²⁵ earlier studies which had reported less favourable responses may have been affected by poor vaccination technique.²⁶

It can be seen from this review that there are enormous differences in the incidence and pattern of TB between different ethnic groups which have implications in prevention, diagnosis and treatment.

Asthma

Studies in parts of Africa such as Nigeria²⁷ have shown a very low prevalence of asthma in adults and children. However, there are other studies including one from the Transkei²⁸ which have shown that the prevalence of asthma increases in children when they migrate from rural to urban areas. Similarly, a survey in the Eastern highlands of Papua New Guinea in 1972 showed a prevalence of only 0.09%²⁹ but by 1980 the prevalence in adults had reached 7.3%³⁰ perhaps due to increased contact with people from North America and Europe and consequently a change in lifestyle. It has been suggested that this remarkable rise might have been due to an increase in the numbers of housedust mite in blankets³¹ or due to a change in diet. However, reports of an apparent large variation in the prevalence of asthma in different parts of the world need to be interpreted with caution as the criteria used for the definition of asthma are often not uniform.

Ethnic differences within the same environment are well established as in Malaysia where asthma is commoner in Malays and Indians than in the Chinese.³² Migration seems to be an important factor in those from the Indian subcontinent (ISC). The prevalence of asthma in children with Asian parents born in the ISC is much lower than in white children in the UK or those born of Asian parents in the UK.³³ Similarly, the children of immigrant families in the UK who were born in the West Indies show a lower prevalence of asthma compared to those born in England.^{33,34} The prevalence of asthma in schoolchildren in Birmingham was found in one study³³ to be 1.5% in Asians and 4.3% in non-Asians (or 5.3% and 9.9% respectively if all 'wheezers' were included). However, it has been suggested that the lower

prevalence in Asians may be related to language problems in the use of the questionnaire by health visitors.³⁵ The prevalence of asthma in those adults who emigrated from the ISC to the UK has not been accurately assessed in the general population. A recent survey of 17 factories in Birmingham has shown a very similar prevalence of asthma in adults of 3 ethnic backgrounds who understand English adequately for the questionnaire. The prevalence rates were 5.5% in Caucasians, 3.7% in West Indians and 3.2% in Asians,³⁶ which were not statistically different. The prevalence rate of asthma in the UK is widely believed to be around 5% in adults.

Adults from the ISC who emigrate to the UK develop asthma at a later age than the indigenous population of the UK³⁷ (mean ages of onset of asthma were 25.9 years and 19.3 years respectively) and the majority were found to develop symptoms of asthma after their arrival in the UK. Caucasian asthmatics were more likely to be current or ex-smokers, to have had a history of childhood bronchitis and wheezing and to have had a past history of pneumonia or pleurisy than their ISC counterparts. A study of children in Birmingham³⁸ has shown that, in children born in the UK, hay fever and positive skin tests to grass pollen, cats and dogs were less common in children with Asian or West Indian parents than in those with Caucasian parents. However, positive skin tests to house dust mites were less common in the Caucasian than in the other 2 groups.

Asian asthmatics are much more likely to be admitted to hospital than whites.^{38,39} In the latter study, there was a 2.5 fold increase in admission rates for the Asian group, assuming an equal prevalence rate in the population. There were no ethnic differences in the length of inpatient treatment required. Possible reasons for the higher admission rates in Asians include less compliance with prophylactic treatment, and a lower threshold for admission by medical staff perhaps due to difficulties in communication and therefore in an accurate assessment of the severity of an asthmatic attack. Poor compliance is a common problem in older Asian asthmatics who often regard regular medication as a stigma to be avoided. Other possible ethnic differences in the clinical features of asthma, such as whether one group of pharmacological agents is more efficacious or in the risk of death from asthma, are unknown.

Sarcoidosis

There are important ethnic differences in the incidence, clinical manifestations and prognosis of sarcoidosis. There is a high incidence amongst the indigenous population of Ireland⁴⁰ and this is also seen in the Irish population living in London.⁴¹ Blacks in

the USA have a much higher incidence of sarcoidosis than whites⁴² and this has also been found in London.⁴³ Asians living in the UK also have a higher incidence than Caucasians, although less than blacks.^{43,44}

Subjects of West Indian origin living in South-East London have been found to have a later age of onset of sarcoidosis than whites. West Indians were more likely to have chest discomfort or pain, less likely to have erythema nodosum, but more likely to have skin infiltration with sarcoidosis than whites.⁴⁵ Erythema nodosum is extremely uncommon in Jamaica.⁴⁶ Patients presenting with erythema nodosum usually have an excellent prognosis and this may be linked to their HLA type.⁴⁷ HLA B8 is strongly linked to spontaneous resolution in sarcoidosis and its frequency is increased in patients presenting with erythema nodosum due to sarcoidosis. However ethnic differences in HLA B8 frequency are as yet unclear. Skin sarcoidosis is commoner in West Indians than Caucasians⁴⁵ and is known to carry a higher risk of progressive pulmonary fibrosis.⁴⁸ Blacks and Asians have a more disseminated disease than whites^{43,49} and as involvement of 3 or more organs by sarcoidosis is known to be a bad prognostic factor⁵⁰ this suggests that the prognosis of sarcoidosis in blacks and Asians is worse than in Caucasians. Two recent studies of sarcoidosis in Asians involved relatively small numbers of subjects but the results suggest that the incidence, clinical severity and prognosis of sarcoidosis in Asians is intermediate between blacks and Caucasians.^{43,44}

The aetiology of sarcoidosis remains unknown but at least some cases may be caused by a transmissible agent.⁵¹ The later age of onset of sarcoidosis in West Indian and Asian immigrants to the UK compared to the indigenous Caucasian population may be compatible with the later exposure to an environmental agent. Seasonal variations in the incidence of sarcoidosis have been found in the UK⁴⁵ and in Japan⁵² and may suggest that environmental factors are important. The differing clinical presentations between ethnic groups might be explained by a different immunological reaction to an environmental agent or agents perhaps with an association with HLA linkage.

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Other respiratory diseases

There are enormous gaps in our knowledge about ethnic differences in many respiratory diseases, even common ones like chronic bronchitis or lung cancer. There has been one study looking at the hospital admission rates for common chest disease in Asians, West Indians and Caucasians.⁵³ Black patients were significantly less likely than the other two ethnic groups to suffer from carcinoma of the bronchus or acute or chronic bronchitis. These differences remained even after adjustment for smoking habits. Any ethnic differences in cell type of carcinoma of the lung in the UK remain unknown.

Conclusion

Important clues about the pathogenesis and pathophysiology of respiratory disease may be deduced by analysing ethnic differences. The work reviewed in this article shows that enormous ethnic differences exist in the prevalence and clinical features of tuberculosis and sarcoidosis. In tuberculosis, this spectrum has Asians at one end and Caucasians at the other but with sarcoidosis, Asians lie in an intermediate position between West Indians and Caucasians. Asians are admitted to hospital with acute asthma more often than non-Asians, although from the limited data available, the prevalence of asthma in the community is not higher in Asians. Cultural differences often necessitate a slightly different approach to treatment. Thus maintenance therapy in Asian asthmatics is often less successful because of poor compliance, and BCG vaccination is still justified for Asian neonates but not for white neonates.

Ethnic differences in diseases are most likely to be observed in recent immigrants but may become gradually less apparent in successive generations. This will partly depend on the contribution of genetic and environmental factors to the aetiology and clinical expression of disease. This is an exciting field and there is considerable scope for further work to elucidate and clarify ethnic differences in respiratory disease both in the hospital and general population.

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