5 The impact of HIV on surgery

"One night after I had been doing some blood tests in a rural area with some local medical colleagues, they went off with some girls from the town. They slept with them, and only one of them used a condom. In the morning I asked them how they could possibly have taken such a risk, since we all knew the prevalence of HIV was quite high in the region. They laughed, saying that you couldn't give up living just because you might get a disease."
A research worker in Central Africa, PANOS Dossier, 1987 (March).

5.1 Introduction

SURGICAL OVERVIEW
Since the dramatic appearance of a completely new and growing range of pathologies in 1981, and the identification of the Human Immunodeficiency Virus (HIV) in 1983 by Françoise Barré-Sinoussi, Luc Montagnier and colleagues at the Institut Pasteur in Paris, enormous efforts have been made to combat this new disease but with only limited success in many developing countries. The reasons are complex and vary in individual countries, but poverty and lack of resources are the biggest drawbacks.

In these environments, HIV-related disease continues to worry medical resources and presents one of the greatest single challenges to the medical practitioner seeking to alleviate suffering in the developing world. As a result, the practice of surgery cannot ignore the impact of HIV and must assess the implications of this new disease. Although much has been written of HIV-related surgical pathology, the preponderance of the literature reflects the experience of surgeons working in well-equipped hospitals in the First World, where HIV prevalence is low, and where there is ready access to a multiplicity of laboratory testing, drug therapies and nursing back-up. From personal experience we try to give you guidelines to help you in this new medical mine-field.

The practice of surgery is everywhere a challenge, and is so especially in the developing world where improvisation often is the order of the day. Be sure therefore to consider the *balance of risk* inherent in any surgical procedure. An operation which is seen as routine in a well-equipped teaching centre may be a serious risk in a rural hospital; likewise an operation traditionally considered routine in an environment of low HIV incidence may prove to have great risk where HIV is common. *You must not underestimate complications expected in HIV patients*, *particularly those not on treatment,* and once a commitment is made to surgical intervention, you must treat these complications aggressively if they arise. Thus you may need to restrict your elective surgery, particularly in certain anatomical regions, considering that HIV disease is progressive.

Nonetheless, ***do not deny emergency surgical intervention to the HIV patient***, who often requires more aggressive and urgent resolution of sepsis.

Many trauma victims are HIV+ve, but their management should proceed along standard lines regardless. Indeed surgical intervention may buy a patient valuable time before his or her eventual demise, and indeed alleviate that process.

Consequently examine the impact of surgical intervention in certain HIV-related states carefully, and question the standard practices of surgical orthodoxy in relation to HIV disease.

Consider *performance status* and *life expectancy* carefully. This is especially true in those parts of the world where HIV prevalence is high but where testing is irregularly available, and where their HIV status is generally not known by patients themselves.

Avoid elective surgery (especially in patients with clinical signs of immunosuppression) in the following (unless you can guarantee close supervision of effective anti-retroviral (ARV) therapy and a count >200/µl):
(a) *cosmetic procedures, especially on the nose and mouth, including routine circumcision*
(b) *complex plastic surgery, especially free flaps*
(c) *neonatal intervention for complex abnormalities*
(d) *open brain surgery*
(e) *tonsillectomy*
(f) *open thoracic surgery*
(g) *open perianal surgery*
(h) *insertion of prosthetic grafts or metal*

Note that after surgery, you often cannot re-start ARV therapy immediately, and this may be a problem (5.8).

Whilst this list is not exclusive, it is also not exhaustive; treat each individual case on its merits. Nonetheless, within a broad perspective, exercise great caution in the above types of surgery. Post-operative infection rates are doubled in asymptomatic HIV+ve patients, and more than trebled in symptomatic HIV+ve patients, especially where the CD4 count is <200/µl.

HISTORICAL OVERVIEW
The most compelling evidence to date suggests that HIV was transferred to humans through transformation of an almost identical simian (monkey) virus in the Congo region in the 1940s or 1950s. The oldest +ve HIV test is from a serum sample of an adult male in Kisangani (formerly Stanleyville), Congo, taken in 1959. Before that there were no deep freezers to store serum. Another +ve sample was found in a lymph node from Congo in 1960.

The emergence of certain diseases, such as Kaposi sarcoma, amongst the homosexual community and intravenous drug abusers in the USA in the late 1970s brought to light a series of ailments related to immune deficiency. Subsequently, an infective agent, one of a group of retroviruses, was identified, and positively linked to further conditions, especially a wasting syndrome seen in Central Africa, known as Slim Disease.

It was then evident that HIV was spread heterosexually and that subsequently this mode of spread was to prove geographically and numerically far greater a threat to populations. The rate of spread is linked to the presence of co-existent sexually-transmitted diseases, principally of the ulcerating variety.

Studies show that a relatively small pool of infected commercial sex-workers could be responsible for 80-90% of the initial disease prevalence in a community. Numbers of cases of HIV disease have increased exponentially, and in many sub-Saharan countries doubled every 9-12months. This trend has been followed in Southeast Asia and the Indian subcontinent.

Initial reactions amongst politicians to the scourge of HIV, which was known to result in inevitable, usually slow and agonizing death through an end-stage described as Acquired Immune Deficiency Syndrome (AIDS), was to deny the problem. The overlay of sexual promiscuity, and in the West, of weird life-styles, served to *exceptionalize* HIV disease, which has been handled differently from other infectious diseases (especially with regard to counselling). Stress was on confidentiality and anonymity and concerns about abuse of a victim's civil rights demanded private individual counselling prior to HIV testing. This has resulted in isolation of the sufferer, contrary to the prior tradition (as in Africa) of understanding illness as a community problem to be discussed fully within the family and then within the village setting.

Thus the HIV patient has often been secluded and even victimized in rural society and even within the family itself. Many women preferred not to know their HIV status, fearing ostracization, because they have little control over their lives and cannot make plans for the future. With the increased availability of anti-retroviral medication however, the *exceptionalization* of HIV disease has become an anachronism.
In some countries, notably Uganda, the inexorable increase of HIV cases seems to have been reversed, principally through strenuous saturated educational coverage, propagated in the main by non-governmental organizations, and by popular fear of the disease.

The advent of ARV therapy has had a significant impact on HIV disease, even in the late stages. However, this therapy remains exorbitantly expensive long-term for most people in developing countries, although WHO is making strenuous efforts to make low-cost drugs available. Single-dose treatments for antenatal women reduce transmission to the unborn child, after needle-stick injuries, and in rape cases. The emergence of resistant strains, however, remains a problem. The development of a vaccine is still at this stage a dream. Viricidal creams may offer some real hope in reducing transmission.

Thus HIV is a fact of life (and death) in the developing world, and surgeons working there must know its implications.

5.2 Pathophysiology

The causal agent of AIDS is known to be HIV which has two known types (HIV-1 and HIV-2), belonging to the family of primate *lentiviruses* (slow viruses), differing by the former having a *vpu* and the latter a *vpx* gene, absent in the other. There is great similarity with the Simian Immunodeficiency Virus (SIV) strongly suggesting a link between these viruses. HIV-2 is more similar to SIV, and HIV-1 has been found genetically to originate from a chimpanzee species. In conformity with other retroviruses, HIV contains a virus capsid whose hallmark is the enzyme, *reverse transcriptase*. This enables a double-stranded DNA copy of the original genomic RNA to be made in host cells. The viral DNA is thus integrated into the lymphocyte genome. The glycoprotein (gp120) envelope of HIV binds to the glycoprotein (gp41) molecule on the surface of certain thymus-derived T-lymphocytes known as helper/inducer cells. This molecule called CD4 is also found on other cells, such as macrophages, monocytes, and even some antibody-producing B-lymphocytes, as well as in brain cells.

The helper/inducer T-lymphocytes are the kingpins of the immune response: when stimulated by antigen contact, they divide and produce lymphokines (such as *interleukin 2* and *interferon*) which control the growth and maturation particularly of cytotoxic/suppressor T-lymphocytes which have a CD8 glycoprotein molecule.

The ratio of CD4 to CD8 gives a good indication of immunological capability. Early on in HIV infection, the CD8 cell number may rise, but there is an inexorable fall in CD4 cell numbers; in the final stages of disease, the CD8 count will also fall.

Virus replication appears to occur mainly in dividing CD4 cells and these cells divide upon stimulation by micro-organism antigens (at least *in vitro*): thus intercurrent infections may stimulate viral replication. Paradoxically, in the final stages of the disease, when CD4 counts approach zero, there may be little active viral replication. *You can think of the CD4 count as the distance a patient is from death; the viral load the speed with which he is travelling there.*

The extensive genetic variability in HIV isolates and the inherent difficulty of blocking the CD4-HIV binding make vaccine development far from straightforward.

Although HIV core antigen can be detected and viral counts are very useful for monitoring anti-retroviral therapy, these tests are rarely available in the developing world. The most widely used ELISA anti-Immunoglobulin antibody test for HIV infection will only become +ve 6wks to 9months after infection, thus producing a 'window' period when HIV is actually present in serum but *not* detected.

This has serious clinical significance; change in the test from -ve to +ve is known as seroconversion. The accuracy of the test and its sensitivity is high; most incorrect results arise from laboratory or deliberate errors, and if a result is clinically suspicious, you should organize a repeat test, preferably using a different laboratory or a different technique (*viz.* radio-immunoassay) with better specificity. The Western Blot method is expensive, however, and is probably not justifiable in most situations in the developing world.

5.3 Transmission & prevention

The 3 most prolific methods of transmission of HIV in the developing world are:
(1) by sexual contact, dominantly heterosexual,
(2) from mother to baby,
(3) by blood products.

Transmission may also occur through
(4) transplanted tissue,
(5) sharps injuries and splashes.
This may occur between drug users sharing injection needles, especially when 'mainlining' (injecting) themselves with IV drugs. Viral particles have, however, been detected in seminal fluid, and pre-ejaculate fluid, vaginal and cervical secretions, breast milk, tears, urine, and saliva, so caution regarding transmission is wise.

(i) Sexual contact.
As simultaneous sexual promiscuity by men is common, there can be no clearly defined risk group; nonetheless certain groups have significantly higher prevalence rates than others, and therefore a high index of suspicion is justified. Such groups are:
army personnel,
those travelling widely in their employment,
  e.g. *truck-drivers, police, and itinerant salespersons,*
attenders at venereal disease clinics, especially when tested
  +ve for syphilis,
men working away from home,
those with high alcohol intake,
male prisoners (through forced rape),
divorced, separated, or young widowed women,
young widows and widowers.

As, however, the spouses of infected persons are at as great risk, the identification by history and direct social questioning of potential HIV individuals becomes at best difficult and time-consuming. Nonetheless identifying a girl as a virgin is helpful in minimizing HIV as a factor in reaching a diagnosis.

The estimated risk factor of transmission from a seropositive man to woman during a single unprotected sexual exposure is c.0·5-0·75%, but seropositive woman to man 0·25%. (There is a considerable range from 0·1% where the viral load is <1700 copies/ml to 20% where the load is >38500/ml).
The risk is zero if viraemia is undetectable.

The risk increases in a violent sexual encounter such as rape, in the deflowering of a virgin, if ulcerative venereal disease is present (up to a factor x10), if non-ulcerative venereal diseases are present, if an intra-uterine contraceptive device is *in situ* and during pregnancy.
It may be 500 times higher in the phase of acute HIV seroconversion. The risk increases x4-x7 in anoreceptive intercourse, and is further increased when jelly with the spermicide, nonoxylon-9, which breaks down the rectal lining, is used. The risk is also present in oral sex, and with artificial insemination.

A condom (female as well as male) is protective, and reducing menstrual bleeding (by use of the combined pill and depot medroxyprogesterone acetate) will also reduce transmission. Male circumcision also reduces transmission.

Restricting sexual activity to a monogamous marriage without extra partners remains the only certain way to avoid HIV exposure by this route. Therefore you should advocate prenuptial HIV testing, and certainly before any pregnancy is considered.

(ii) Vertical transmission of HIV from mother to baby varies between 15-45% if there are no interventionist strategies used; estimates are that transmission occurs in ⅓ before delivery, in ⅓ during delivery, and in ⅓ after delivery. It seems possible to reduce transmission to 2-3% with the antenatal use of antiretroviral drugs (a single dose of nevirapine appear to be sufficient), arranging delivery by Caesarean section, and avoiding mixing breast feeding with bottle feeding of milk substitutes.

Whilst the adoption of mandatory Caesarean section for HIV-mothers may have theoretical justification, the morbidity and mortality inevitable in such a policy in the developing world outweigh the advantages notwithstanding the costs of screening and surgery. Previous policies of restricting breast-feeding have actually been shown to be harmful, and *are not recommended*.

Other practices, however, reduce risks of transmission: protocols developed to prevent blood exchange from foetus (low-pressure) to mother (high-pressure) in potential rhesus sensitization are applicable up to the moment you clamp the umbilical cord:
(1) Treat infections which disrupt the placental barrier, particularly malaria and toxoplasmosis because these increase transmission of the virus. Malnutrition also allows increased transplacental viral transmission.
(2) Reduce prolonged labour by use of prostaglandins and oxytocin. Treat chorio-amnionitis with antibiotics.
(3) *Avoid external cephalic version and amniocentesis*; clamp the umbilical cord as early as possible. The longer the baby is protected in labour from direct contact with the mother's blood and secretions the better.
(4) *Avoid artificial rupture of membranes* and make episiotomies at the last moment. If membranes are already *ruptured, reduce contact time by use of oxytocin.*

N.B. Foetal scalp electrodes and foetal scalp blood collections are contra-indicated.

(5) Be very careful with instrumental deliveries, preferably using rubber cup vacuum extractors to prevent abrasions of the foetal head; better avoid them altogether. Washing of the vagina with povidone iodine before instrumental delivery or after rupture of membranes is probably a sensible precaution. Rinse babies immediately after delivery in warm water.

(6) During Caesarean Section, try to deliver the foetus with intact membranes; *do not use the scalpel to open the whole thickness of the abdominal wall*, lest the baby is cut. Suctioning of the baby after delivery pushes maternal blood up its nose and is unnecessary; wiping is usually sufficient.

Transmission during breast feeding appears to increase if the mother seroconverts during this time, if breast feeding is mixed with other feeds, and if the nipple is cracked or eczematous, or the baby has mouth ulcers. Abandoning breast feeding implies the ready availability of milk substitutes, rarely the case for the poor in low-income countries, and removes the natural transmission of protective immunoglobulin to the baby. However, expressed breast milk can be pasteurized (kept at 62·5°C for 30mins, or heated just up to boiling and then cooled) to eliminate HIV, as well as Hepatitis B virus (HBV). Supply it then in a small cup rather than in bottles with teats as these are difficult to sterilize properly. Nutrients and micro-nutrients are preserved but IgA antibody activity is lost, and diarrhoea is then a frequent problem. Proper attachment of the baby to the breast and preventing nipple damage also reduces the risk. Heat treatment is not possible for colostrum, however, because it curdles and there is a high viral load in colostrum.

Correct Vitamin A deficiency, which increases the risk of transmission.

N.B. Transmission of HIV from seropositive baby to surrogate breast-feeding mother has occurred, and vice versa from seropositive surrogate mother to baby.

(iii) Transfusion of blood products entails a significant risk (3.6), especially where laboratory testing is unreliable. Because of the window period, apparently safe blood products may actually be contaminated. In order to reduce this risk, encourage long-standing donors whose HIV-ve status can be followed over a considerable period of time (and are therefore unlikely to seroconvert), unlike schoolchildren who may become newly sexually active. Discard blood from a new donor deliberately; accept it only if he tests -ve on a subsequent visit after nine months. Select blood donors on a voluntary basis, thus removing a financial incentive for donation.

The risks from transfusion are cumulative, rising with numbers of units transfused. Furthermore the risk of using products pooled from many donors is also higher; thus *do not use Fresh Frozen Plasma and pooled Platelet Concentrate*. The use of Factor VIII concentrate is likewise risky but may be essential in treatment of haemophiliacs requiring surgery; render it safe by heat treatment.

Use blood transfusion therefore very sparingly; educate anaesthetists concerning the safety of working with suboptimal Hb levels, and learn the appropriate strategies. Various strategies can avoid risks:

(a) Autologous blood.
Take 1L of blood from an adult; treat him with maximal doses of ferrous sulphate for 2wks; then take a further 1l at the same time as transfusing 500ml of the previously collected blood. In this way you can prepare 1500ml (3 units) of blood for elective surgery.

(b) Intraoperative haemodilution.
Take 1l of blood immediately prior to surgery and replace it with crystalloid. The fresh and platelet-rich blood is then immediately available for re-infusion if needed; blood viscosity is also incidentally lowered and this may be an advantage, especially in vascular surgery.

(c) Peroperative blood salvage (Autotransfusion).
Blood from clean traumatic injuries of the chest or abdomen, or from an ectopic gestation, is ideal for this treatment; it can be life-saving. Also, it carries no risk of hepatitis or HIV, and it will be perfectly cross-matched. Autotransfusion is thus very useful.

CONTRAINDICATIONS.
Do not attempt autotransfusion if:
(1) There is an offensive smell when you open the abdomen.
(2) The abdomen is grossly contaminated.
(3) The blood is obviously haemolysed.
(4) A woman is more than 14wks pregnant with a ruptured amniotic sac. (Her blood will be contaminated with amniotic fluid containing large quantities of thromboplastin. If you transfuse this, it could theoretically cause disseminated intravascular coagulation (DIC). Nonetheless you can use blood in a contaminated peritoneal cavity on occasion under antibiotic cover without untoward effect if you are absolutely desperate.

N.B. The presence of fresh clots is not a contraindication to autotransfusion.

THE VACUUM BOTTLE METHOD is the best. Buy vacuum bottles, or prepare them by closing blood-taking bottles containing 150ml 3·8% citrate-dextrose immediately after they have been sterilized, before the steam in them has had time to condense. Clamp a taking set, introduce one of its needles into the abdomen, as if you were doing a 4-quadrant tap, and then put the other needle into the bottle and remove the clamp. To fill the bottle insert another sterile needle connected by way of a heparinized suction catheter to a vacuum pump into the bung. You may be able to collect up to 3l of blood this way. If the vacuum is imperfect, and does not fill the bottle, apply suction with a vacuum (water) pump connected to a sterile needle inserted through the bung.

A U T O TRANSFUSION
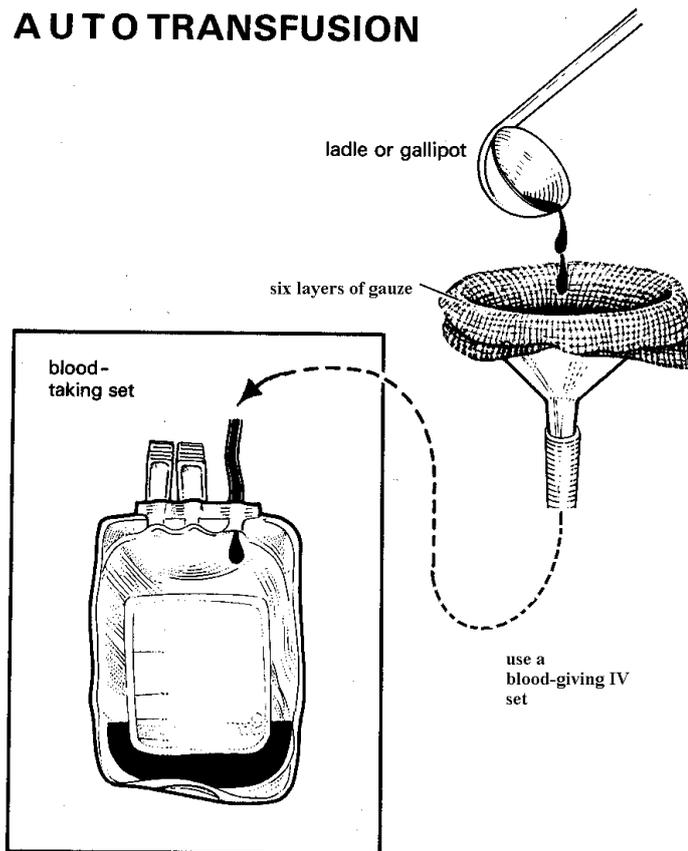
Fig. 5-1 AUTOTRANSFUSION using a funnel. This is also useful if the patient has a ruptured spleen. Use 6 large pieces of gauze, and collect the blood through a blood-giving IV line into an empty citrated blood-collection unit.
Kindly contributed by Stephen Whitehead of Maua Hospital, Kenya.

THE SOUP LADLE METHOD is less satisfactory, but is useful when you cannot use a vacuum bottle because there are too many clots. Keep the equipment (5-1) ready sterilized. Put the patient into 15° head-down position, make a small opening in the peritoneal cavity to begin with, and be prepared to catch the blood, as it escapes, with a sterilized stainless steel soup ladle or gallipot. Then complete the incision and ladle out the rest of the blood. The right hypochondrium may be the easiest place to collect it. Pour it through a small metal funnel, and collect it through a blood-giving set into empty blood transfusion packs pre-primed with citrate anticoagulant. The filter in the drip set will remove smaller clots.

   N.B. You can also use a filter made of 6 layers thicknesses of gauze *but beware that if the gauze is contaminated by glove powder, the autotransfused blood may kill the patient!*
You can also squeeze blood out of soaked laparotomy pads after they have been agitated in saline.
Alternatively, you will find a sump useful. This is a conical vessel with a handle and holes towards its tip. Insert it deep in the abdomen; blood will flow in through the holes and can be sucked out.

   CAUTION !
(1) Either transfuse the blood immediately, or throw it away.
(2) *Do not use it for someone else*.
(3) Use prophylactic antibiotics

There are expensive commercial autotransfusion machines available, but they all work on the system of (1) aspirate, (2) anticoagulate, (3) filter, (4) centrifuge, (5) wash, (6) re-infuse.

N.B. Directed blood transfusion (where blood is collected from relatives or friends) has almost all the pitfalls of undirected transfusion.

   (iv) Transplantation (of kidneys, allograft skin etc) carries the risk of HIV transmission.

   (v) Sharps injuries and splashes.
Risks of transmission of HIV to health personnel are small but real. Use routine double-gloving for surgical procedures, especially when you may encounter sharp pieces of bone, or use wires, drills or chisels; some prefer to use a glove half a size greater on the outside. The use of different coloured gloves may highlight damage to the glove material more easily. Wear a non-sterile glove under a sterile one if economy dictates. (*Do not use recycled gloves for operating*, except as the first in double-gloving, unless economy dictates!). Long arm gloves are useful for surgery involving deep ingress into the abdominal cavity. Special Kevlar gloves are useful (and re-usable) as the interior glove because they cannot be penetrated by needles or blades: this makes their initial high cost worthwhile. They are however cumbersome to work with. Sterile cotton gloves can be worn outside the latex glove where wires are used in Orthopaedic surgery; the wire will snag on the cotton before tearing the latex.

Blood splashes are also important especially to the open eye (with risk rates estimated at 1·5%). Use protective eye-wear therefore, especially where spraying is likely, *e.g.* orthopaedic drilling. However, wrap-around plastic goggles are inconvenient for those with spectacles, and attachment of sides to the spectacles is a reasonable alternative. Masks also help protect the mouth from splashes.

Careful operating is, however, probably more important than trying to prevent injury. Avoid operating if possible when you are over-tired! Likewise drug users can avoid HIV transmission by using unused sterile needles, and discarding these carefully.

The estimated risk of seroconversion with a penetrating hollow needle-stick injury is 0·3% and with a solid needle is 0·03%. Reduce the use of cutting needles (you can close an abdomen readily using a blunt-ended needle) and preferably employ a no-touch surgical technique. Introduce rigorous adoption of theatre routines: *do not hand sharps from scrub-sister to surgeon and vice-versa.* Create a neutral zone where sharps are placed in a receiver by only one person at any given moment. *Do not use hands as retractors, and the surgeon's fingers to guide needles* (2.3). Draw up multivial solutions using an unused sterile needle. Glove up for venepuncture and handling blood samples.

Most injuries to health-care workers arise from careless handling of sharps:

| Recapping of needle	40%
Improper disposal of sharps	32%
Contamination in open wound	25%
Other	3%

LOW COST SHARPS CONTAINER
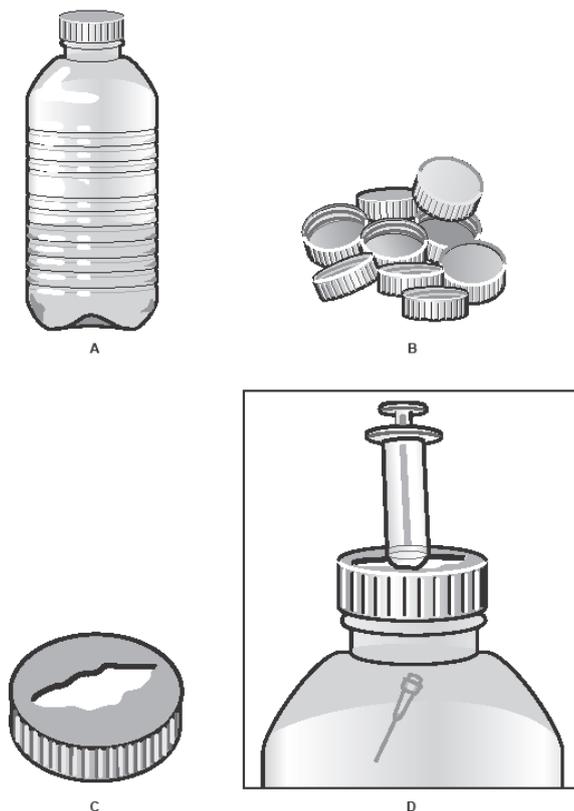
Fig. 5-2 LOW-COST SHARPS CONTAINER WITH NEEDLE REMOVAL DEVICE.
A, Ordinary plastic bottle. B, Bottle tops. C, Bottle top with hole cut out.
D, Syringe inserted through hole and needle eased off inside bottle.
After Onayade AA, Omotoso AO, Olafimihan VB. Hospital biohazard control: low-cost device for safe collection and disposal of hypodermic needles. Tropical Doctor (2006):36(4)215.

Discard needles uncapped; separate and dispose of other sharps (*do not leave them for someone else*) in a dedicated, labelled, non-breakable, puncture-proof, watertight container with a keyhole opening large enough but too small to admit a hand. Fix this to a wall, and empty it when ¾ full, and incinerate it. *Do not over-fill the container.* (You should probably avoid expensive specially manufactured containers as they may be utilized for another purpose by cleaners). A useful home-made container can be made from an ordinary mineral water bottle with its screw-top pierced with an elliptical hole (5-2A); thrust a needle attached to a syringe through this hole and with minimal manipulation pull the syringe back, thus detaching it from the needle (5-2D). Put non-sharps in other containers in order not to waste the space in the sharps container; *do not separate needles from syringe with your fingers*!

Adopt a hospital sharps-injury policy in order to advise *all* health workers on precautions and action to take after exposure, depending on facilities available. Discipline staff not taking precautions. Introduce a post-exposure prophylaxis/treatment policy if you don't already have one in your hospital. Remember to wash the part injured by a needle-stick immediately, and cleanse it with betadine.
Use the low-cost de Montfort medical waste incinerator.
In the laboratory, heat-treat serum at 56ºC for 30mins before testing; pipette solutions using a teat *not your mouth!*

A practice that assumes every patient is a HIV risk, and all blood may be contaminated, is likely to result in far fewer accidental seroconversions than one that attempts to identify individual high-risk patients.

The HIV+ve health worker is extremely unlikely to transmit HIV to patients except sexually; the risk of a surgeon passing HIV to a patient has been estimated at 1:800,000.

5.4 Sterilization

Wear gloves when cleaning spills. Dilution by washing is important. If alcohol is used, wipe the surface several times because alcohol evaporates. Establish the rule, **"You spill it, you clean it."**
Dispose contaminated materials safely; *do not put them on a rubbish tip* where they may be scavenged!
Ordinary laundry is effective for cleaning soiled linen after thorough soaking.

Chemical disinfection is acceptable only for instruments such as endoscopes which cannot tolerate heat. Pull out and clean light carriers and biopsy carriers, and wash internal tubes thoroughly before placing them in antiseptic. These may be:
 (a) Chlorine-releasing solutions
    * (readily neutralized by blood or tissue),
 (b) Ethanol 70% (for 15mins):
    (higher and lower concentrations are less effective),
 (c) Isopropyl Alcohol (2-propanol) 70% (for 15mins),
 (d) Povidone Iodine 2.5% (for 15mins),
 (e) Formaldehyde 4% (for 30mins),
 (f) Alkaline-buffered Glutaraldehyde 2% (for 10mins)
    (*Cidex,Asep,Omnicide Tegodor*) effective for 14days, once prepared, if kept away from direct sunlight,
 (g) Hydrogen Peroxide 6% (for 10mins),
 (h) *Virkon* (balanced blend of peroxygen compounds, surfactant and organic acids in inorganic buffer at pH2.6, sold as a stable powder, is non-corrosive, non-bleaching, non-toxic and not a transport hazard: a fresh 1% solution is used for 30mins).

  CAUTION!
The following solutions are NOT recommended: Spirit Solutions <70%, especially <50%, Cetrimide (*Cetavlon*) or Chlorhexidine (*Hibitane*), Formalin 0.1%, Quarternary Ammonium Compounds (*e.g.* Dettol, Roxenol, Flavine etc).

* Chlorine-releasing solutions are excellent disinfectants.

Their power is expressed in 'available chlorine': 1% = 10g/l = 10,000 ppm (part per million) = 3·33 chlorometric degrees

N.B. Chlorine corrodes iron and stainless steel, so these disinfectants must not be stored in stainless steel containers; equipment is easily corroded and should be rinsed well after disinfecting.

Sodium Hypochlorite solutions (Liquid bleach, Javel) are unstable:

Neat disinfectant (domestos, Chloros, Sterite)	contain c.100,000 ppm
Strong hypochlorite solution BP	contains >80,000 ppm
Most supermarket brands	contain c.50,000 ppm
Milton	contains c.10,000 ppm

HIV is inactivated by 5,000 ppm solution in 1 minute, by 50ppm in 10mins; at this low dilution it is *very* unstable so must be freshly made, used and discarded.

Calcium Hypochlorite (70% available chlorine) and Bleaching Powder (35% available chlorine) sold as tablets, granules or powder, both decompose gradually if not protected from heat and light.

Sodium Dichloroisocyanurate 0·5% (NaDCC: 60% available chlorine) and Tosylchloramide sodium (Chloramine T: 25% available chlorine) sold as powder or tablets, are comparatively stable.

Use solutions of 1,000 ppm for general disinfection of wards, theatres and laboratory benches.

Clean contaminated surfaces with 5,000 ppm which is left in contact for 30mins before rinsing off.

Recommended	dilutions	of chlorine-	releasing agents
	Available Chlorine	Clean condition (*e.g.* cleaned medical equipment)	**Dirty condition** (*e.g.* blood spills, soiled equipment)
Available Chlorine required		0·1% (1g/l, 1000pcm)	0·5% (5g/l, 5000pcm)
Dilution			
Sodium Hypochlorite Solution	5%	20ml/l	100ml/l
Calcium Hypochlorite	50%	1·4g/l	7·0g/l
NaOCC	60%	1·7g/l	8·5g/l
NaOCC-based tablets	1·5g per tablet	1 tablet/l	4 tablets/l
Chloramme	25%	20g/l	20g/l

RECOMMENDED DILUTIONS OF DISINFECTANTS
WHO AIDS Series (2), Guidelines on Sterilization and High-Level Disinfection Methods effective against HIV. Geneva 1988

Standard autoclaving at 121ºC at 1 kg cm^2 or use of a hot air oven at 170ºC for 2hrs eliminates HIV (as it does the hepatitis B virus, which is much more easily transmitted). Thus place all surgical instruments which tolerate heat, and all reusable surgical sundries in disinfecting fluid and then clean them (someone wearing non-sterile gloves) free of blood or tissue and then sterilize them by heat.

5.5 Testing & visual recognition

Combo kits are now available which detect IgM as well as IgG, and so reduce the *window period* when a common screening test may show -ve in the presence of early infection (and high risk of transmission owing to high viral loads).

As most erroneous results are from laboratory errors rather than deficiencies of the test, repeat surprise results. Repeat confirmation of -ve results likewise for safety, after 3-6 months. Oral tests are now available.

Though the theoretical model of insisting on counselling for HIV tests as promoted in the First World is commendable, it may not be practical in the developing world situation where resources are few and trained manpower limited. It has been shown that a short description of the facts of HIV disease without full discussion of the social implications will lead to fear and despair rather than a positive attitude to the disease; thus limited counselling may be more detrimental than none at all.

If tests are only done when a patient has been fully counselled, many patients will go untested. Furthermore a possible HIV-ve result may thus be denied a patient who is too scared to ask for a test, assuming as many do in areas of high HIV endemicity, that any severe illness is probably the dreaded disease that leads to certain early death. To put pressure on a patient to make up his mind on whether or not to have a test which may reveal a fatal illness is like asking a patient with a pathological fracture whether he wants an X-ray to be done if it might reveal a malignancy. Indeed even the counselling becomes something with a stigma attached for the patient.

In areas of high endemicity, an HIV test may be important to exclude HIV infection as a diagnosis, rather than confirming the presence of the disease, and thus giving a patient hope when he had long given up ideas of recovering from illness.

Where HIV is prevalent, and testing difficult or impossible, an awareness of the clinical presentation of HIV-related disease is essential. As any body system can be affected; HIV does not manifest itself usually by a single identifying pathology. Therefore look for the usual significant tell-tale signs in patients, especially to give clues as to the underlying pathology of the presenting condition. *HIV has made new diseases common, and changed the diagnostic spectrum.*

Certain conditions have a very high association with HIV, whereas others less so; it is the sum total of the clinical picture that is important. Because HIV affects any system, always take a meticulous general history and make a full examination.

Perhaps the most striking features of untreated HIV patients recognizable before any medical interview is undertaken are the following (seen obviously mainly in the face):
(1) Facial rash, typically seborrhoeic dermatitis,
(2) Lymphadenopathy,
(3) Herpes Zoster scarring (5-3),
(4) Parotid swelling (5-12),
(5) Unilateral ptosis (5-14),
(6) Weight loss; hair changes & premature ageing.

Where you see these features, concentrate the remainder of the medical history and examination for diagnostic purposes on further HIV-related conditions. Although, of course, patients with HIV may have non-HIV-related illness, inherently it is more likely that the illness is indeed HIV-related. For example a patient with clear signs of immunosuppression complaining of headache is much more likely to have HIV-related causes of headache than a brain tumour.

Gradation of severity of symptoms and signs is related to dropping CD4 counts, but this test is not available in most hospitals, although you can gauge it by the total lymphocyte count.

5.6 New pathologies & new strategies

In every area, HIV has an impact; not only are new pathologies seen, but many well recognized problems become more severe. We provide a brief overview here, but detailed discussion is in the main body of the text. Of note is that prior to treatment, there may be several diseases present simultaneously with HIV. Consequently one symptom may be caused by different pathologies, and further, different symptoms may have separate pathologies. So in HIV disease, Occam's famous razor, *"Numquam ponenda est pluralitas sine necessitate"* ('Plurality must never be posited without necessity') is inevitably blunted.

A. SKIN DISEASES (34.4)
In the skin, HIV directly attacks antigen-presenting dermal dendritic cells and Langerhans cells, which take up antigens, process them and present them to unexposed T-lymphocytes in lymph nodes, after which they themselves migrate to the skin to exert a protective immune effect. Impairment of this system leads to microbial invasion and malignant change. Furthermore, contact between HIV-traumatized dendritic cells and T cells during antigen presentation causes a surge in HIV replication.

A fine facial rash is virtually diagnostic; new skin affections in HIV disease are very common, found in >50% of HIV patients presenting in hospital, and almost in 100% in the terminal stages of the disease. Idiopathic maculopapular eruptions are frequent and pruritic; these papular dermatoses must be distinguished from urticaria and lesions due to insect bites which occur on exposed skin. (Some of these may respond to dapsone; they do not respond to steroids). Itching is often severe and needs a sedative or antihistamine.

Opportunistic infections, such as tinea, candidiasis, and scabies, especially crusted and Norwegian types, may be florid and widespread.

Bacterial skin infections, especially with *Staphylococcus aureus* are more common. Likewise allergic skin reactions are more common, and may be florid and life-threatening: frequent culprits are thiacetazone, sulphonamides, streptomycin, and pyrazinamide.

Some dermatitis may be secondary to other conditions, *e.g.* HIV-related malnutrition leading to pellagra. Some malignant skin conditions may show a more aggressive pattern: this has been reported with malignant melanoma. Several skin ailments are common with high HIV association, with *Herpes Zoster* having a high predictive value, and *Herpes Simplex* on the vulva and buttocks; eosinophilic folliculitis has only been seen in HIV+ve patients, particularly where the CD4 count is <400/µl.
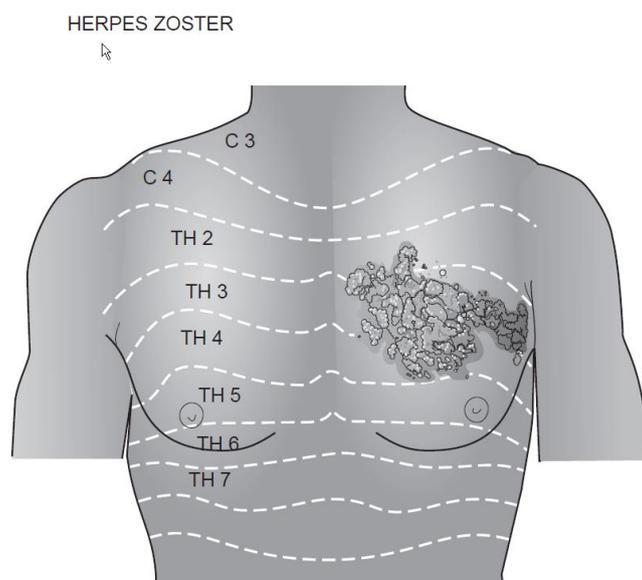
HERPES ZOSTER

Fig. 5-3 HERPES ZOSTER. Blisters, classically ending in the midline

Increased photosensitivity to sunlight and therapeutic irradiation is common.
Typical manifestations of skin disease (34.4) are:
> **Aggressive psoriasis** (5-7),
> **Bacillary Angiomatosis**,
> **Candidiasis**,
> **Condylomata** (5-13),
> ***Cryptococcus* ulcers**,
> **Eosinophilic folliculitis**,
> **Florid *tinea corporis***,
> ***Herpes zoster*** (5-3),
> **Kaposi sarcoma.** (5-4,11),
> ***Molluscum contagiosum*** (5-4),
> **Multiple *herpes simplex***,
> **Pyoderma gangrenosum**,
> **Seborrhoeic dermatitis** (5-6),
> **Stevens-Johnson syndrome** (5-5).

It is probable that some of these skin infections destroy skin grafts, especially *Herpes Zoster* and *Molluscum contagiosum*.

Pressure sores are, alas, all too common in the debilitated advanced HIV+ve patient; these are often deep and resistant to healing: prevent them! Gloves, filled with water and tied, make excellent soft supports.

Malignant melanoma in white people is 3 times as common in HIV disease.

## MOLLUSCUM CONTAGIOSUM
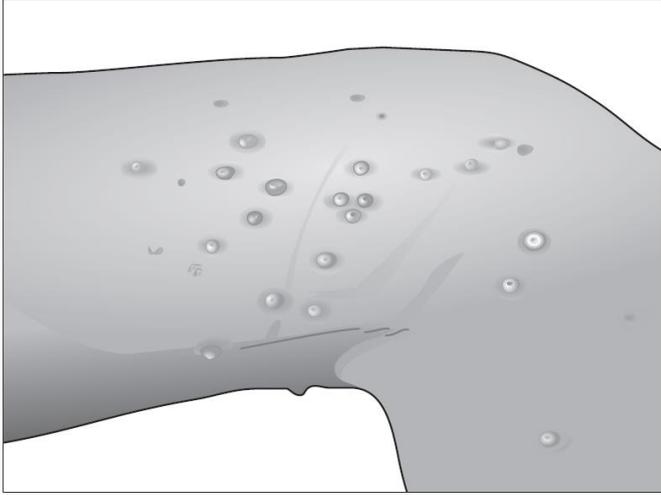
Fig. 5-4 MOLLUSCUM CONTAGIOSUM, producing multiple typically punctuate lesions.

STEVENS-JOHNSON SYNDROME
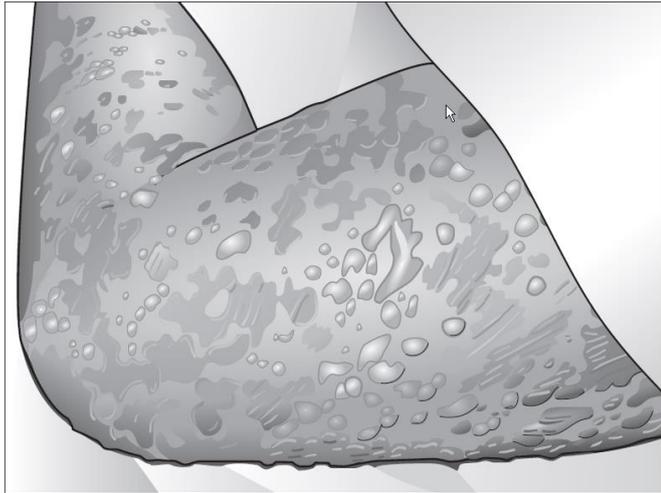
Fig. 5-5 BULLOUS EPIDERMOLYSIS (Stevens-Johnson syndrome), is a widespread blistering reaction that looks like a burn wound.

SEBORRHOEIC DERMATOSIS
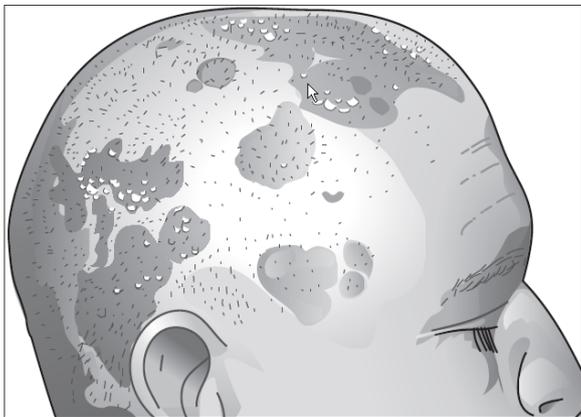
Fig. 5-6 SEBORRHOEIC DERMATOSIS, which usually affects scalp, groins, and perineum, but can be widespread.

PSORIASIS
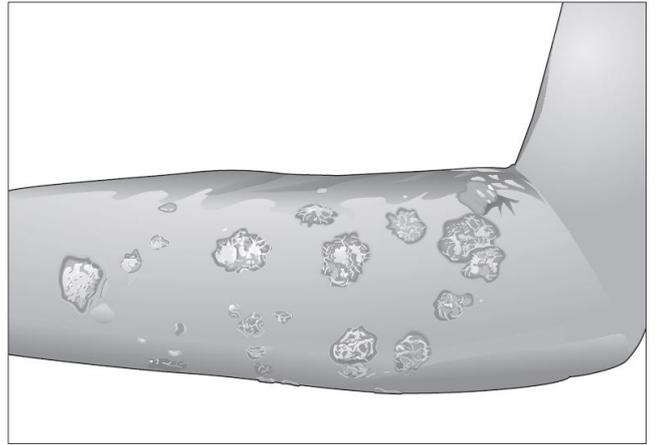
Fig. 5-7 AGGRESSIVE PSORIASIS.

B. SOFT TISSUE DISEASE

Kaposi sarcoma (KS) in its aggressive widespread form is now recognized as virtually diagnostic of HIV disease (34.10).

CLASSICAL KAPOSI SARCOMA

Fig. 5-8 CLASSICAL KAPOSI SARCOMA, typically on the leg, producing violet nodules and cutaneous ulceration.

Cellulitis (6.22), arising without history of diabetes mellitus or trauma, is a common manifestation of HIV; the causative organisms remain *streptococcus* and *staphylococcus* and the disease responds to intravenous penicillin or cloxacillin, rest and elevation of the affected limb. There is, however, frequent skin necrosis requiring debridement and subsequent skin-grafting. This may occur with *pseudomonas aeruginosa* infection where the result is known as ecthyma gangrenosum. Facial cellulitis is potentially life-threatening owing to possible spread of organisms to the brain through the cavernous sinus, and requires aggressive intravenous antibiotic therapy.

NECROTIZING FASCIITIS
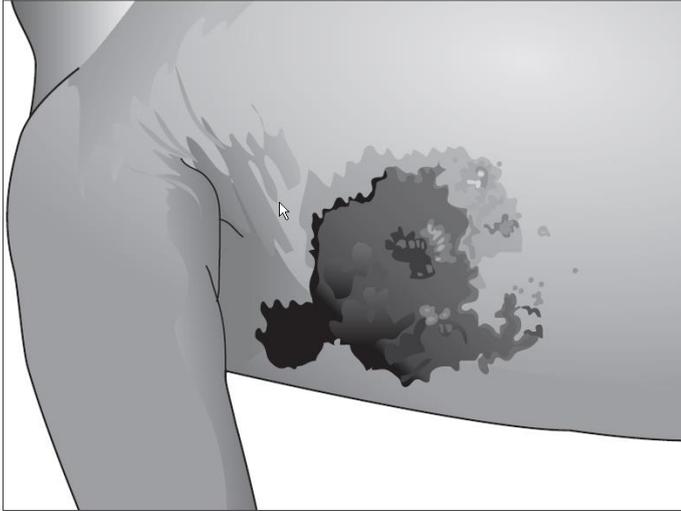
Fig. 5-9 NECROTIZING FASCIITIS, which is classically on the scrotum, but can appear in the perineum, abdominal wall, neck, limbs or indeed anywhere.

Necrotizing fasciitis (5-9, 6.23), describes soft tissue infection initially remaining hidden until the blood supply to the skin is affected by increasing oedema and inflammation; thereupon there is rapidly advancing necrosis, if there is excessive collagenase production by haemolytic *streptococci* or *staphylococci* and *peptostreptococci*. The scrotum (Fournier's gangrene) and abdominal wall (Meleney's gangrene) are common sites, but you may also see necrotizing fasciitis associated with HIV in the limbs and neck. This may occur in infants as well as adults.

Pyoderma gangrenosum represents a very painful necrotizing non-infectious ulceration, especially in a non-healing wound, often associated with fever. This responds to a short course of prednisolone 60mg/day (if the CD4 count is >50/μl), application of zinc oxide cream and maybe dapsone. *Debridement makes it worse!*

Recurrent infections and abscesses (6.2), multiple and frequently recurring in skin, and soft tissue are also typical in HIV disease; standard methods of treatment are effective, but attention to every focus of sepsis is essential. Pus swab microscopy is useful, though the causative organism is most often staphylococcal, it may not be so and is sometimes Gram-ve. *Discourage the use of antiperspirant 'roll-ons'* because these may clog up skin pores causing abscesses.

There is chronic staphylococcal carriage with decreasing immune competence, and therefore colonization of foreign bodies such as catheters is high. The incidence of post-operative wound infections increases dramatically in HIV+ve patients, especially if the CD4 count is <200/μl.

Abscess formation, especially *de novo*, in normally clean anatomical sites should give rise to suspicion of HIV disease; in this category are breast abscesses in non-lactating women (6.13), muscle (pyomysositis) (7.1), thyroid (6.12), abdominal wall, penile (6.21) and retroperitoneal abscesses (6.15). Submandibular and neck abscesses (6.11) are often related to pre-existing lymphadenopathy and may be tuberculous.
Pressure sores often arise from the combination of inertia, cachexia and neuropathy in HIV disease.

Leiomyosarcomas in children are unusual lesions noted to be associated with HIV and specifically to exposure to Epstein-Barr virus. The lesions occur subcutaneously, in the respiratory and gastro-intestinal tract, and even in the kidney. They appear not to be common in Africa to date.

Muscle atrophy is frequent in debilitation; specific wasting syndromes are also seen with rises in CPK levels and increased numbers of macrophages in muscle biopsy specimens.

Lipodystrohy is a generally abnormal degeneration of fatty tissue, seen in advanced HIV disease, where fat is lost in the extremities, buttocks and face (especially in men) and is laid down in the neck, abdomen, back and breasts, (especially in women). This is not so well-recognized in poor-resource settings where malnutrition and HIV-related Slim disease are so common, and the condition appears to be related to the length of time on antiretroviral therapy. There is an associated tendency to type 2 diabetes mellitus. No specific therapy has yet been identified.

Other rare malignancies found are embryonal tumours, and Merkell cell carcinoma.

C. LYMPHADENOPATHY (17.1)

Persistent generalized lymphadenopathy has long been recognized as one cardinal feature of HIV disease and represents significant immunosuppression as related by depressed CD4 counts; the presence of epitrochlear lymphadenopathy is virtually diagnostic of HIV affliction.

Typically lymph node enlargement is symmetrical, with small rubbery nodes palpable; these show follicular hyperplasia. Cystic degeneration often occurs, especially in the parotid and submandibular regions. Where nodes are larger, non-symmetrical, matted and firm, other pathology is usually found, principally tuberculosis, Kaposi sarcoma, or lymphoma. These are usually large B cell anaplastic, Burkitt, or aggressive Hodgkin (Grade II) types.

Histoplasmosis in Latin America, *leishmaniasis* in South America and infection with *penicillium marneffei* in the Southeast Asia are increasingly common associations of lymphadenopathy and hepatosplenomegaly with HIV. In children with HIV, BCG immunization produces a lymphadenitis.

D. ORAL DISEASE

Oral candidiasis (5-10) is a very well-known manifestation of HIV disease, which may present in erythematous, pseudomembranous, hyperplastic forms or angular stomatitis.

ORAL CANDIDIASIS
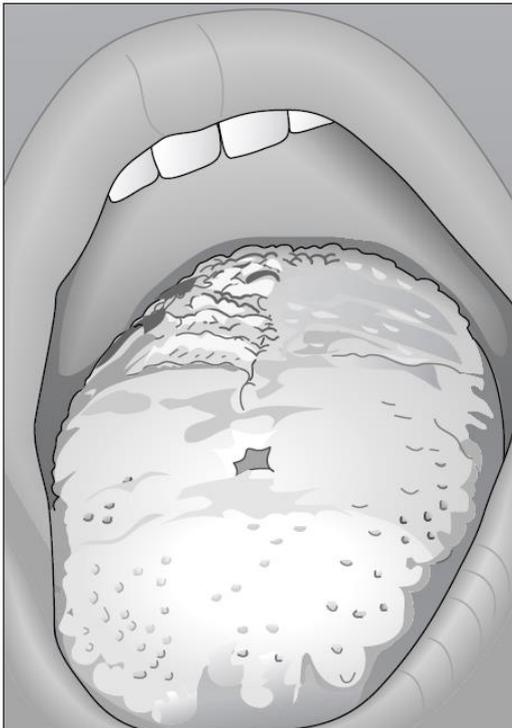
Fig. 5-10 AGGRESSIVE ORAL CANDIDIASIS, often extending into the pharynx and oesophagus.

White warty projections (hairy leucoplakia) occurring particularly on the lateral aspects of the tongue and cheeks are diagnostic of HIV disease.

Periodontal disease is common: linear gingival erythema worsens to necrotizing ulcerative gingivitis and periodontitis. Advanced necrosis may lead to external ulceration on the cheek, or even to cancrum oris (31.5). In these cases the demarcation of necrosis is usually clear.

Herpetic ulceration of keratinizing epithelium is common.

Recurrent aphthous ulcers are more severe and long-lasting. Some may be due to *histoplasmosis.*

Tonsillitis is common and severe, often with ulceration, either in combination with generalized lymphadenopathy or alone. Development into a tonsillar abscess is not uncommon (6.7).

Oropharyngeal carcinoma is 3 times as common with HIV disease.

Kaposi sarcoma (31.8) lesions on the palate or gums (5-11) are manifestations of systemic gastro-intestinal involvement. Non-Hodgkin Lymphoma is also frequently seen.

KAPOSI SARCOMA ON THE GUMS
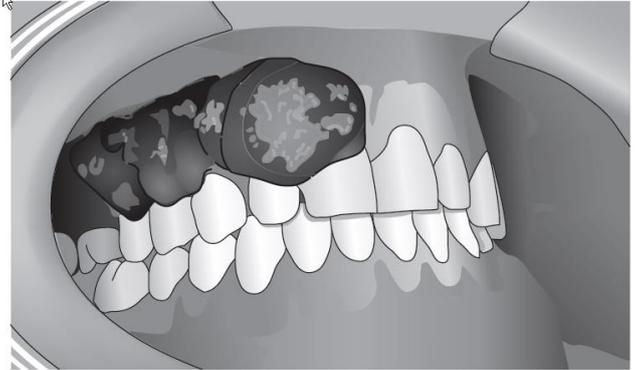
Fig. 5-11 HIV-RELATED KAPOSI SARCOMA, typically on the gums or palate: (*remember always to look inside the mouth!*)

E. NASAL DISEASE

Recurrent rhinitis and sinusitis are the consequences of mucociliary dysfunction in the nose and sinuses, with increased atopy, often complicated by bacterial or fungal infection (the latter if CD4 counts are <50/μl).
Nasal tumours are usually lymphomas or Kaposi Sarcoma.

F. EAR DISEASE

Hearing loss of both sensineural and conductive types can occur. There may be direct central neurological damage, effects of HIV directly on the VIIIth cranial nerve, but the causes below are more common. However, *do not forget that anti-TB drugs and ARVs may be directly ototoxic.*

Acute otitis media, especially with effusion, owing to obstruction of the Eustachian tube by lymphadenopathy, is frequent and often recurrent, and may result in rupture of the eardrum. Almost all HIV+ve children have had at least 5 episodes by the age of 5yrs, the frequency being related to the drop in CD4 count.

Otosyphilis leading to sensineural hearing loss occurs often suddenly with rapid progression in one or both ears: it appears that HIV disease may activate or accelerate pre-existing syphilis.

Otalgia and facial palsy (Ramsay Hunt syndrome) is caused by *Herpes zoster* affecting the geniculate ganglion; the herpetic rash appears in the ear, and the facial palsy never recovers.

Otitis externa is often florid with necrosis, and may be accompanied by invasive fungal infection.

G. SALIVARY GLAND ENLARGEMENT (17.5)

Parotid enlargement is a typical early sign of HIV disease; its cause is varied, including lymphadenopathy (as part of generalized lymphadenopathy), salivary and extraparotid lympho-epithelial cyst formation, and lymphocytic infiltration (due to direct infiltration by CD8 lymphocytes). This may represent a beneficial response to HIV infection, and patients with salivary gland enlargement seem to experience slower progression of the disease. Frequently, unilateral parotid swelling is followed some time later by swelling of the contralateral side.

PAROTID SWELLING

Fig. 5-12 PAROTID SWELLING, often bilateral, of cystic soft texture.
N.B. Nasogastric tube only in situ to help nutrition because of orophayngeal and oesophageal candidiasis.

H. EYE DISEASE

Keratitis is a severe, rapidly deteriorating infection involving the cornea caused by either: bacteria, fungi, *microsporidia, Herpes simplex,* or *Herpes zoster*. The cornea is affected in the latter through the nasociliary branch of the ophthalmic division of the Vth cranial (trigeminal) nerve. Progress occurs to multiple small dendritic and then geographic ulceration and frequently to perforation. Healing by scarring may give rise to iris adhesions leading to glaucoma, and inevitably corneal opacification. Once perforation occurs, however, or if a staphyloma develops, the eye is lost.

Bacterial conjunctivitis comes as acute or subacute infection, either staphylococcal or gonococcal.

Conjunctival carcinoma (28.15) was soon found as a more frequent pathology in Uganda, being first described in Guadeloupe as probably related to HIV, having been noted as an oddity much earlier. *(This pattern mimics the story of Kaposi Sarcoma).* There appears to be an increased susceptibility to ultraviolet light in the presence of human papilloma virus-16 infection.

A small lesion with an irregular surface 2-5mm in diameter appears on the medial side of the limbus usually, spreading onto cornea and underlying sclera. Recurrence after excision is fairly common. Where tumour extends into the sclera, resulting in necrotizing scleritis, the eye is lost.

Kaposi sarcoma appears as a slightly raised pigmented lesion found on the eyelid, conjunctiva or inside the orbit. This may be isolated or multifocal; recurrence after treatment is usual.

Molluscum contagiosum consist of raised umbilicated lesions; when they affect the eyelids, they may become large and numerous; an associated follicular conjunctivitis may occur due to viral shedding.

Cytomegalovirus (CMV) retinitis is the most common cause of impaired vision in HIV patients: in 30% it is bilateral; early signs are narrowing of the retinal vessels, resulting in perivascular exudation and haemorrhage prior to retinal infarction. CMV is common in those patients who have had TB; it does not appear to occur if Herpes Zoster was contracted earlier. Toxoplasma is a rarer cause of chorioretinitis.

Keratoconjunctivitis sicca (extreme dryness of the conjunctiva), reminiscent of the Sjøgren syndrome, occurs in HIV patients, and in particular in association with the Stevens-Johnson syndrome, and toxic epidermal necrolysis.

Diffuse lymphocytosis syndrome occurs as a malignant condition where there is perivasculitis of retinal vessels and lacrimal gland involvement.

I. CARDIOPULMONARY DISEASE

Cardiomyopathy occurs, often with sudden dramatic cardiac collapse: its aetiology is multifactorial.

Spontaneous pneumothorax (36.1) occurs especially in *pneumocystis carinii* pneumonia, which accounts for up to 60% of pulmonary infection in HIV disease. This occurs frequently in conjunction with *cytomegalovirus.* Other infections in the lung are mainly with bacterial pathogens and *mycobacterium*: in low-and middle-income countries, tuberculosis is extremely common as a manifestation of HIV disease. Pleural effusion is a common consequence, and empyema thoracis (9.1) likewise.
However, not all effusions are due to tuberculosis: they may be secondary to lymphoma, Kaposi sarcoma, or serious bacterial infection.
Open thoracic surgery is fraught with serious pulmonary complications and is ill-advised.

Tuberculous pericarditis and pericardial effusions (9.2) are common.

J. OESOPHAGO-GASTRIC DISEASE

Oesophageal candidiasis. Oral candidiasis (5-10, 30.4) is a very frequent manifestation of immune deficiency. Infestation with candida may spread further into the pharynx and oesophagus, where if very copious will give rise to symptoms of dysphagia. It may be absent in the mouth though present in the oesophagus! Complete oesophageal obstruction can occur.

Diffuse oesophagitis may be due to *herpes simplex*, and result in ulceration; discrete ulceration is more likely due to *cytomegalovirus*. There may be profuse haemorrhage. Some of these ulcers are, however, idiopathic. They often result in strictures.

Tuberculosis may affect the oesophagus without being present elsewhere; a broncho-oesophageal fistula may result; the oesophagus is too friable to attempt stenting in this circumstance.

K. THE ACUTE ABDOMEN

(1) PERITONITIS (10.1)
You will see the causes of peritonitis as in HIV-ve patients; HIV-positivity does not of course necessarily imply an HIV-related pathology as the cause. Indeed some common causes of peritonitis, such as gynaecological pelvic inflammatory disease (PID), are more common and more severe in HIV+ve patients. Likewise pelvic abscesses (from any cause, but especially PID) are more common and more extensive.

Nonetheless you may see HIV-related pathologies frequently; these include:
   Primary peritonitis: most common,
   Spontaneous bowel perforation, especially in the distal
      ileum (usually due to *CMV*) or colon,
   Tuberculous peritonitis (16.1) in the following forms:
      Multiple peritoneal seedlings with ascites,
      Tuberculous mesenteric lymphadenopathy
         (with or without ulceration),
      Ileocaecal tuberculous mass (Tuberculoma),
      Tuberculous colitis (mimicking ulcerative colitis),
      Tuberculosis of Fallopian tubes and ovary,
      Abdominal wall sinus.
   Cryptococcal peritonitis, multiple superficial small white
nodules seen on the omentum and serosal surfaces,
   Mesenteric thrombosis (12.14), usually a venous infarction,
   Colitis (in adults), from enteropathic *E. coli* or *CMV,*
mimicking amoebic colitis,
   Necrotizing enterocolitis (in adults and infants beyond the
neonatal period;10.4),
   Acalculous cholecystitis (caused by *cryptosporidium, CMV,
microsporidia,* lymphoma or KS).

In late stages, the gallbladder may perforate, but perforations may be multiple and small with inflammatory exudation.

Other HIV-related conditions may give rise to severe abdominal pain:
   HIV-pancreatitis (15.11,
   Severe HIV-cystitis,
   Retroperitoneal abscess (6.15),
   Necrotizing fasciitis of the abdominal wall (6.23),
   Abdominal wall abscess,
   Intestinal wall haemorrhage from Kaposi sarcoma
      (mimicking colitis).

There may be a complex mass of adhesions with all of the above, including bowel perforation. Of course tuberculosis may affect any abdominal organ, including the pancreas, liver and spleen. The classic 'doughy' abdomen occurs in c. 50% of cases.

An ascitic tap will only demonstrate AAFB's in 25% of cases, but a raised adenosine deaminase level helps to confirm the diagnosis. However in areas of high endemicity, a high lymphocyte count in the ascitic fluid would be sufficient to justify TB treatment.

(2) INTESTINAL OBSTRUCTION (12.2)
Causes of intestinal obstruction may again be non-HIV related, but specific HIV causes are:
   Tuberculous adhesions/mass/intestinal stricture,
   Lymphoma of small bowel,
   Kaposi Sarcoma of small and large bowel,
   Mesenteric Lymphadenopathy,
   Intussusception (12.7).

Tuberculous adhesions are often thick and unyielding (and may be detected as septa on ultrasonography in an ascites-filled abdomen). A tuberculous mass usually occurs in the right iliac fossa but any site may be affected; an intestinal stricture occurs in the ileum in 70%, in the jejunum in 15%, and in both in 15%.

In a few cases, the signs of intestinal obstruction may mimic a paralytic ileus thought to be related to an HIV-neuropathy.

L. ABDOMINAL MASS

Lymphoma or tuberculoma is likely to be the diagnosis in a younger patient; tuberculous abscess of the liver or spleen are not rare, but common local conditions should still head the diagnostic list in HIV+ve patients, especially where, as in schistosomiasis, HIV appears to have little impact on the disease pattern.

Do not assume a right iliac fossa mass to be a walled-off acute appendix! Whilst the diagnosis of an abdominal mass follows standard principles, *keep HIV-related conditions in mind*.

M. HEPATO-BILIARY DISEASE

Liver abscess (15.10), especially tuberculous, is not uncommon.

Hepatitis is common: either with *hepatitis B* or *herpes* virus, *cryptococcus,* or induced by drugs. Granulomatous hepatitis occurs with fungal infections or *mycobacteria.*

Hepatoma is 7 times as common with HIV disease, but the effects of Hepatitis virus exposure are probably more important.

Acalculous cholecystitis has been discussed previously under '*Acute abdomen'.*

Cholestatic jaundice (15.7) may arise from several types of HIV-related pathology:
   papillary stenosis,
   sclerosing cholangitis,
   lymphadenopathy in the porta hepatis, especially TB.
Cryptosporidium and *cytomegalovirus* have been implicated; this is not necessarily a late complication of HIV disease.

A pancreatic mass may be tuberculous, lymphoma or adenocarcinoma, behaving more aggressively, often associated with portal vein thrombosis.

N. GYNAECOLOGICAL DISEASE

Pelvic inflammatory disease, **pelvic lymphadenitis and pelvic sepsis** (23.1), especially post-abortal (23.2), are more common and more virulent in HIV-disease. They are promoted by the use of intra-uterine contraceptive devices; recurrent abortions, primary subfertility due to HIV disease and permanent infertility due to previous infection are very frequent consequences. Recurrent sexually-transmitted infections are very common.

Tuberculous infection of tubes and ovaries is common. Dense matted adhesions are frequently found with perforation into bladder, small, large bowel or rectum. Low rectovaginal fistulae, unrelated to obstetric trauma are seen in sexually active women and children <5 years.

Cervical carcinoma is 10 times more frequent, affects younger females, and is more aggressive; recurrence is common.

Herpetic vulvovaginitis, often ulcerative, is common and huge extensive vulval condylomata very often seen. Their presence in young girls does not necessarily imply sexual abuse; long-standing condylomata may however develop into carcinoma.

Ovarian lymphomas of Burkitt-type are seen.

Nonspecific chronic pelvic pain has been a difficult but regularly seen problem in HIV patients.

O. OBSTETRIC PROBLEMS

Pregnancy worsens the HIV condition if in the late stages; wasting contributes to maternal and perinatal mortality; puerperal sepsis (22.14) is more common and more severe.
Although Caesarean section reduces the transmission of HIV to child, *it is not practical to advocate such a general policy*. Introduce practices to reduce transmission (5.3).
Unusual infections, *e.g.* peritonitis after postpartum tubal ligation, or pubic osteomyelitis after spontaneous labour, are seen.

Puerperal psychosis may be difficult to differentiate from HIV-cerebral encephalopathy.
Good contraception (*and that usually does not mean the contraceptive pill*), is needed in HIV+ve women. *The contraceptive pill is a bad option* because ARV therapy and antibiotics (especially rifampicin) interfere with their absorption and so they become far less effective (unless 2 pills a day are taken). Fever, vomiting diarrhoea and the AIDS dementia syndrome also interfere with effective use.
The dangers of IUD's are overstated, but Depo-Provera is probably the drug of choice.

P. UROLOGICAL DISEASE

Neuropathic bladder is a common problem in HIV disease; it may present with irritative symptoms of urgency and frequency, which respond to anticholinergic therapy *e.g.* imipramine. Less commonly there are obstructive symptoms leading to urinary retention. Where the neurogenic bladder is due to Guillain-Barré syndrome or transverse myelitis, expect spontaneous recovery. Otherwise a trans-urethral incision of the prostate provides a remedy in men, and intermittent self-catheterization in women.

Urethral stricture (27.9) may also cause acute urinary retention; the stricture is usually more severe than in non-HIV patients. This commonly presents in HIV+ve patients through its complications, namely periurethral abscess and fistula formation. The development of 'watering can' scrotum and perineum is frequent. *Do not perform an open urethroplasty because it has a high complication rate*.

Fournier's gangrene (6.21,23) is a very high risk in HIV patients following urethral injury. It may often, however, occur *de novo*.

Prostatic abscess (6.19), **tuberculous and non-specific prostatitis** are specific HIV-related problems, frequently resulting in urinary retention. Tuberculous prostatitis mimics prostatic carcinoma completely, even to the extent of giving rise to raised prostate specific antigen (PSA) serum levels.

Focal segmental glomerulonecrosis is the commonest cause of HIV-related renal impairment; renal tuberculosis remains rare but consider it in chronic sterile pyuria.

Although common in the HIV population, epididymitis shows no real differences in presentation and treatment with the non-HIV population.

Tuberculous epididymitis is however more common; the lesion is typically firm.

HIV-related cystitis may be aggressive and extremely debilitating. The predominant symptoms are painful urinary frequency, suprapubic pain and haematuria (micro- or macro-scopic) without any demonstrable urinary tract infection. Cystoscopy reveals a highly characteristic uniformly congested appearance with no ulceration and no significant reduction in bladder capacity. The histological appearance is like a non-specific interstitial cystitis without mast cells, with no *cytomegalovirus* found.

Urinary tract infections occur in c.15-20% of males with advanced HIV disease (CD4 <200/µl), most commonly with *pseudomonas aeruginosa.*
All types of sexually transmitted infections are inevitably common in HIV+ve patients, and therefore a combination of diseases is frequent.

Balanitis co-existing with chancroid, condylomata or with malignancy. This may be in the form of squamous carcinoma or Kaposi sarcoma. There may be a continuum of histological change from condyloma to squamous carcinoma, suggesting a synergistic interaction between the papilloma virus and HIV. Malignancy of the foreskin however remains rare; frankly necrotic ulcerative penile lesions are usually due to chancroid. Patients may request circumcision (27.29) hoping thereby to avoid recurrent penile ulceration; this may then of course occur on the glans penis itself. The operation of circumcision is not without risk: severe necrotizing fasciitis of the penis can occur post-operatively. There appears, at least in certain cases, to be a microangiopathy associated with balanitis; this may be the predisposing factor in the development of necrotizing fasciitis and it may be exacerbated by increased tension when LA is used in a penile block. You should therefore perform the operation only under GA or using a caudal block.

Penile abscess (6.21) *de novo* is diagnostic of HIV infection. The infection usually spreads from the penis to the scrotum, rather than the reverse as in the classical Fournier's gangrene. In the absence of urethral stricture or diabetes mellitus, necrotizing fasciitis of the penoscrotal tissues is likewise diagnostic of HIV disease.
Don't necessarily refuse a request for circumcision in HIV+ve patients on traditional or social grounds; there may be a protective role in HIV transmission in the act of circumcision. The epithelium of the exposed glans penis in the circumcised male changes from columnar to stratified squamous, and may thus be more resistant to ulceration.
However, the morbidity and, in some cases, mortality of circumcision, especially where medical resources are scarce, may make this procedure dangerous.

Do not underestimate the possible complications of elective circumcision, especially if you use a LA ring block: necrotizing fasciitis, abscess and also the risk of haemorrhage, particularly where thrombocytopenia is present, are serious problems. Though these complications are quite common with HIV+ve patients, they can also occur to others.
Recommendations for circumcision to prevent HIV transmission fall in the same category as the use of condoms: although it may help, it does not get to the root of the problem. You must carefully counsel your patient that circumcision does not protect him from HIV infection, but may just lowers the risk.

Condylomata may be very profuse on the foreskin and may encroach onto the glans penis and into the urethral meatus.

Erectile dysfunction is very common in HIV disease, and seems to have a multifactorial origin; treatment with sildenafil and related drugs pose huge moral and ethical issues.

Q. ANORECTAL DISEASE (26.2)

You will find a variety of anorectal lesions in HIV+ve patients, and their severity relates closely to CD4 levels; in all patients they are common, although they are particularly numerous (c. 30%) in homosexuals, where they have a somewhat different pattern. As many practitioners have a natural reluctance to examining the anal region, they are often referred to as 'piles'; however haemorrhoids are *per se* not part of the spectrum of HIV anal pathology.
Many of the lesions are resistant to treatment, and their aetiology is not known; however, this does not mean that you can do nothing for patients with these conditions. However, do *not* undertake elective anorectal surgery lightly: many authors have reported poor or absent wound healing often after many months. Distal septic complications such as meningitis may also occur.

Idiopathic anorectal ulcer appears first as a mucosal laceration within the anal canal, and gives rise to symptoms identical to the classical anal fissure, i.e. pain and bleeding *per rectum*. However, you will see no anal skin lesion on gentle parting of the buttocks, because the lesion is internal, usually just proximal to the dentate line. Furthermore there is rarely anal sphincter spasm, and often diarrhoea rather than constipation. Pain is persistent, usually associated with some intermittent bleeding *per rectum*, particularly after defecation.
The mucosal defect then deepens and becomes palpable as an ulcer with smooth benign-feeling edges. As this ulcer deepens further, it may penetrate into the vagina or urethra or appear as a large fistula externally.
No single agent has been implicated in this lesion, although in some cases *cytomegalovirus, chlamydia trachomatis* (26.11), and *herpes simplex* virus have been found.
There is commonly associated infection, with patients reporting pus draining *per rectum*.

Superficial breakdown of perianal skin with excoriation is often associated with chronic diarrhoea; control of loose stools is therefore obviously important. Vesicular excoriation is due to *herpes simplex*. Careful examination to exclude fistulae and abscesses is vital.

Fistulae (26.3) in HIV+ve patients are often complex and multiple. They are frequently high or intersphincteric (intermediate) and are therefore not amenable to simple laying open. In fact, even for low superficial fistulae, the laying open may result in non-healing perianal wounds, especially if CD4 counts are <200/μl.

Many fistulae arise from sepsis, but some as a result of extension of the idiopathic anal ulcer described above. In these cases, the fistula is wide and may readily admit the examining finger. Fistulation can occur to the outside skin, but also to the vagina or bladder. This occurs both in adults and small children. If the fistula was not present at birth, it is pathognomonic of HIV-disease.

Anal and perianal warts (26.6) are often very extensive; their excision or diathermy ablation surprisingly results in rapid wound healing, presumably due to an epithelial growth factor in the papilloma virus. Contact tracing in poor-resource environments is a pipe-dream, and therefore recurrence by reinfection is frequent. Moreover, if not all condylomata are removed, and they can extend far up in the anal canal, they quickly re-establish themselves. *Beware when using diathermy on these lesions: HIV may be transmitted by the smoke,* so always wear a mask and aspirate away the fumes.

PERIANAL CONDYLOMATA
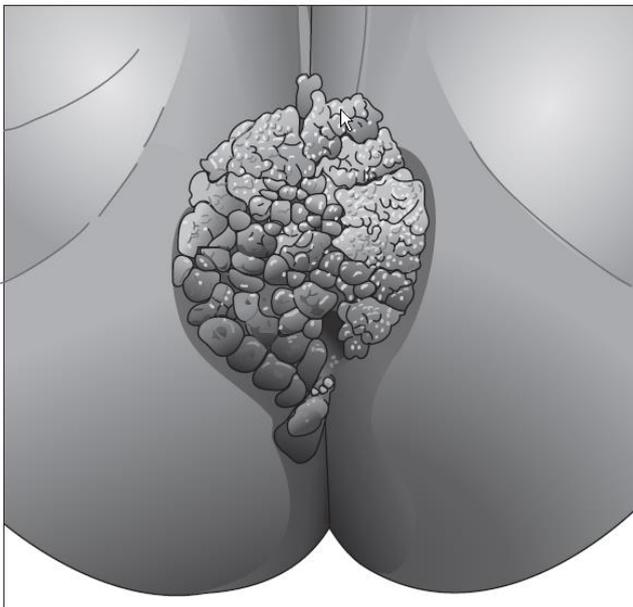
Fig. 5-13 CONDYLOMATA (warts), often extensive with underlying neoplastic change.

Squamous carcinoma (26.7) may be heralded by the neoplastic change seen in anal intra-epithelial neoplasia (AIN), or be the result of chronic infestation by condylomata, especially if florid, or arise *de novo*. The incidence of HIV-related anal carcinoma is rising and it is 60 times more common than without HIV disease, but this may be mostly due to the risks of ano-receptive sexual intercourse.

(**Lymphoma** and **Kaposi sarcoma** may also be found at the anus.)

Proctitis: Just as in colitis, the rectum may be affected by a severe inflammatory process; *cytomegalovirus, herpes simplex, chlamydia or* enteropathic *E. Coli* may be the cause.

R. VASCULAR DISEASE

Any major artery can be involved; the pathology affects mainly the adventitia with leucocytoclastic vasculitis of *vasa vasorum* and periadventitial vessels, proliferation of slit-like vascular channels, chronic inflammation and fibrosis. There is associated medial fibrosis with loss and fragmentation of muscle and elastic tissue, and similar fragmentation in the internal elastic lamina of the intima, with calcification.

Arterial occlusion (35.2) **or aneurysm formation** (35.8) are the end result; the former is much more common, but increasing numbers of aneurysms are seen in HIV+ve patients.

Arterial occlusion in limbs results obviously in gangrene; in poor-resource countries, patients rarely present with claudication, and the deterioration of symptoms is usually too rapid to allow early presentation. Thus arterial reconstruction is hardly ever an option; you should also have serious qualms about using prosthetic material in HIV+ve patients as the vessels take sutures poorly, and secondary infection of the graft is a very definite risk, often with fatal outcome. Results of surgery for atheromatous disease (*i.e. not HIV-related*) in HIV+ve individuals may however be more successful.

Thrombosis may also occur in mesenteric vessels, or cerebral arteries resulting in a cerebro-vascular accident. Aneurysms tend to occur in the carotid and superficial femoral arteries, although any artery may be involved and multiple lesions are seen. Spontaneous arteriovenous fistulae also result.

Deep vein thrombosis occurs with 10 times greater frequency, though you will detect less than 1% of cases clinically. Risks of surgery are obviously further increased when you take this statistic into consideration, especially as you can use prophylactic anticoagulants only with reluctance in the presence of thrombocytopenia.

S. ORTHOPAEDIC PROBLEMS

There is increased risk of infection especially when implants are used; you may see late infection long after implants have been inserted, where surgery has often been done before seroconversion.
The larger the implant, the bigger the problem: bone infections then often fail to respond to antibiotics, removal of the implant, debridement and subsequent sequestrectomy.
Never put implants in open fractures in HIV patients!

Thus non-operative methods are usually more suitable, especially when they are obvious signs of immunosuppression (CD4 levels <200/µl); external fixators are preferable if practical. Remove implants as soon as possible, once their effectiveness is over. Explain fully the merits and demerits of internal fixation before you carry out any such operation.

Adult bone infection (osteomyelitis) (7.3) occurs usually in the lower femur or upper tibia, often bilaterally; *staphylococci* are usually found, but *salmonellae* and gut organisms are often seen. Despite appropriate treatments, infections frequently do not resolve and amputation may be necessary.

Septic arthritis (7.17) occurs more frequently in HIV-disease, especially if joint replacements have been inserted. Knee, hip, shoulder, ankle, elbow and wrist are commonly affected by the same organisms as osteomyelitis.

Tuberculous arthritis affects HIV-patients similarly to non-HIV: primarily the spine (32.4), and then the hip and knee are involved. Relapse is not uncommon after treatment; except where immune competence is reasonable (CD4>200/µl) avoid surgery to decompress the vertebral column to relieve paraplegia or arthrodese painful destroyed joints.

Reactive HIV-arthritis causes painful swelling and joint effusion, especially of knees and ankles, and may be acute (mimicking septic arthritis) or more insidious, usually bilateral and sometimes migratory; recurrence frequently occurs in the same joint which had been quiescent for months.
The arthritis may arise as a result of reaction of diarrhoea bacterial fragments carried in the circulation: aspiration yields opalescent fluid filled with leucocytes. Chronic debility results with permanent joint stiffness where relapse occurs (often with resolution of physical signs)
Where rheumatoid arthritis, Reiter's disease or ankylosing spondylitis occur with HIV disease, their response to anti-inflammatory drug treatment is usually poor.

Inflammatory conditions of tendons and ligaments, *e.g.* tennis elbow, Achilles tendinitis, plantar fasciitis are common, and usually recur after treatment.

T. NEUROLOGICAL DISEASE

Transverse myelitis, leucoencephalopathy, progressive dementia, and encephalitis, occur through the strong affinity of HIV for neuronal cells.

UNILATERAL PTOSIS

Fig. 5-14 UNILATERAL PTOSIS, usually without pupillary changes.

Neuropathies and myelopathies are common, resulting in facial palsy (especially at seroconversion), ptosis (5-14), impotence, paraparesis, urinary retention or incontinence.

Opportunistic cerebral infections with *toxoplasmosis, cytomegalovirus, herpes simplex,* and *blastomycosis* are common.

Cryptococcus **meningitis** is a typical manifestation of advanced HIV-disease; tuberculous meningitis is more common in HIV-patients and often results in secondary hydrocephalus involving the basal cisterns.

Herpes zoster may affect the *motor* roots in HIV-disease: a claw hand may result.

U. HAEMATOLOGICAL DISEASE

Pyrexia without obvious cause is frequent.

Chronic anaemia is common with bone marrow suppression of single or multiple cell lines. Infiltration of bone marrow with leishmaniasis or toxoplasmosis is seen. There is a drop in levels of interleukin 4 & 5, needed in haemopoiesis.

There is an increased risk of bleeding in HIV disease; when thrombocytopenia is overt this may be catastrophically serious. Platelet numbers may be satisfactory, but their function not so.

Idiopathic thrombocytopenia responds to splenectomy, but in HIV-patients the risks of *pneumococcal* and other sepsis, including malaria, outweigh the advantages.

All these complications may be correlated to CD4 cell counts and can therefore give an indication of the stage of advancement of the disease, and also of its regression with treatment:

CD4 count	Infectious complication	Non-infectious Complication
>500/µl	Acute HIV syndrome	Persistent generalized Lymphadenopathy Skin rashes Salivary gland swelling Guillain-Barré disease Myopathy Aseptic meningitis Colitis
200-500/µl	Pneumonias Pulmonary TB Herpes zoster Kaposi sarcoma Oral *candidiasis* Recurrent skin infections Primary peritonitis	Carcinoma Cervix B-cell lymphoma Anaemia Mononeuritis multiplex Lymphocytic interstitial pneumonitis Oral hairy leucoplakia Idiopathic thrombo-cytopaenia Gingival erythema Seronegative arthritis Vasculitis
<200/µl	*Pneumocystitis carinii* Pneumonia Extra-pulmonary/ Miliary TB Necrotizing fasciitis Cellulitis Chronic mucocutaneous herpes simplex Oesophageal *candidiasis* Anal ulcer/ Perianal excoriation	Wasting Peripheral neuropathy Non-Hodgkin's lymphoma Cardiomyopathy Encephalopathy Myelopathy/ Radiculopathy Dementia
<100/µl	Disseminated herpes simplex *Toxoplasmosis/ Blastomycosis* *Cryptococcal* meningitis Chronic c*ryptosporidiosis* Chronic *isosporiasis* Oesophageal *candidiasis* Respiratory *candidiasis* Salmonella (non-*typhi*) septicaemia	Lipodystrophy
<50/µl	Disseminated *cytomegaloviris* Necrotizing gingivitis/ Cancrum oris	CNS Lymphoma Pancreatitis

CD4 count	WHO Stage
>500/µl	I
200-500/µl	II - III
<200/µl	IV

The T-cell profile changes with drop in levels of CD4 cells and rise in CD8, with drop in ratio CD4/CD8 <2; there is a total drop in T-cells late in the disease. However, a T-cell leukaemia may occur with rise in numbers.

Leucopenia is common with especially a lymphopenia; a leucocytic response to infection is often not present. However, **leukaemia** can develop after ARV treatment is started.

Immunoglobulins, especially IgE, are raised, and so plasma viscosity goes up, with rise in ESR. Total globulin levels rise, with drop in albumin/globulin ratio.

5.7 HIV & tuberculosis

Tuberculosis (TB) can affect any organ in the body, and so is found in surgical patients either as coincident pulmonary disease, or as primary cause of their complaint (*e.g.* TB lymphadenitis (17.4), TB arthritis (32.3), abdominal TB (16.1), gluteal sinuses, epididymal TB (27.23) etc.) The advent of HIV disease has severely increased its incidence throughout the world, and in many countries TB is a strong indicator of HIV disease.
You may see bovine TB where immunization of cattle and pasteurization of milk is not routine.

Extra-pulmonary TB is an even stronger indicator of HIV. Therefore test for HIV in every TB patient. Dissemination is more common as the CD4 counts fall <200/µl. There may be TB outside the lung without it being inside the lung!

The clinical diagnosis of TB can be difficult; especially in lymph nodes, but also in pus and other solid organs, aspiration for acid-alcohol fast bacilli (AAFB) by direct smear microscopy or using Ziehl-Neelsen (ZN) staining is useful, especially if histology is not available. Use simpler cold staining methods: flood the smear with concentrated carbol fuchsin for 10mins without heating, and wash with water; then flood the smear with Gabbet's methylene blue for 2mins and again wash with water. Dry the smears as for ZN staining. Recent methods (Gene Xpert) detecting DNA sequences by using a polymerase chain reaction (PCR) through nucleic acid amplification tests are very sensitive even in HIV+ve patients and can detect rifampicin resistance; if the equipment is available, the cartridges are now inexpensive, easy to use and recommended by WHO.

Gabbet's methylene blue: Methylene Blue 1G, Absolute Alcohol 30ml, Concentrated Sulphuric Acid 20ml + Distilled Water 50ml.

Naked eye appearances of caseation are virtually diagnostic, but may be confused with necrotic lymphoma. Tuberculin (Mantoux and Heaf) testing is no longer reliable, except for children <3yrs who have not had BCG.

In areas of high TB endemicity, you may be able to diagnose TB by a lymphocytosis on pleural fluid, pericardial fluid or simply the presence of para-aortic lymphadenopathy on ultrasound. Pleural fluid usually has fibrinous strands visible on ultrasound.

It is important to screen sputum also for AAFB ('open PTB') in every patient for good infection control, especially in the community. A chest radiograph may not show classical apical disease, but rather lower lobe infection; there is less cavitation and a miliary pattern is common (especially when the CD4 count is low). It is important to perform radiography when treatment is finished, and to file films properly for future cross-reference.

Do not start treatment without arranging contact tracing, especially babies and infants, and notification.
Special charts are available in many countries. Follow your regional regime, or otherwise, the WHO approved standard, using a directly observed treatment scheme (DOTS):
  Intensive Phase: 2months Isoniazid (H), Rifampicin (R), Pyrazinamide (Z), & Ethambutol (E), followed by
  Continuation Phase: 4months HR.

Extend this continuation phase to 5months for TB epididymitis, 6months for spinal TB with neurological problems, TB pericarditis and meningitis, and 9months for renal TB. (An alternative is 6months of Isoniazid and Ethambutol.) *Do not use Ethambutol in children <10yrs.*

If the patient has had treatment before, initial treatment is probably best in hospital: use longer treatment phases:
  Intensive Phase: 2months Streptomycin (S), plus HRZE, followed by 1 month HRZE, and then,
  Continuation Phase: 4months HRE.
Do not use Streptomycin in pregnancy; or (and Ethambutol) to children <10yrs. Thiacetazone is no longer routinely used.

Dosages are weight-dependant: as the patient improves and he gains weight, so you may need to alter the dosage; these are daily oral doses:

Weight	Isoniazid (H)	Rifam-picin (R)	Pyrazin-amide (Z)	Etham-butol (E)	Strepto-mycin (S)
5-9kg	50mg	75mg	250mg	-	-
11-20kg	100mg	150mg	500mg	-	-
21-33kg	200mg	300mg	1000mg	800mg	500mg
34-50kg	300mg	450mg	1500mg	800mg	750mg
>50kg	300mg	600mg	2000mg	1200mg	750mg

Fixed dose combinations may be available, and help patient compliance; twice or thrice-weekly regimens are being introduced to make DOTS easier, but dosages will then differ.

Control neuropathy with Isoniazid with Pyridoxine (Vitamin B6) 50mg tid; prophylactic treatment is 20mg od. Most of the problems with HIV treatment occur with rifampicin which induces liver enzyme breakdown of ARVs making them less effective; generally start anti-retrovirals after the intensive 2month phase of TB treatment. Rifabutin is an alternative to Rifampicin.

If the CD4 count is <50/µl, however, start ARV treatment as tolerated, but avoid nevirapine and substitute efavirenz which is much more expensive. Otherwise start ARV treatment after 2wks of anti-TB therapy.

The main drawback with TB drugs is their side-effects, which are often shared by anti-retroviral drugs:

Toxicity	*TB Drug*	*ARV Drug*
Neuropathy	H	d4T, ddC, ddI
Hepatitis & Rash	R, H, Z, S	NNRTI's
Nausea	Z	ddI, AZT, PI's
Visual loss	E	-
Hearing & Balance loss	S	-

(N.B.Names of ARV drugs in 5.8)
(Note, however, that visual loss is usually the result of CMV retinitis rather than a side-effect of TB drug therapy)

If a patient is already on ARV treatment when you diagnose TB, *don't stop the ARV drugs!*

If patients do not complete their treatment courses, or if many different treatment regimens are used, resistant strains are likely to develop. Multi-resistant TB has surfaced in some parts of the world: 2months of streptomycin are then recommended but get specialist help; the possibilities of untreatable TB, if combined with HIV, would be disastrous. For these reasons, prophylactic treatment of HIV+ve patients with isoniazid is only recommended where tuberculosis is not so prevalent: *follow national programme guidelines!*

5.8 Treatment

The virus multiplies at an alarming rate: within a week of seroconversion there are 10^{7-8} RNA copies/ml. In 6-12 months the viral load reaches an equilibrium where it can usually be maintained by medication for several years.

ARV therapy has proved remarkably successful, though eradication of viral reservoirs has not been possible. You should maintain long term treatment, though this is still expensive; however costs have come down dramatically through WHO campaigns; so use this resumé if you can. Unfortunately still only c.50% of people with HIV needing treatment worldwide are getting it.

A willingness and commitment to long-term therapy is essential; consider the financial costs, and the potential barriers ahead. Treat co-morbidities, and manage psychosocial issues: *the drugs are not the whole story*! A combination of drugs is necessary; otherwise early drug resistance is inevitable, and further treatment practically impossible.

Reduction of viral loads by 70-80% is usually possible with at least 95% adherence to drug regimes, but about 30% of patients default treatment.

Agents can be divided into:

Type	Abb.	Function	Name	Abb.
Nucleoside Reverse Transcriptase Inhibitors	NRTI Cat I	Mimic normal building blocks of HIV-DNA	stavudine zidovudine	d4T AZT
	NRTI Cat II		didanosine lamivudine zalcitabine	ddI 3TC ddC
	NRTI Cat III		abacavir	ABC
Nucleotide Reverse Transcriptase Inhibitors	NtRTI	*as* NRTIs	tenofovir emtricitabine	TDF FTC
Non-Nucleoside Reverse Transcriptase Inhibitors	NNRTI	Directly inhibit early stages of replication	delavirine efavirenz nevirapine etravirine	DLV EFV NVP ETR
Protease Inhibitors	PI	Directly inibit last stages of replication	amprenavir indinavir nelfinavir ritonavir saquinavir atazanavir lopinavir darunavir	APV IDV NFV RTV SQV AZV LPV DRV
Dideoxy-nucleotide reductase inhibitor	Hydroxy-urea	Promotes NRTI activity	Hydroxy-urea	

The main drawback of these drugs is their side-effects and interactions with other drugs (especially TB treatment, which often means taking 6 or more drugs), and hence their tolerability.
Avoid Efavirenz during pregnancy.
Certain combinations are contra-indicated either because they work as antagonists, or are excessively toxic to peripheral nerves or bone marrow. Other toxic side-effects, potentially fatal, are: pancreatitis, hypersensitivity reactions (including Stevens-Johnson syndrome) and lactic acidosis (with d4T, ddI or AZT): this presents with abdominal pain and dyspnoea. Long-term side-effects are lipodystrophy, osteodystrophy and insulin resistance.

Occasionally you will need to substitute one drug for another of the same type: get advice about this.
Nonetheless you should warn patients of potential side-effects, *e.g.* vivid dreams with starting EFV, rash with NVP, anaemia with AZT, peripheral neuropathy with d4T or ddI.

Recommended initial therapy is one NRTI from Category I, one from Category II, and one NNRTI. Use an extra NRTI from Category III if the viral load is <55,000 copies/ml: monitoring of viral load and CD4 counts is important.

Normally treatment was only started if the CD4 count was <200/μl, though evidence now suggests it may be better to start when the count is <500/μl. Treatment is necessary regardless for clinical stages III & IV, co-infection with TB or Hepatitis B (include TDF and 3TC or FTC), pregnancy (avoid AZT if HB <80g/l) or where the partner is HIV-ve.

Other combinations are 3 NRTI; 2 NRTI + PI; 2 NRTI + 2PI; or NNRTI + PI. *Do not use two NRTI's alone*; PI's are metabolized by cytochrome P450 which is inhibited by ritonavir.
This enhances their efficacy if used in combination, but adds significant side-effects, especially metabolic. Combination drugs are available. Both d4T and ddI are being phased out because of their toxicity.
Follow nationally agreed guidelines, as with TB therapy.

Screen patients for anaemia, TB, Hepatitis B and syphilis and treat these before starting ARV therapy. Try to get renal and liver function tests done. *Do not forget to do the pregnancy test in women of reproductive age!*

Treatment for children should also follow nationally agreed guidelines: use first-line therapy with RTV-boosted LPV for babies <3yrs and EFV for those >3yrs, together with 2 NRTIs

Sudden discontinuation of all therapy usually results in viral rebound within a month with 'wild-type' HIV strains; discontinuation of therapy even when no detectable virus is found for 3yrs almost always results in viral rebound in 3months.
This means that if you have severe complications after abdominal surgery resulting in your patient not being able to take his medication, all the problems described may emerge. Consider carefully therefore before you undertake complex elective procedures in the abdomen.
New types of drugs on the horizon are *fusion inhibitors* and *integrase/CCr-5 inhibitors*.

Recurrence of HIV-related disease if no antiretrovirals are used is virtually inevitable with many complications, but especially so with TB and malignant disease such as Kaposi sarcoma or lymphoma.
Co-infection with hepatitis B hugely increases the mortality.

Treatment to reduce mother-to-child transmission is now standardized: use zidovudine 200mg at the onset of labour. If pains turn out to be false labour, try a repeat dose of 200mg at the actual onset of labour. Alternatively advise a dose at 28wks' gestation at home, in case premature labour occurs, with instructions as to when to take the drug.

Further, use one 6mg dose to the new-born baby (in liquid form) between 48 and 72hrs after delivery, or at discharge. For babies under 2kg, reduce the dosage to 2mg/kg. If the baby vomits <1hr after taking the medication, repeat the dose. Should the baby be born <2hrs after the mother had her dose, supply an immediate dose to the baby, and repeat this at discharge.

Post-exposure prophylaxis (PEP): after a sharps injury or splash onto mucosal surfaces, wash the affected part immediately in warm water. For a case of rape, obtain specimens, but *do not use a douche*. Clean a human bite wound by copious rinsing. Significant injuries warrant ARV treatment: a single drug regime of zidovudine 200mg tid for 4wks reduces the risk of seroconversion by 80%, but adding another category NRTI drug (*e.g.* lamivudine 150mg tid) will further reduce the risk. Severe injury, gang rape, rape with immediate life-threatening injury, or inadvertent HIV-affected blood transfusion warrant addition of a PI drug also despite side-effects.

Obviously HIV testing of the victim and the source is mandatory; stop treatment if a HIV-ve result is confirmed from the source (but this may still only signify the 'window' period). An HIV quick test may be -ve even with high viral loads in the period of early seroconversion. A hospital policy on PEP is advisable: some may claim a needle injury otherwise to obtain antiretroviral drugs surreptitiously.

Adjuvant therapy: in Kaposi sarcoma, and HIV-related lymphoma, chemotherapy will not eliminate malignancy, so you should give antiretroviral therapy in addition. *If you do not, recurrence is inevitable*.

You might also consider antiretroviral treatment when inserting metal into bone, in order to prevent septic complications, but this area is still controversial.