

Conference Report

The pathology of AIDS

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With an estimated 17 000 cases world wide, the acquired immune deficiency syndrome (AIDS) is now described as pandemic. Behind this figure lurks another and even more disquieting one: for every known case of AIDS between 50 and 100 people are infected with the AIDS virus (HTLV-III). How many of them will go on to develop AIDS is unknown, but estimates suggest that about a quarter will develop signs and chronic symptoms of the disease within five years.

The prognosis remained uniformly poor, said Dr N S Galbraith, from the Communicable Disease Centre, Colindale, speaking at a recent symposium on AIDS organised by the Royal College of Pathologists (Monday 25 November). The British tally at October 1985 was 241 cases, and the number was doubling every eight months or so. Of those patients who had developed the syndrome in or before 1982, 92% were already dead.

Although AIDS remains incurable and can be prevented only by implementing appropriate public health measures and promoting responsible health education, more and more is being learnt about the nature of the virus and the pathogenesis of the disease. There is considerable genetic variation between different isolates of the virus, although a single antibody can be used to detect the virus in all European and North American patients. HTLV-III is tropic not only for T4 cells but also for glial cells and monocyte cell lines—a most worrying finding, said Professor L Montagnier, from the Pasteur Institute, Paris, for that meant that even if the immune deficiency syndrome proved to be treatable patients might go on to develop neurological sequelae. Commenting on the disease mechanism, he suggested that an autoimmune process, in which the body mounted an antibody response first to infected T cells and then to non-infected T cells, was more likely than a direct cytopathic effect.

From man to monkeys

Observation of the disease in man has triggered off a wealth of research in animals, especially monkeys, in whom three distinct retroviruses have been found. One, which is very like HTLV-III, causes a syndrome similar to AIDS in Asian macaque monkeys. These monkeys also develop symptoms if they are infected with a retrovirus that is prevalent (but apparently harmless) in African green monkeys. Giving a fascinating glimpse of the relevance of simian AIDS to disease in man, Professor R A Weiss, from the Institute of Cancer Research, London, said that the antibodies isolated from the African monkeys cross react with the human AIDS virus. Furthermore, antibodies against the AIDS virus isolated from prostitutes in Senegal were more specific to the African green monkey virus than to HTLV-III. This strengthened the belief that West African patients with AIDS, in whom the

pattern of disease was different from that seen in European and North American patients, were infected with a different retrovirus.

Turning to factors that predispose people carrying HTLV-III to go on to develop AIDS, Dr A J Pinching, from St Mary's Hospital Medical School, London, re-emphasised Professor Montagnier's view that both pre-existing immunosuppression and excessive antigenic stimulation were important. Excessive antigenic stimulation was especially relevant among homosexuals with multiple partners and repeated sexually transmitted infections. It might also explain the high incidence of AIDS in infected women who became pregnant: the fetal graft was providing the stimulation. The state of activation of a person's T cells at or around the time they met the HTLV-III might, therefore, determine whether or not they would later develop AIDS. On the vexed question of whether or not immunological abnormalities might be used to predict outcome Dr Pinching said that in most cases the best marker for the severity of the cellular immune defect was the clinical picture. Monitoring the level of antibody to the AIDS virus did not have much predictive value either, for although the titre fell when patients developed full scale AIDS there was no clear change until the patient was obviously ill.

With screening tests to detect antibody to the AIDS virus now widely available what, asked Dr Mortimer, from the Middlesex Hospital, did a positive test mean? (Equally important, what did a negative one mean—for patients exposed to the virus might not seroconvert until eight weeks later, and possibly a good deal longer after that.) A positive test implied two things: past experience of the virus and continuing excretion of the virus by the patient. Low titres of antibody implied either very early or late infection (or a poorly carried out or unreliable assay). He believed that a range of tests should be used so that equivocal tests could be repeated. Reference centres had been set up in Colindale, at the Middlesex Hospital, and in Edinburgh, and when in doubt pathologists should send serum samples to them for confirmation of weakly positive results.

Counselling

Whether or not counselling at risk groups actually has an effect on their behaviour was discussed by Mr J Green, a clinical psychologist from St Mary's Hospital, London. Although he had no answer to those who argued that his patients might simply be lying, Mr Green said that his studies on homosexual patients had left him convinced that counselling did persuade them to change to safer sex. He also believed that counselling should be carried out irrespective of whether the person at risk was antibody positive or not—or chose not to find out—as the advice was the same in all those circumstances. Anyone who did want to know his or her antibody status could, however, get the test done. General practitioners could arrange tests through the 50 or so regional laboratories.

The setting up of good counselling services for antibody positive patients seems to have lagged a little behind the screening process. In Mr Green's view it was probably best carried out by informed,

sympathetic medical staff, for few centres were likely to have the resources to employ trained counsellors. Among the at risk groups haemophiliacs needed special support and should not be counselled in genitourinary clinics, said Professor A L Bloom, from the University of Wales, who went on to reassure the audience that no patients in Britain had seroconverted after being given heat treated factor VIII concentrate.

AIDS remains a clinical diagnosis

Although the day was dominated by the pathologists, the clinicians had their turn. Professor M Adler, from the Middlesex Hospital, London, emphasised the importance of maintaining a high index of suspicion, particularly when a young person in an at risk group presented with a syndrome similar to glandular fever or a pyrexia of unknown origin, which are common in the 20% or so of patients who develop an acute, overt illness when they encounter the virus. Chronic infection might also be subclinical, though some patients develop minor infections, lymphadenopathy, or the AIDS related complex (defined as two or more symptoms or signs present for three months or longer plus two or more abnormal laboratory tests consistent with AIDS). In patients who present with progressive lymphadenopathy—nodes of 1 cm or more in two or more non-contiguous extrainguinal sites present for three months or more and not due to any other cause—the risk of going on to develop AIDS is uncertain, but clinical pointers to a poor prognosis include oral candida, a raised erythrocyte sedimentation rate, lymphopenia, herpes zoster, and, paradoxically, an involution of the enlarged lymph nodes.

End stage AIDS in the United Kingdom was heralded by *Pneumocystis carinii* pneumonia in 36% of patients, other opportunistic infections in 28%, and Kaposi's sarcoma in 28%. The range of opportunistic infections that may be encountered was discussed by Professor A J Zuckerman, from the London School of Hygiene and Tropical Medicine. *Mycobacterium avium intracellulare* and *M tuberculosis* were the commonest bacterial pathogens. Cytomegalovirus, Epstein-Barr virus, herpes simplex, hepatitis B virus, and

non-A non-B infections were the commonest viral pathogens. Candida and cryptococcus the commonest fungal infections, and pneumocystis, toxoplasma, and cryptosporidium the commonest protozoal infections. A simple message to the clinician from this list would be think of AIDS in patients at risk with, for example, severe dysphagia (caused by oral and oesophageal candidiasis), diarrhoea (caused by cryptosporidium or cytomegalovirus), or recurrent and severe perianal ulceration (caused by herpes simplex). He went on to emphasise that clinicians will be seeing increasing numbers of patients with evidence of central nervous system disease, who may present with behavioural changes or dementia.

Once a patient in hospital is known to have AIDS full precautions should be taken to protect clinical and laboratory staff, as well as to preserve the patient's dignity and confidentiality as far as possible, said Dr A M Geddes, from East Birmingham Hospital. He presented encouraging data to show that no health service staff in the world had contracted AIDS from a patient, although in one study 26 out of 1758 tested had seroconverted. Of these, all but three had been in high risk groups. In a study from San Francisco that started in 1981, of 160 staff looking after patients with AIDS, 35% had reputedly had needle stick injuries but none had yet seroconverted. Needlestick injuries were eminently preventable, and most would be avoided if staff stopped resheathing needles and drip cannulas from infected patients. Precautions should be similar to those enforced for hepatitis B infections, but he added that it was prudent to exclude staff from the ward if they had cold sores, upper respiratory tract infections, or eczema (one unsubstantiated report has suggested that patients with extensive eczema may be at risk) and if they were pregnant (to avoid the chance of them contracting and then transmitting cytomegalovirus infection).

Repeated speakers spoke of the high risk to dentists among professionals at risk. Pathologists undertaking necropsy examinations need only adopt the same procedures as they already do for cases of hepatitis B. On a lighter note, those professionals who care for our souls have apparently also been concerned about the spread of AIDS, on this occasion via the communion chalice. One course of prophylactic action suggested was that the host could be dipped in the wine before being handed on to the communicant.

A recently married young woman had a total thyroidectomy for cancer of the thyroid. Is it safe for her to become pregnant?

Because the long term prognosis in thyroid carcinoma is variable, careful preconception counselling is advisable. By itself pregnancy should not adversely affect the course of the disease. The dose of thyroxine for replacement therapy will require careful monitoring to ensure that the mother remains euthyroid throughout the pregnancy.—G J LEWIS, consultant obstetrician and gynaecologist, Stourbridge.

An apparently healthy European nurse in her late 40s working in the hills on the Indian subcontinent developed palpitations, arrhythmia, and a continuous feeling of constriction in the chest that was aggravated by exertion. At sea level her blood pressure and pulse are normal. What might be the cause of her symptoms, what investigations are advised, and what treatment would help her?

In the absence of more clinical details it would be impossible to give a definite opinion on the cause of this patient's symptoms. Clearly, ischaemic heart disease and angina pectoris must first be excluded. A careful history, electrocardiogram, and a trial of sublingual nitroglycerin might help to establish that diagnosis. She might need an exercise stress test and treatment with nitrates, β -blockers, Ca^{++} antagonists, and even coronary bypass surgery. Under similar circumstances, however, one must always remember the possibility of high altitude pulmonary oedema.¹ This condition is not rare and occurs more often on the re-entry to high altitude (around 3000 m) of those individuals already living at high altitude rather than newcomers. Symptoms may occur any time from three hours to 10 days after arrival. Dry cough, palpitation, precordial discomfort, and breathlessness are important symptoms. Headache, nausea, and vomiting occur commonly. Frank pulmonary oedema with frothy pink sputum may rarely occur. Examination shows tachycardia, tachypnoea, and crepitation over the lungs. In severe cases cyanosis with pronounced features of peripheral vasoconstriction are

seen. Chest radiography shows features of pulmonary oedema, more prominent around the para hilar region. Electrocardiogram may be normal or may show right ventricular hypertrophy. Familiarity with the clinical features of high altitude pulmonary oedema and with the means of avoiding the condition is important. Most cases may be avoided if the subject does not attempt to ascend too rapidly after arrival in the hills. Above 2130 m ascent of more than 300 m a day should be avoided.² Treatment consists of absolute bed rest and prompt descent to below an altitude of 2400 m. Oxygen therapy at high flow rates and diuretics have been found to be helpful.—I S ANAND, professor of cardiology, Chandigarh.

- 1 Heath D, Williams DR. Man at high altitude. Edinburgh: Churchill Livingstone, 1981:151-68.
- 2 Anonymous. See nuptuse and die. *Lancet* 1976;ii:1177.

While swimming in the sea an asthmatic doctor developed an acute attack of asthma—possibly related to the prior consumption of beer. He became more distressed than usual, presumably because of the continued effort to remain afloat. During the swim he experienced quite severe bilateral shoulder pain that persisted until shortly after arriving on the beach. This was a novel experience for him. Is it a recognised phenomenon in acute asthma?

The bilateral shoulder pain described is not a phenomenon which I have previously noted as being associated with asthma. Apart from referred diaphragmatic pain there are other possible explanations. Cramp or ischaemic pain in the shoulder muscles associated with the effort of swimming, cold, and perhaps hypoxia might explain it. Alternatively, angina pectoris could occur in these circumstances and although presumably the pain came on before it was possible to use a bronchodilator aerosol, angina has been described in association with beta agonists in some patients.¹—J MORRISON-SMITH, honorary consultant physician, Birmingham.

- 1 Tattersfield AE. Bronchodilators in the prevention of asthma. In: Clark TJH, ed. *Bronchodilator therapy*. Auckland: Adis Press, 1984:79.