

HIV and the Cervix

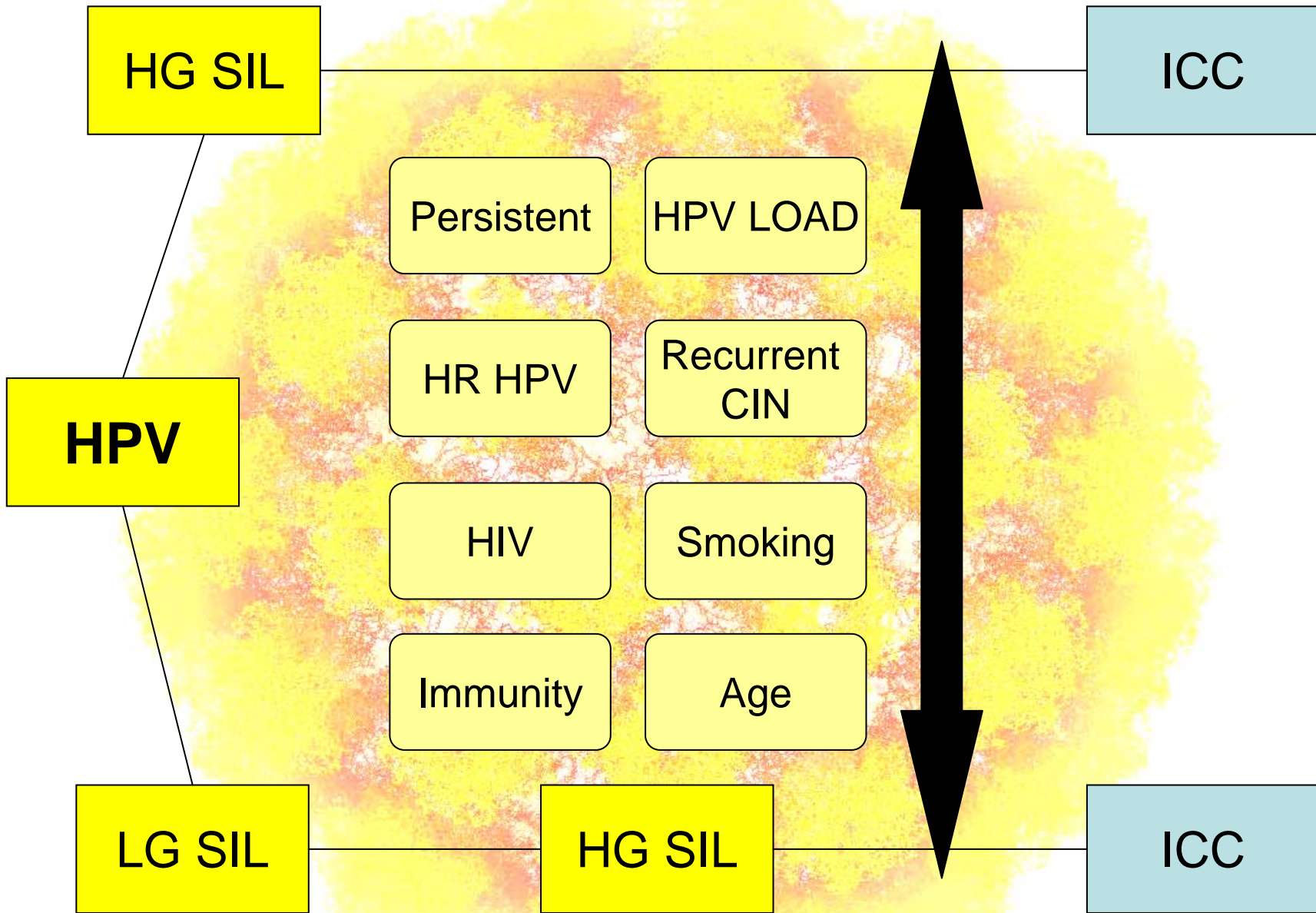
The Cervix and HIV

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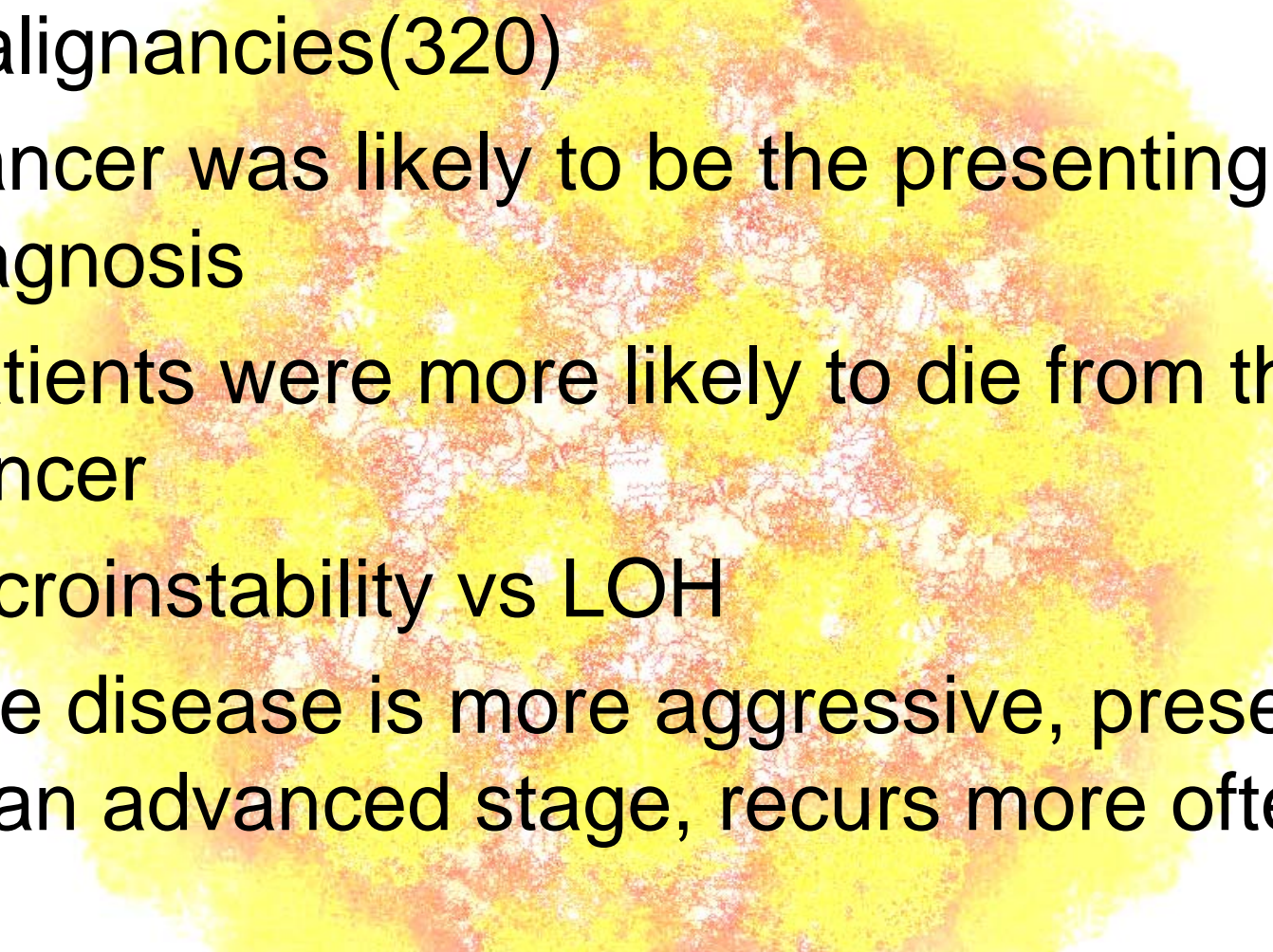


Cancer of the Cervix

- CDC definition- 1.3% of all women- 13yrs.
- No increase in ICC. 1995,1997,1998.
- Sentinel Hospital Surveillance System for HIV positive women- 1998.
- Most common AIDS related malignancy in women-1998.
- Marginally significant increase- 1999.

Cancer of the cervix

- 2000, both SA and Uganda marginal increases.
- 2000, RR for ICC was 5.4.
- 2006, Cape Town. No excess risk, women were 6 years younger- stage of presentation was the same.

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- CD4 counts were higher than with other malignancies(320)
 - Cancer was likely to be the presenting diagnosis
 - Patients were more likely to die from this cancer
 - Microinstability vs LOH
 - The disease is more aggressive, presents in an advanced stage, recurs more often.

HPV

- HPV satisfies KOCH'S principles.
- HIV and cancer of the cervix are endemic.
- Canadian Women's study: Women between the ages of 15-44, prevalence of 73,6% in HIV +ve women and 52.5% in HIV -ve women.
- As high as 95% in HIV infected women and 22% in uninfected women.
- 2%-3% of HPV progresses

HPV Subtypes

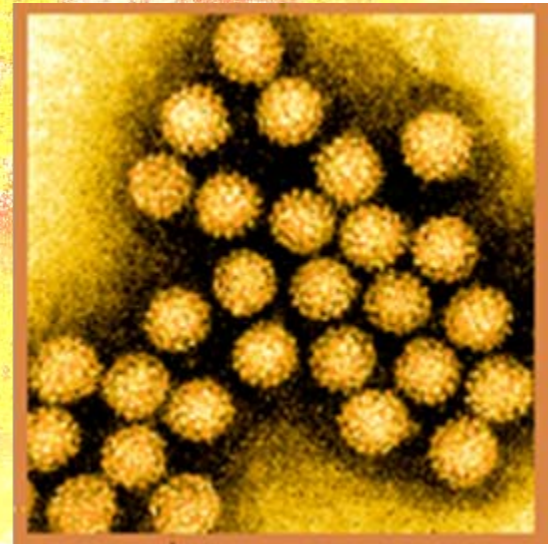
- HIV +ve women are more likely to be infected with HPV types of high oncogenic risk.
- Infected with multiple HPV types.
- Incidence of High risk types increase with immunosuppression.
- Increase of Low risk HPV in HIV +ve pat assoc with HG SIL.
- HIV increase the oncogenecity of HPV and increase the activity of low risk HPV.

Persistent HPV

- Cumulative prevalence of persistent HPV infection (more than 2 positive test results) was higher among HIV +ve than among HIV-ve women (87% vs 52%–73%).
- More likely than the latter group to shed HPV DNA continuously
- Persistent HPV infection was correlated with CD4+ cell counts.

HPV load

- High HPV load was associated with a 10-fold increased risk of CIN among women with severe immunosuppression.
- HPV integration versus episomal HPV



CIN

- 7% to 42% in the Northern Hemisphere.
- Recent Cape Town Study- 50% and Zambia 76%
- Aggressive course, progress rapidly and recurs (62% to 87%)
- Independent of residual disease.
- HIV seropositivity and HIV induced immunosuppression have emerged as independent risk factors (CD4 450).

Immunity of the cervix

- Independent of systemic immune reactions.
- Cervix possesses a local immune system which has all the characteristics of a mucosa associated lymphoid system.
- Both HIV and HPV affect the immune system.
- Decreased Langerhans cells.

Immunity of the cervix

- Inverse ratio of CD4:CD8.
- CSW resistant to HIV 1. Increase in CD4 T cells, 10 fold increase in RANTES exp, increase in B cytokines.
- HPV can modify cytokine production.
- HIV will make cytokine production worse.
- IL 2, IL 4, IL10 increased.

Haart CIN and ICC

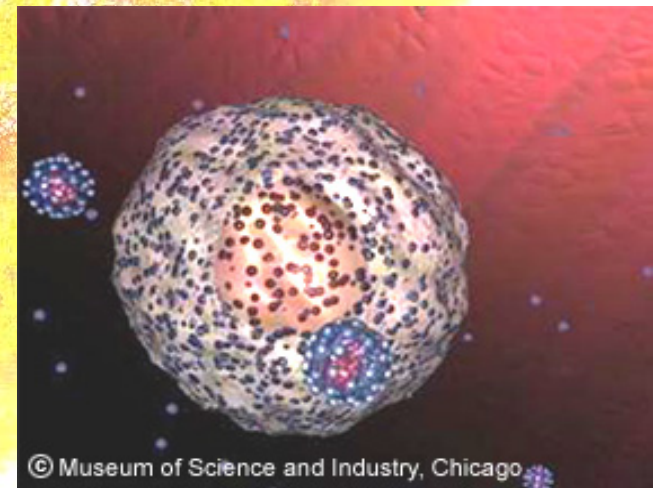
- Significant regression of SIL from 69% to 53%, but no change in HPV load- Direct effect of nucleoside on HPV.
- WIHS-Higher rates of regression.
- Small Italian study – HAART reduced other illnesses but not ICC.
- HIV as an independent co-factor.
- 2 Italian studies HAART increase immunity without changing the prognosis of CIN.

Viral-interactions

- Direct action of HIV proteins on HPV-infected epithelial cells.
- Direct or indirect immune based interaction
 - mutual increase in transmissibility
 - local immune compromise
 - compromise of mucosal integrity
 - mutual alteration of gene expression.
- Activation of both early and late HPV genes by HIV.

The cervix and HIV

- Cervicovaginal HIV-1 DNA
 - Shedding HIV – related to lower immunity.
 - Cell associated and free HIV1 in CIN
- Cervical ectopy/Visible lesions
 - Oral contraception
 - Nuristerate
 - Pregnancy/puberty
- Cervical mucus



IN CONCLUSION.....



- Prevention-technologies
- HPV Vaccines
- ✂ Circumcision
- Treatment of CIN
- Treatment of HPV
- Extending ARV's to patients with less advanced disease