ABC of AIDS

MICHAEL W ADLER

RANGE AND NATURAL HISTORY OF INFECTION

THE SEROCONVERSION ILLNESS

Glandular fever like illness
Acute encephalopathy
Acute myelopathy

A positive test indicates:

- ☐ Exposure
- ☐ Persistent infection
- ☐ ? Infectiousness

It does **not** indicate AIDS

Infection with the human immunodeficiency virus (HIV) can produce a very varied clinical picture, ranging from an acute seroconversion illness to full blown AIDS many years later. Infection may be asymptomatic or symptomatic.

Acute infection following first exposure to the virus is usually asymptomatic and may occur up to about six weeks after the contact. When symptoms do occur they are often non-specific. A glandular fever like illness has been described at the time of the acute seroconversion. The patient suffers from fever, malaise, lethargy, myalgia, arthralgia, lymphadenopathy, and sore throat. An acute reversible encephalopathy with disorientation, loss of memory, and consciousness and personality change has also been described at seroconversion, as has acute meningitis, myelopathy, and neuropathy.

Probably not all of those who have seroconverted will progress to chronic infection. Those who do not probably go into a latent phase of infection. Nevertheless, it is prudent to assume that the individual is still infectious despite this latency. The development of more sophisticated tests will help to clarify whether this is true or not. A positive antibody test to HIV indicates only that a person has been exposed to the virus and not that he or she has gained any natural immunity.

Chronic infection may also be asymptomatic. The clinical features described consist of cytopenias, minor opportunistic infections and skin conditions, lymphadenopathy, and the AIDS related complex (ARC). More recently, peripheral neuropathies, myelopathy, and encephalopathy have been seen in patients before they have developed AIDS.

Persistent generalised lymphadenopathy*Prospective studies of persistent generalised lymphadenopathy*

No of patients	Follow up (months)	No (%) developing AIDS	Investigators
42	Median 22	8 (19)	Mathur Wagh 1983
42	Longest 60	12 (29)	Mathur Wagh 1986
90	8-19	15 (17)	Metroka 1983
70	Longest 16	0 (0)	Abrams 1983
200	Longest 61	16 (8)	Abrams 1985
100	Median 24 (9-50)	13 (13)	Middlesex 1987

The lymphadenopathy seen in chronic infection has been termed the persistent generalised lymphadenopathy syndrome (PGL). The definition of this syndrome is:

Enlarged nodes at least 1 cm in diameter in two or more (non-contiguous) extrainguinal sites that persist for at least three months in the absence of any current illness or medication known to cause enlarged nodes.

The nodes are symmetrically affected, and those most often enlarged are in the posterior and anterior cervical chains and axillary and submandibular regions. Other less common sites are submental, postauricular, epitrochlear, and retroperitoneal. About a third of patients also have associated splenomegaly. Lymph node biopsy usually shows benign follicular hyperplasia followed by follicular involution at a later stage. Mostly there is no need to undertake such biopsies. The indications for doing so are covered next week.

Several series of patients with persistent generalised lymphadenopathy have been studied prospectively for a number of years. The proportion with the syndrome who progress to AIDS varies from 10 to 30%, but the proportion increases the longer the patients are followed up.

AIDS related complex

The AIDS related complex is diagnosed in a person who presents with any two or more signs/symptoms which have been present for three months or longer and any two or more abnormal laboratory values

Symptoms/signs

Fever: $\geq 38^{\circ}\text{C}$ intermittent/continuous
 Weight loss: $>10\%$
 Lymph nodes: persistent generalised lymphadenopathy
 Diarrhoea intermittent/continuous
 Fatigue that reduces physical activity
 Night sweats

Laboratory abnormalities

Lymphopenia, leucopenia
 Thrombocytopenia
 Anaemia
 Reduced ratio of CD4:CD8 (>2 SD)
 Reduced T helper cells (>2 SD)
 Reduced blastogenesis
 γ Raised globulins
 Cutaneous energy

Patients who have some of the constitutional symptoms and signs of AIDS without the opportunistic infections or tumours found in the end stage disease are described as having the AIDS related complex (ARC). The term covers a wide range of disease. The concept is of less use now that an antibody test has been developed but can still be of use to the clinician in identifying particularly ill patients, some of whom will progress to full blown AIDS. More useful clinical indices for judging prognosis are covered next week.

Finally, a series of minor opportunistic infections and skin conditions can be found with chronic HIV infection. These include seborrhoeic dermatitis and hairy leukoplakia as well as viral, fungal, and bacterial infections and are described in detail in next week's article.

Progression

Not everyone infected with HIV develops AIDS. Cohort studies give some idea of the natural history. Recent actuarial analysis of five cohorts over three years showed a differing rate of progression from infection with HIV to AIDS—8% in Danish homosexual men to 34% in New York homosexual men. Intravenous drug abusers in New York also had a high rate of progression. The different rates of progression might be accounted for by more virulent cofactors for progression in some of the groups and the fact that some of those studied had been infected for longer than the three years studied. Nevertheless, there is no doubt that the longer the natural history is observed the greater the proportion who will progress from seroconversion to AIDS. The incubation period for this progression ranges from two and a half to five years. Certain clinical features and laboratory values have been found to be useful in judging which patients are more likely to progress to AIDS once they have become infected with the virus. These are covered next week.

Opportunistic infections and tumours

Cases of AIDS by disease category

	USA (%)	UK (%)
<i>Pneumocystis carinii</i> pneumonia	64	46
Other opportunistic infections	22	24
Kaposi's sarcoma	14	21
Kaposi's sarcoma and <i>P carinii</i> pneumonia		7
Other tumours		2

The two main clinical manifestations of AIDS are tumours and a series of opportunistic infections. Kaposi's sarcoma is the commonest original tumour described, but other tumours are now being described. These are non-Hodgkin's lymphoma (usually extranodal) and squamous carcinomas of the mouth and anorectum. Most patients in the USA and UK present originally with *Pneumocystis carinii* pneumonia followed by other opportunistic infections and Kaposi's sarcoma.

Because infection with HIV can manifest itself in many ways, from asymptomatic infection to full blown AIDS, the Centers for Disease Control have attempted to classify the range of HIV infection into four groups.

The many opportunistic infections associated with AIDS affect virtually any system of the body. *Pneumocystis carinii* pneumonia is the commonest opportunistic infection and presenting feature in patients with AIDS both in the USA and UK. Other organisms can also cause pneumonia in patients with AIDS: bacteria (*Haemophilus influenzae*, *Streptococcus pneumoniae*, *Branhamella catarrhalis*, group B streptococcus, and mycobacteria) viruses (cytomegalovirus and herpes simplex) and fungi (cryptococcus). Infections also occur affecting the central nervous system. The organisms are

Opportunistic infections—syndromes

Syndrome	Features	Common organisms			
		Protozoa	Viruses	Bacteria	Fungi
<i>Lung</i>	Cough, shortness of breath, fever, hypoxia Chest x ray infiltrates	<i>P carinii</i> pneumonia	Cytomegalovirus Herpes simplex virus	Mycobacteria* Gram positive <i>Str pneumoniae</i> <i>H influenzae</i> <i>B catarrhalis</i> Group B streptococcus	Cryptococcus
<i>Central nervous system</i>	Meningitis/encephalitis or focal signs	Toxoplasma	Cytomegalovirus Herpes simplex virus Progressive multifocal leucoencephalopathy (papovavirus)	Mycobacteria*	Aspergillus Cryptococcus Candida
<i>Gut</i>	Dysphagia High volume diarrhoea Bloody diarrhoea/colitis	Cryptosporidium Isospora belli Microsporidia	Cytomegalovirus Herpes simplex virus	<i>Mycobacterium avium intracellulare</i> <i>M tuberculosis</i> Salmonella	Candida
<i>Pyrexia of undetermined origin</i>	Fever Weight loss± lymphadenopathy		Consider all pathogens and focal or disseminated infection		

**M tuberculosis* and atypical mycobacteria

Classification system for human immunodeficiency virus

Group I	Acute infection
Group II	Asymptomatic infection
Group III	Persistent generalised lymphadenopathy
Group IV	Other disease
Subgroup A	Constitutional disease
Subgroup B	Neurological disease
Subgroup C	Secondary infectious disease
Category C-1	Specified secondary infectious diseases listed in the CDC surveillance definition for AIDS
Category C-2	Other specified secondary infectious diseases
Subgroup D	Secondary cancers
Subgroup E	Other conditions

Median survival after initial diagnosis

	Median survival (months)	
	USA	UK
Kaposi's sarcoma	31	21.2
<i>Pneumocystis carinii</i> pneumonia	9	12.5
Other opportunistic infections	4.5	

protozoal (toxoplasma), viral (cytomegalovirus and herpes simplex), bacterial (mycobacteria), and fungal (aspergillus, candida, cryptococcus). Finally, the gastrointestinal tract can be infected with protozoa (cryptosporidium, isospora belli, and microsporidia), viruses (cytomegalovirus and herpes simplex), fungi (particularly candida), and bacteria (mycobacterium avium intracellulare, mycobacterium tuberculosis, and salmonella).

In Africa patients with AIDS may have Kaposi's sarcoma as well as a diarrhoeal wasting syndrome (Slim's disease) and opportunistic infections. These infections, however, are more representative of the background organisms found in that continent, such as tuberculosis, cryptococcus, and cryptosporidiosis.

The clinical spectrum is enlarging all the time. The originally described manifestations of Kaposi's sarcoma and *Pneumocystis carinii* pneumonia may have represented the presentation of a short incubation illness, and possibly those who develop AIDS after a longer period may have different clinical presentations. This already seems to be occurring, with the appearance of new clinical phenomena such as other tumours and neurological disease. Other conditions increasingly recognised as part of end stage disease are lymphoid interstitial pneumonitis, granulomatous hepatitis, and an enteropathy.

The median survival of patients after diagnosis of AIDS varies with the presenting manifestation. In America survival is about nine months for patients with *Pneumocystis carinii* pneumonia and 31 months for those suffering from Kaposi's sarcoma. In the UK the figures are similar, with a median survival of 12.5 months for patients with *Pneumocystis carinii* pneumonia and 21 months for those with Kaposi's sarcoma.

Professor Michael W Adler, MD, FRCP, is professor of genitourinary medicine, Middlesex Hospital and Medical School, London.