Chronic Disease of Liver and Lungs in New Guinea

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New Guinea has some specific and unusual advantages for the epidemiological study of diseases; this, and its nearness to Australia make it a particularly attractive place in which to work for the academic exposed to a heavy administrative load in his office.

The Highland peoples mix little with the Coastal people and have different cultures, geographical surroundings, and climates. Highlanders are usually sweet-potato eaters whereas the Coastal people usually eat taro and sago and have more protein from fish. The lack of mixing has resulted in a virtual absence of tuberculosis in the Highlands, which were only 'opened up' by Europeans in the 1930s, whereas the disease was introduced into the Coastal people by the London Missionary Society a long time ago, and it is rife in many areas.

The Western and Eastern Highlanders are separate and different peoples although they live in similar geographical surroundings. There are many linguistically and culturally separate clans or tribes that are territorial, exogamous named groups which mix little with other groups a few miles away. Between the Chimbu people near Mt Wilhelm in the Eastern Highlands and the Enga people at Baiyer River, near Mt Hagen, in the Western Highlands, there are three other linguistically separate groups. A study of haptoglobin groups in the Fore people (Eastern Highlands) showed that the frequency of Hp^1 was highly significantly different in two clans or villages separated by two miles (Blackburn and Hornabrook, 1969).

The urban population is small and localised to a few larger towns such as Port Moresby, Lae, Madang, Rabaul, Goroka and Mt Hagen; the rural population is much larger and often static. The people of New Guinea are intelligent and keen to have health improvement and so are most co-operative in epidemiological studies. Alcohol has never been made by these people and its introduction by Europeans is slow in many rural areas. The lack of adequate medical care has limited the widespread use of antibiotics.

On a first visit by one of us (CRBB) in September 1964 to set up an epi-

demiological study of cirrhosis of the liver, it was noticed that a great many people in rural areas had a chronic cough and cor pulmonale was found to be a common cause of death in those dying of heart failure. It was decided to add an epidemiological study of chronic non-tuberculous lung disease to the study of liver disease.

METHODS

Highland sub-populations, living at 4,000 to 7,500 feet, are being compared with each other and with people on Kiriwina Island, where the highest feature is 150 feet. In neither area is tuberculosis prevalent, and malaria control measures have been in force in both places for some years.

Clans or villages are selected for study if they fulfil the following criteria:

1. they are relatively isolated yet accessible;
2. they are close enough to a hospital to have access to treatment;
3. they appear to have the same social structure as that which had been traditional;
4. they might be expected to have no rapid social or economic change in the next five to ten years.

It is important to study 'static' rather than 'mobile' populations so that the same people can be seen year after year and so that those who are ill may visit the local hospital and have a diagnosis attached to their illness. Although there is a marked resistance to autopsies it is hoped that proximity to a hospital will increase the chances of their performance.

The nature and purpose of the studies have been explained through interpreters to each clan or village visited and to groups of councillors and village chiefs.

Data process cards are written out for each person in a clan or village, between 100 and 600 as a rule, using the census books. The census order is preserved so that on a subsequent day when the clan is visited a 'caller' can give to each person, and his or her family, their card, which is then presented to the examiners and the relevant data obtained and recorded. Figure 1 shows Enga people waiting to be examined, and Fig. 2 shows some Trobriand Island women, with their heads shaved for mourning, waiting with their cards.

A usual team consists of two or three doctors, two students and two technicians and such a team can examine 120 to 300 people in a day, 10 a.m. to 3 p.m., depending on the extent of the physical examination and variety of tests carried out. A maximum study would include questioning for smoking and cough, physical examination for hepatosplenomegaly, jaundice, and

Fig. 1. Enga people waiting for medical examination.

Fig. 2. Trobriand Island women, with heads shaved for mourning, waiting with data cards.

oedema; physical examination of the chest, including the detection of a moist cough; recording of body build, height and weight; measurement of peak expiratory flow rate, forced expiratory volume and forced vital capacity; and, sometimes, skin testing with helminth antigens. Usually, a particular field study does not include all of these. From those seen in such a field survey some are selected for special study in the local hospital on a subsequent day. The data from these field cards are transferred to cards for computer analysis on our return to Sydney.

Special studies are carried out in hospital. Liver protocols include collection of blood for liver function tests, a variety of BSP retention and excretion tests, and liver biopsy where indicated. The latter is carried out only in the operating theatre after checking the bleeding time: the tissue is prepared for light microscopy and, often, for electron microscopy. The lung protocol includes ventilatory studies using spirometry, measurement of lung volumes by the helium method, of transfer factor by the carbon monoxide method, and of blood gas tensions and pH, using electrodes. Chest X-rays are made on persons having special studies.

The aims of the studies of both chronic liver disease and chronic lung disease are:

1. to define their prevalence and incidence;
2. to determine their causation and aggravating factors;
3. to suggest preventive public health measures and to eliminate or minimise them;
4. to relate our findings to similar or identical conditions occurring in Australia and other Western countries.

CHRONIC LIVER DISEASE

Jaundice, cirrhosis of the liver, and hepatoma are known to be common in the people of Papua and New Guinea, as in many other developing countries, and the significance of jaundice and ascites is appreciated by the villagers. The pattern of liver disease seen in patients in hospital has been described (Ma *et al.*, 1968) and the histological diagnoses of 102 patients who had adequate liver biopsies are set out in Table 1. It is notable that 26 had changes of acute hepatitis, cirrhosis or carcinoma of the liver, and 47 had portal tract changes. The cirrhosis usually conformed to the pattern described in active chronic hepatitis (Mistilis and Blackburn, 1970).

In field surveys about 15 per cent of about 13,000 people examined had enlarged livers but those over the age of thirty years had a greater incidence. Re-examination of sub-populations one to three years after the initial survey

showed that 67 to 94 per cent of women over the age of thirty years had hepatomegaly on one or more occasions. Hepatomegaly was usually modest, between 2 and 4 cm below the right costal margin in inspiration.

There appeared to be some relationship to splenomegaly since few people had splenomegaly without hepatomegaly, although the reverse was common. In the people living above Gembogl in the Eastern Highlands, at an altitude

TABLE 1. Histological Changes in Liver Biopsies Obtained from 102 Patients in Hospital in New Guinea

Histological diagnosis	Number of patients
Acute hepatitis	11
Cirrhosis	7
Carcinoma of the liver	4
Myeloid metaplasia	5
Amyloidosis	3
Cellular infiltration and fibrosis of portal tracts	47
Miscellaneous minor changes	11
Normal	14

of about 7,000 ft, where malaria transmission either does not occur or is negligible, hepatomegaly was still common. There was little or no histological evidence that malaria was the cause of hepatomegaly.

On each survey some persons were selected for more detailed study. Standard tests of liver function and percutaneous liver biopsies were carried out on over 300 persons seen in the surveyed populations. These detailed studies were carried out in regional hospitals where adequate operation and transfusion facilities were available.

In most of the liver biopsies definite abnormalities were easily recognised. Portal tract cellular infiltration and fibrosis were very common and only 20 per cent had neither change. These two changes occurred in varying degrees of severity and in various combinations. Some portal tracts, which had mild fibrosis, contained a heavy cellular infiltrate; in other tracts fibrosis was more prominent and the cellular infiltrate less marked. Typically, the inflammatory infiltrate consisted mostly of lymphocytes and a few macrophages but in some, plasma cells or neutrophil and eosinophil granulocytes predominated (Arter *et al.*, 1968).

Portal tract fibrosis was usually accompanied by some cellular infiltration but it often occurred alone. Apparently inactive lesions consisted of heavily sclerosed, almost acellular portal triads, in which the identity of the inter-

lobular bile ducts and hepatic arteries was frequently lost. Such changes were seen in both small and enlarged tracts and the fibrous tissue was dense and collagenous.

The distribution of abnormal portal tracts was characteristically focal and those minimally involved were seen close to markedly fibrosed or heavily infiltrated ones. Fibrosis and infiltration were always confined to the immediate vicinity of the portal tracts, and stellate extensions penetrating into the adjacent parenchyma were rare. The bile duct epithelium, other portal structures and the parenchymal cells of the limiting plates were of normal appearance in most instances. Ductular proliferation was not a feature.

Re-biopsy of 42 subjects, two or three years after the first procedure, showed the portal tracts to be unchanged in 21, to have more severe changes in 10, and less severe in 11. One native whose biopsy was normal in 1965 showed the changes of inactive cirrhosis in 1967. Only two biopsies with cirrhosis have been seen in the whole survey series and only one with hepatoma.

No statistically significant abnormalities were found in serum bilirubin levels, serum glutamic oxaloacetic transaminase and serum alkaline phosphatase levels, BSP retention, total serum protein levels, and serum albumin concentrations. There was a significantly increased concentration of gammaglobulin in the serum of those persons who had cellular infiltration of their portal tracts.

It has not yet been possible to relate the portal tract changes to age, sex or the presence of an enlarged liver. There is no evidence that these portal tract changes lead to cirrhosis or to hepatoma. We do not know the cause or causes of these changes and have no evidence, epidemiologically, histologically or by electron microscopic examination, that they are due to dietary toxins such as cycosin or mycotoxins. The changes resemble those seen in some helminth infestations, for example, *Dirofilaria immitis*, but no causal relationship has been established (Grudzinskas and Blackburn, 1969). The temporal distribution of the lesions and their apparent lack of progression suggest that they result from some undefined episodic insults which recur throughout life.

Bromsulphthalein, injected intravenously, is cleared more rapidly than in the normal Australian, little conjugated dye reappears in the circulation, and detailed studies suggest that the dye is transferred unusually rapidly from the circulation into the bile. Rose Bengal clearance appeared to be normal so it is not thought likely that an unusually high liver blood flow is the important factor. One may speculate that this finding reflects induction of a protein synthetic pathway, perhaps an enzyme itself, by some dietary substance but we have no direct evidence for this.

CHRONIC LUNG DISEASE

The results obtained during the survey in 1965 and 1966 were published in 1967 (Woolcock and Blackburn, 1967). Persons with established chronic lung disease have a chronic productive cough, often with purulent sputum. They have coarse rales on auscultation but rhonchi are rarely heard. Chest movement becomes limited but obvious chest overinflation is not commonly seen. Chest radiographs show areas of fibrosis, especially in the upper zones, evidence of pleural adhesions, and sometimes depression of the diaphragms.

The values for the Wright Peak Flow (WPF) readings in subjects with no abnormal findings on examination correlate well with height and agree with values previously reported in European subjects. This instrument has proved most satisfactory for detecting abnormality of lung function in these people. However, it is of no help in demonstrating the nature of the abnormality. For this reason, we have also recorded forced vital capacity (FVC) and forced expiratory volume in one second (FEV_1) in the adult population and, in 1969, 30 people in the Western Highlands with clinical evidence of lung disease had detailed studies of lung function performed. These studies were repeated on 18 people in the Trobriand Islands in 1970.

The results of the studies at Baiyer River were published recently (Woolcock *et al.*, 1970). Both the epidemiological and the special study abnormalities in the Trobriand Island population are remarkably similar to those found in the Highland population.

As with the WPF, the FEV_1 and FVC results in normal New Guineans are the same as those in Europeans and patients with lung disease in New Guinea have both values reduced with a low FEV_1/FVC ratio indicating airways obstruction. However, in some people with clinical evidence of lung disease, this ratio was only moderately reduced, suggesting that in these patients there may be lung restriction in addition to airways obstruction. This suggestion is supported by the finding of normal lung volumes in all subjects, even in those with a severe reduction in FEV_1 who might be expected to be overinflated. Although the fractional uptake for carbon monoxide was normal, there was evidence of gross inequalities of ventilation-perfusion ratios in the lungs. These inequalities were sufficient to cause low oxygen and high carbon dioxide tensions in the arterial blood of more than half the subjects studied.

We have been able to study four excised and inflated lungs from autopsies on people dying with this disease. In each lung there was severe bronchitis and bronchiolitis as well as emphysema. There were dense pleural adhesions requiring excision of the lung from the chest cavity and in some there were patches of parenchymal fibrosis. Such abnormalities would cause a combination of restrictive and obstructive patterns of lung function and severe inter-

Fig. 3. Typical non-ventilated, smoky New Guinea hut.

ference with the distribution of ventilation and perfusion within the lungs, and this is what we have demonstrated

In many ways, chronic lung disease in New Guinea appears to be similar in nature and aetiology to chronic obstructive lung disease in European people. Thus, a chronic productive cough and a reduced FEV_1 are universal and carbon dioxide retention in the arterial blood is frequently seen. The patients usually die of an acute infection, usually pneumonia, while some develop cor pulmonale. *Haemophilus influenzae* appears to be the important pathogen in the New Guinea population (Blackburn *et al.*, 1970) as it is in Europeans.

On the other hand, there are some important differences. First, the disease appears to be equally as common in women as men in New Guinea; secondly, dyspnoea is not a common symptom in the New Guinea population and patients with marked lung function abnormalities are able to walk long distances; thirdly, we have been unable to demonstrate any reversible component in the airways obstruction of the New Guineans; and fourthly, the New Guineans appear to have more lung fibrosis in association with their airways disease than Europeans with chronic obstructive lung disease.

The reasons for these differences are not all clear. In New Guinea, recurrent untreated lung infections are probably a major factor in causing bronchitis, bronchiolitis, and lung fibrosis. Several factors are probably important in contributing to this lung damage. These include tobacco smoking, long hours spent in non-ventilated, extremely smoky huts (Fig. 3) (Cleary and Blackburn, 1968), poor hygiene, including crowded living conditions and

infrequent washing and perhaps sensitivity to moulds found in the thatch of their huts since precipitins to these moulds have been found in the sera of subjects with lung disease (Blackburn and Green, 1966).

In the New Guinea population it is apparent that infections start in infancy and are more common throughout life than in European populations. In addition, these airway and parenchymal infections probably resolve less completely than in European populations who have a higher standard of living and the benefit of antibiotic therapy. With Dr S. C. Wigley we have been studying a group of school children in Port Moresby for four years and a number have been found to have chest radiograph abnormalities associated with WPF meter readings below those of their contemporaries. In many cases these abnormalities have persisted from year to year. It seems probable that if the abnormalities do not resolve, these children will suffer from chronic lung disease in adult life, especially if they smoke and continue to have repeated chest infections.

The studies on the prevalence, aetiology and nature of chronic lung disease in New Guinea are continuing and have already been most rewarding in regard to our thinking about chronic obstructive lung disease in European populations.

In this work we have had the greatest co-operation from the native peoples, from the staff of the Baptist Mission at Baiyer River, from Dr R. F. Scragg and the medical staff of the Department of Public Health in the areas where we have worked, and from the Institute of Human Biology, headed by Dr R. W. Hornabrook.

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