Kaposi Sarcoma in HIV Infected Patients

DR ADAM NOSWORTHY

SPECIALIST PHYSICIAN AND MEDICAL ONCOLOGIST

WITS UNIVERSITY

DONALD GORDON MEDICAL CENTRE

Wits Oncology

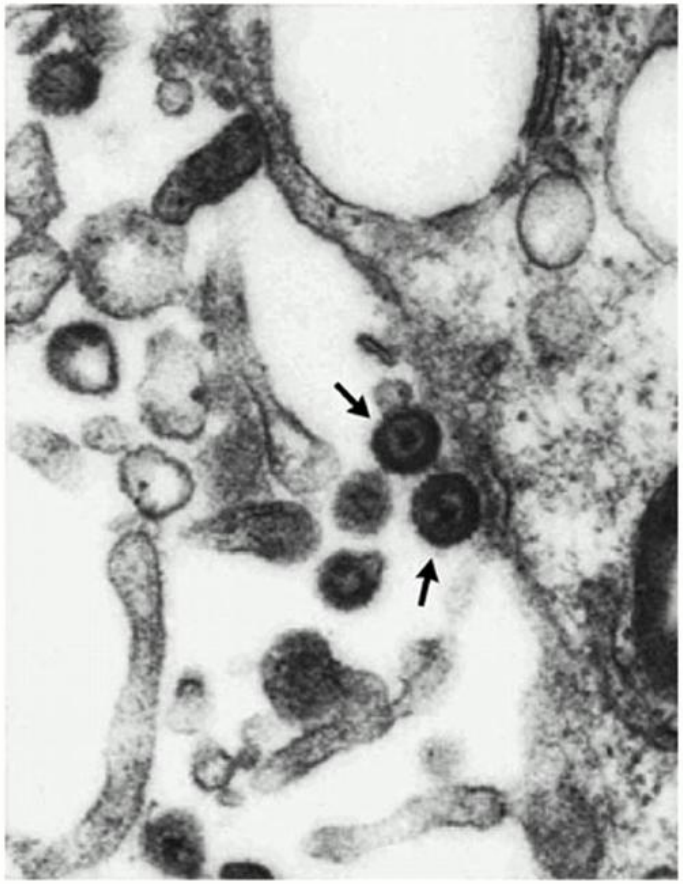
KAPOSI'S SARCOMA

- First description amongst 5 men of "idiopathic multiple pigmented sarcomas of the skin" – 1872.
- Hungarian Dermatologist – Moritz Kaposi.

KAPOSI'S SARCOMA
Clinical Variants

- Epidemic Kaposi's Sarcoma:
  - 1981 – more than 50 healthy young homosexual men described with KS involving lymph nodes, organs and mucosa.
  - Far more aggressive than classic KS – often lung and GIT involvement.
  - Often paired with life-threatening infections.
  - Affected homosexual men with AIDS >20 times more frequently than male patients with haemophilia.

KAPOSI'S SARCOMA
Human Herpes Virus 8 (HHV8)



- Epidemiological evidence – including geographical distribution prompted speculation regarding infectious cause for KS as well as sexual transmission.
- 1994 – Chang et al identified DNA fragments of previously unrecognised herpesvirus in KS lesion from patient with AIDS.

KAPOSI'S SARCOMA
Human Herpes Virus 8 (HHV8)

- 8th Human Herpes Virus – most associated with disease in immunocompromised hosts.
- Disease – results either from reactivation of latent virus or proliferation of growth-transformed cells.
- Herpes viruses are divided into three subfamilies – both HHV8 and EBV members of the gammaherpesvirus subfamily.

KAPOSI'S SARCOMA
Pathogenesis of HHV8

- HHV8 infects both lymphatic and blood vascular endothelial cells.
- Production of lymphangiogenic growth factors that are involved in the pathogenesis of KS lesions.
- Lymphatic reprogramming of blood vascular endothelial cells.
- Both lymphatic and blood vascular endothelial cells undergo a shift in gene expression profile.

KAPOSI'S SARCOMA
Interaction of HHV8 and HIV

- Despite evidence supporting pathogenic role for HHV8 in development of KS, infection alone is not a potent risk factor – co-infection with HIV markedly increases risk.
- HIV may promote HHV8 replication indirectly by impairing immunity of host.
- If HHV8 replication is necessary to sustain KS lesion then decreases in HIV viral load should lead to decrease in KS tumour burden.

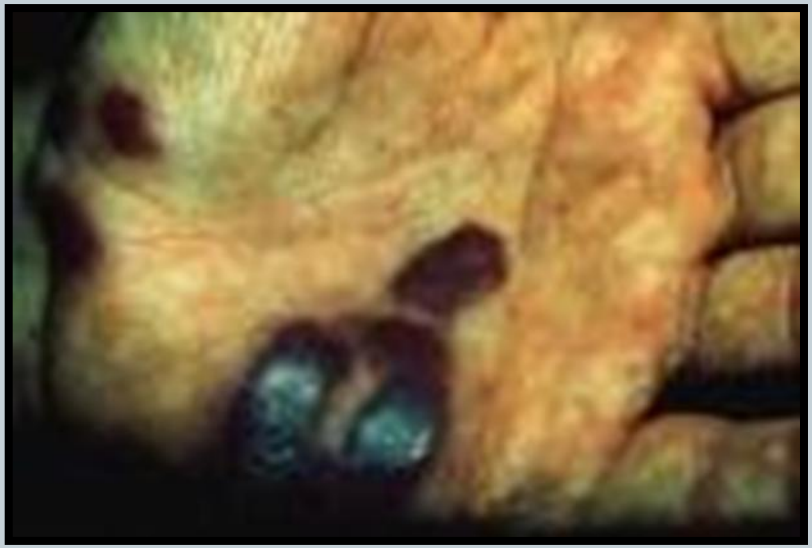
KAPOSI'S SARCOMA
HHV8 Infection Rates

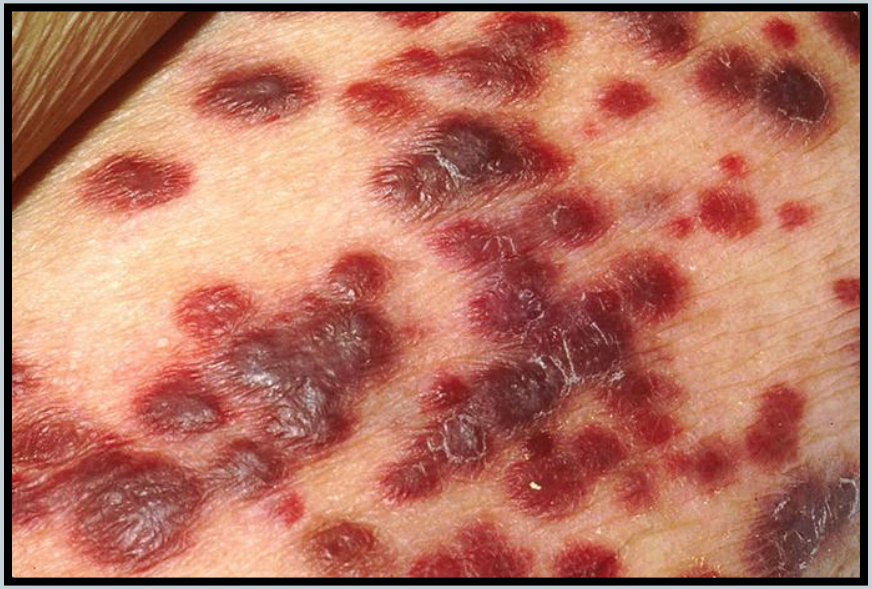
- Infection rates parallel incidence of KS – low rates in USA and parts of Europe, intermediate rates in Mediterranean countries and highest in Central Africa.
- Seroprevalence of HHV8 amongst blood donors:
  - Japan – 0,2%
  - USA – 10%
  - African Countries – 50%

KAPOSI'S SARCOMA
HHV8 Transmission

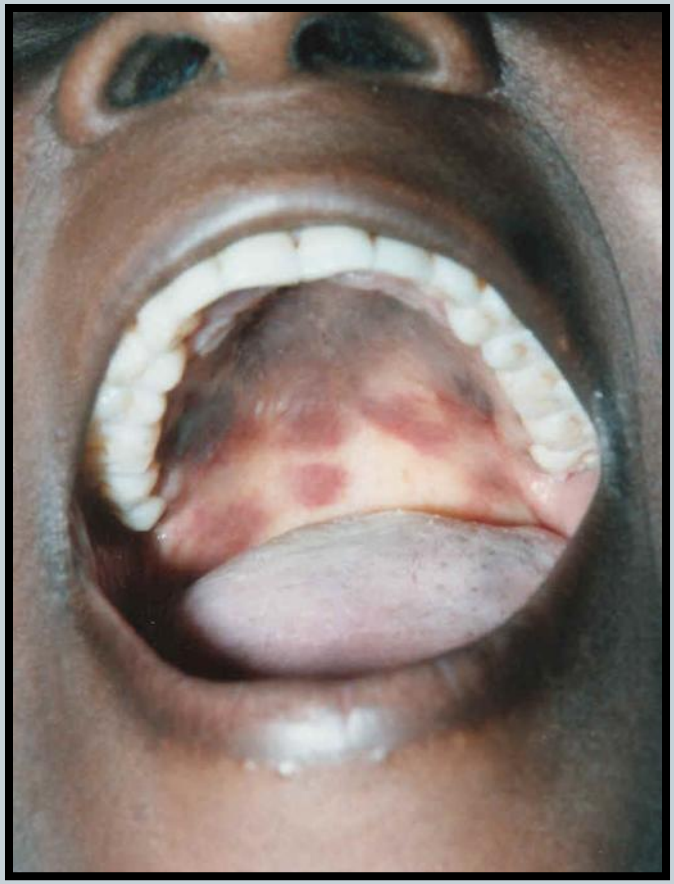
1. Sexual transmission – predominates in developed countries.
2. Vertical transmission tends to predominate in African countries where infection is endemic.
3. Some form of non-sexual transmission – exact mechanisms unknown but may include saliva.
4. Primary infection appears to be asymptomatic.

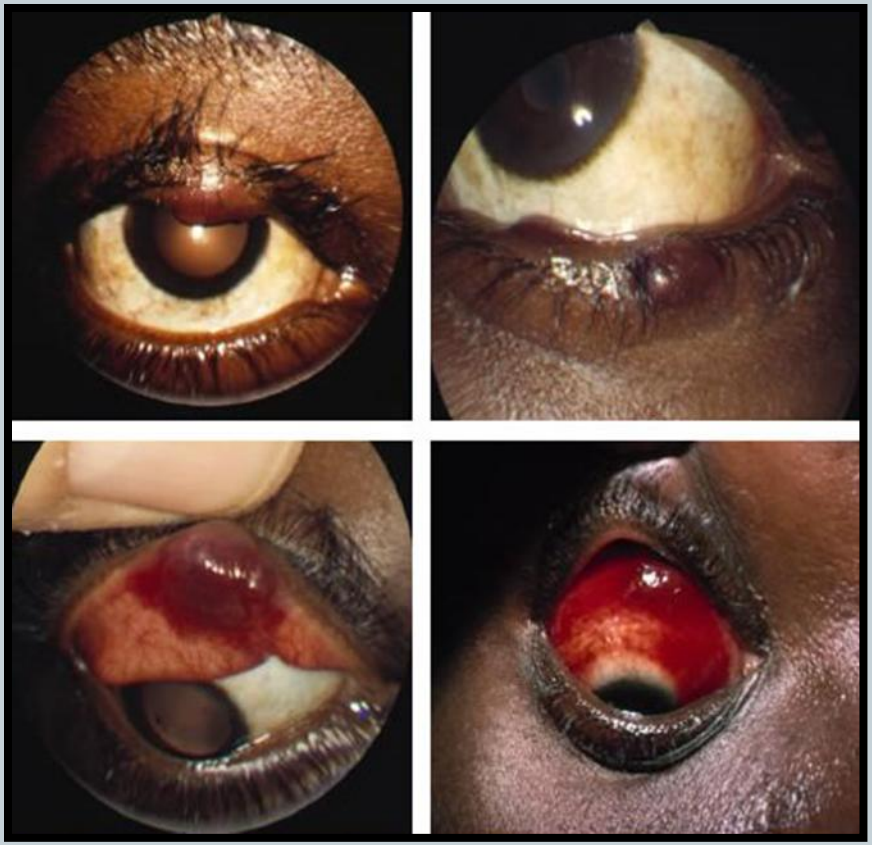
KAPOSI'S SARCOMA
Classic Cutaneous Involvement



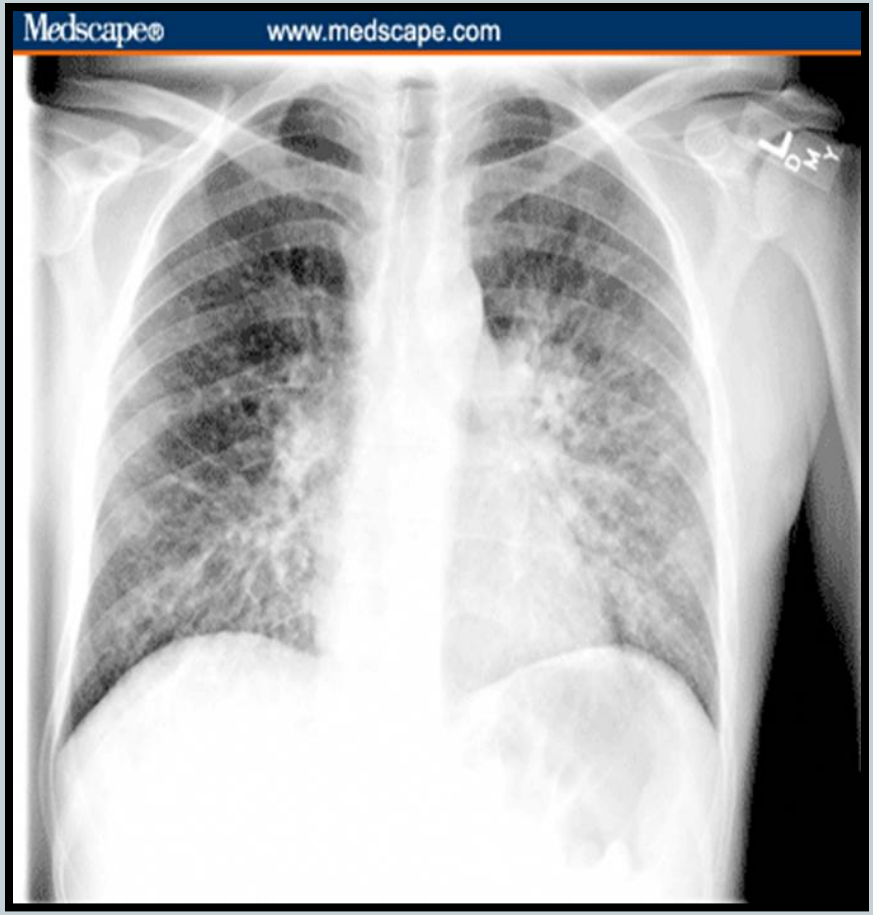


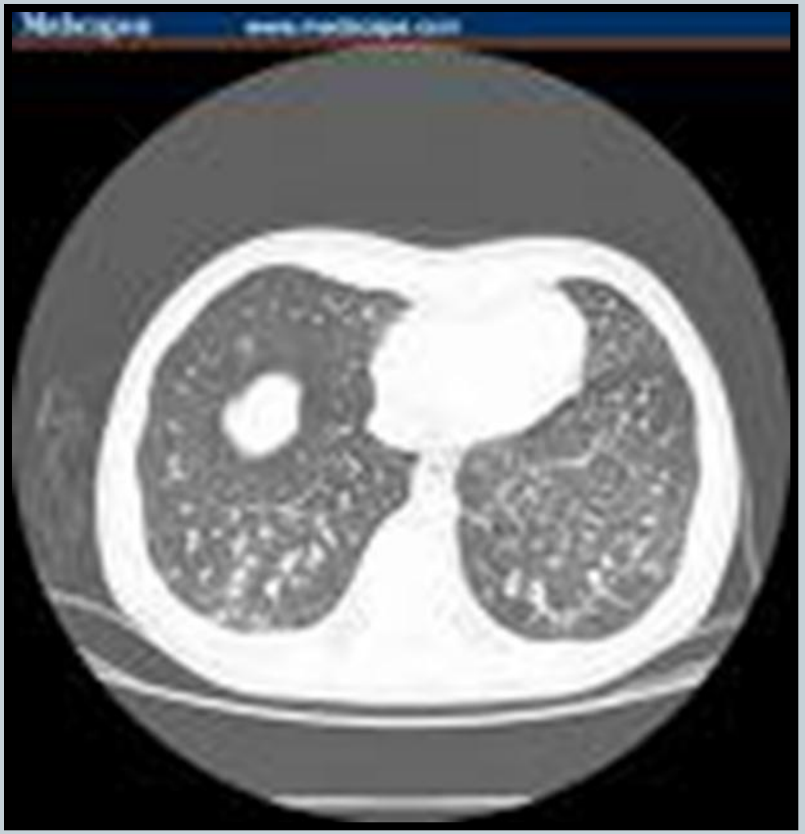
KAPOSI'S SARCOMA
Mucocutaneous Involvement



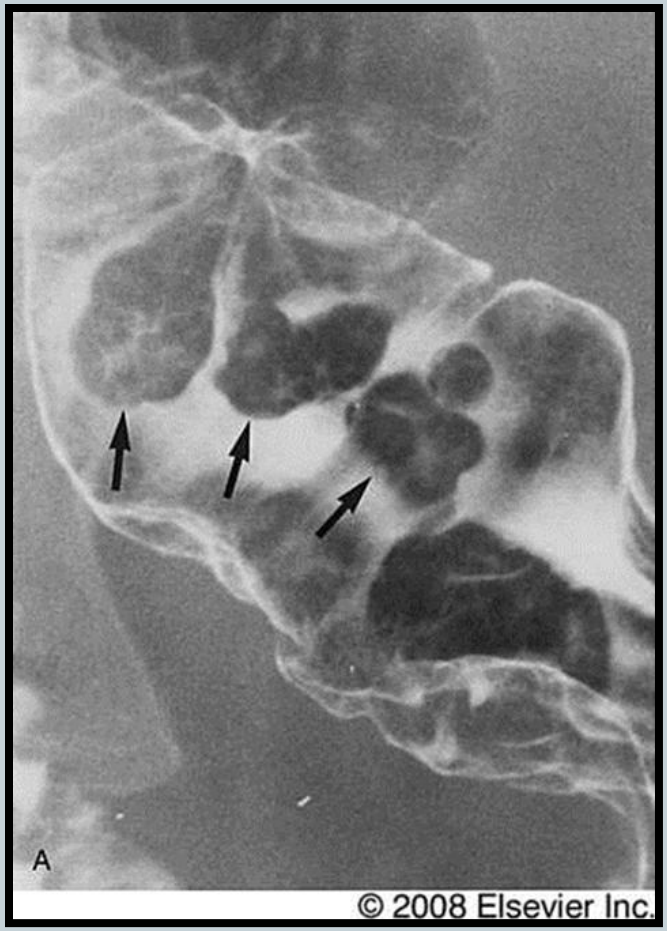


KAPOSI'S SARCOMA
Pulmonary Involvement

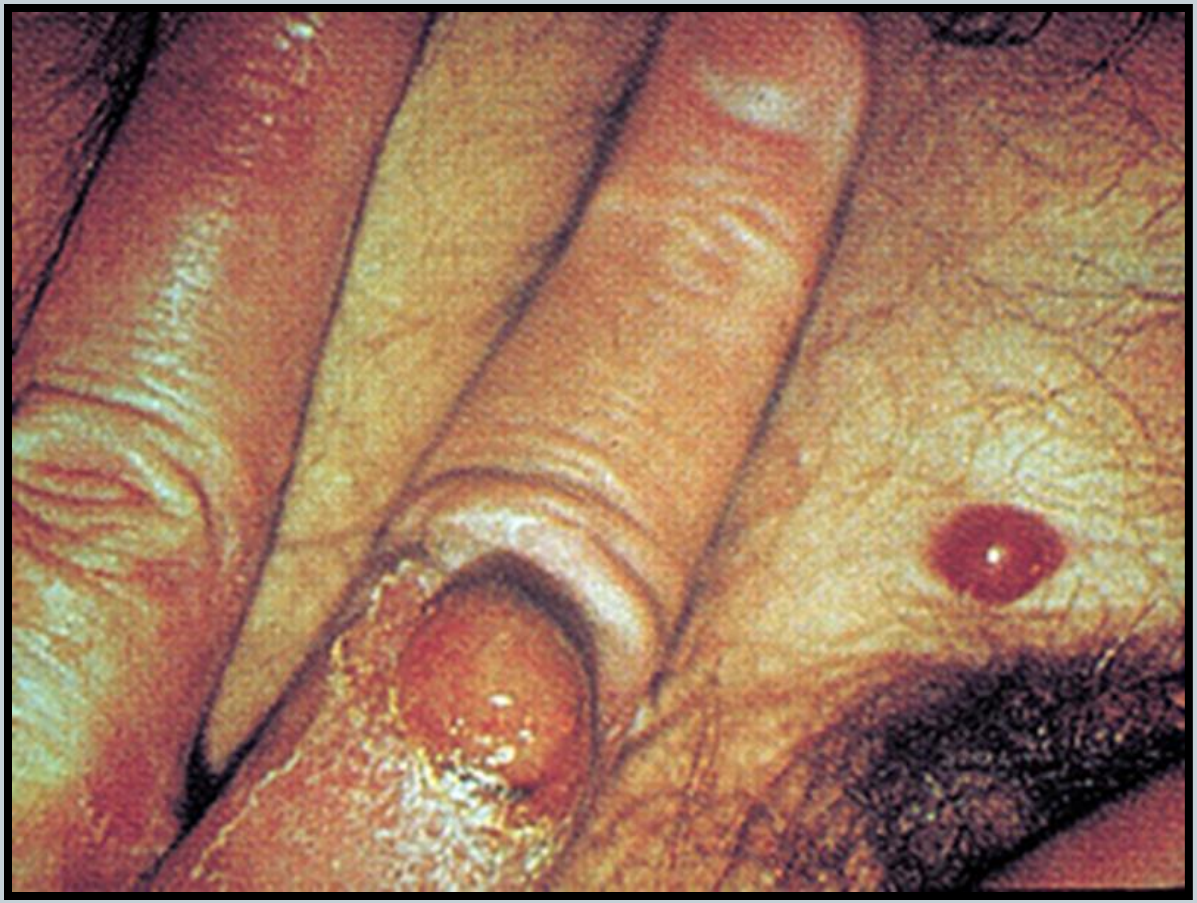




KAPOSI'S SARCOMA
GIT Involvement



KAPOSI'S SARCOMA
Differential Diagnosis – Bacillary Angiomatosis



KAPOSI'S SARCOMA
Staging

	Good Risk	Poor Risk
Tumour (T)	T0 – Confined to: •Skin. •Lymph Nodes. •Minimal Oral Involvement.	T1 : •Tumour associated oedema. •Extensive Oral lesions. •GI Involvement. •Any other organ involvement.
Immune System (I)	I0 – CD4 > 200/μl.	I1 – CD4 < 200/μl
Systemic Disease (S)	S0 – No history of: •Opportunistic Infection. •Thrush. •B-symptoms. Good Performance status.	S1 – History of: •Opportunistic Infection. •Thrush. •B-symptoms. Poor performance status.

Aids Clinical Trial Group (ACTG) of the National Institute of Health Staging

KAPOSI'S SARCOMA
Treatment

- Goals of therapy:
  - Symptom palliation.
  - Prevention of disease progression.
  - Shrinkage of tumour to alleviate oedema, organ compromise and psychological stress.

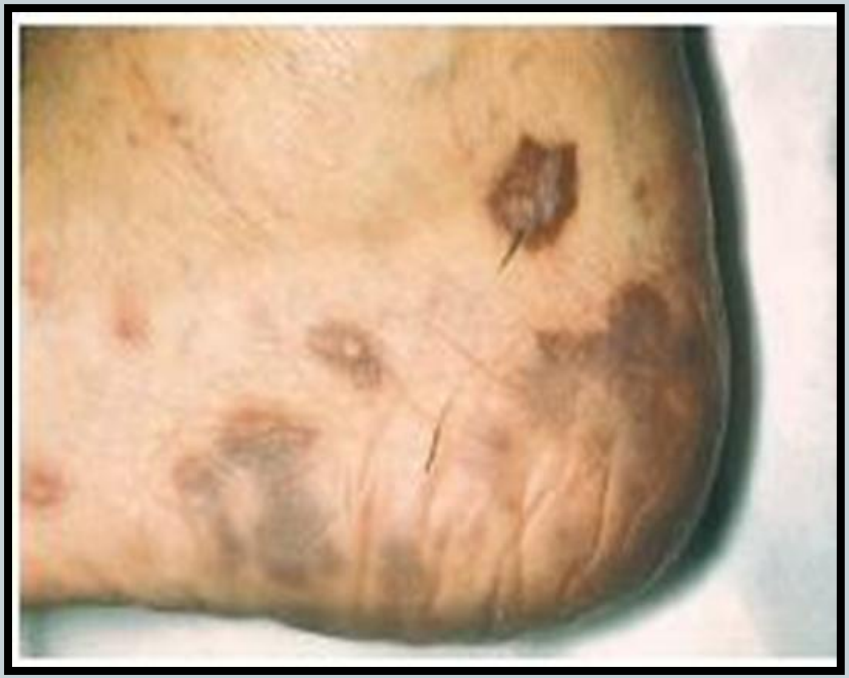
- **ALL** patients should receive HAART irrespective of CD4 count or viral load – variety of other options depend of extent of disease and rate of tumour growth.

KAPOSI'S SARCOMA
HAART

- HAART is associated with:
  - Decreased proportion of new KS cases.
  - Regression in size of existing KS lesions.
  - Possibly improved survival with or without chemotherapy.
- Immune reconstitution due to control of HIV most likely explanation for survival benefits.
- HIV protease inhibitors:
  - Anti-angiogenic properties.
  - Block development and progression of KS lesions in nude mice.

KAPOSI'S SARCOMA
Local Therapy - Radiation

- Useful for management of localised bulky disease or for cosmesis BUT does not influence development of new lesions in untreated areas.
- Discomfort from radiation is frequent but resolves within two weeks of treatment.

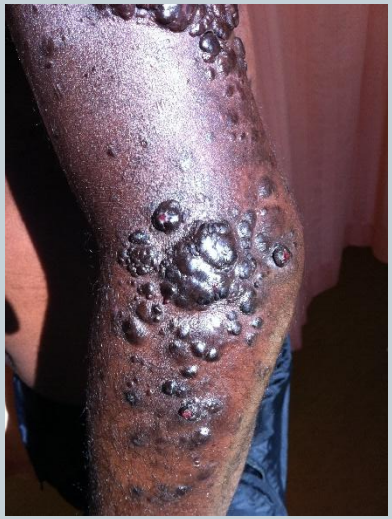


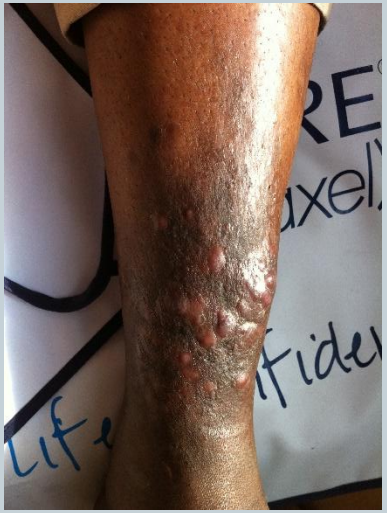
KAPOSI'S SARCOMA
Local Therapy – Intralesional Chemotherapy

- Injected directly into KS lesion – multiple injections may be required for larger lesions.
- Second series of injections usually needed three to four weeks later.
- Lesions usually fade and regress but don't typically resolve completely.

KAPOSI'S SARCOMA
Systemic Chemotherapy

- Generally accepted indications for systemic therapy include:
  - Widespread skin involvement (usually more than 25 lesions).
  - Extensive cutaneous KS unresponsive to local treatments.
  - Extensive oedema.
  - Symptomatic visceral involvement.





KAPOSI'S SARCOMA
Systemic Chemotherapy

- Liposomal Anthracyclines:
  - Theoretical advantage of longer plasma half-life, higher tumour concentrations and less toxicity in non-target organs compared with conventional anthracyclines.
  - Standard first line therapy for KS in USA.
  - Diminished cardiotoxicity permits higher cumulative dosing lengthening duration over which agents can be used (R35 000 / treatment).
  - State Hospital standard – Adriamycin / Bleomycin / Vinblastine (R800 / treatment).

KAPOSI'S SARCOMA
Systemic Chemotherapy

- Taxanes:
  - Potentially more toxic than anthracyclines but has striking efficacy in second-line treatment.
  - Two potential interactions between paclitaxel and antiretroviral therapy:
    1. Dexamethasone premedication required for taxane administration – may further immunosuppress and exacerbate KS.
    2. Paclitaxel metabolism involves cytochrome P450 – profound paclitaxel-related toxicity demonstrated in at least two patients – caution with indinavir / ritonavir / saquinavir / nevirapine.

CANCER IN HIV POSITIVE PATIENTS