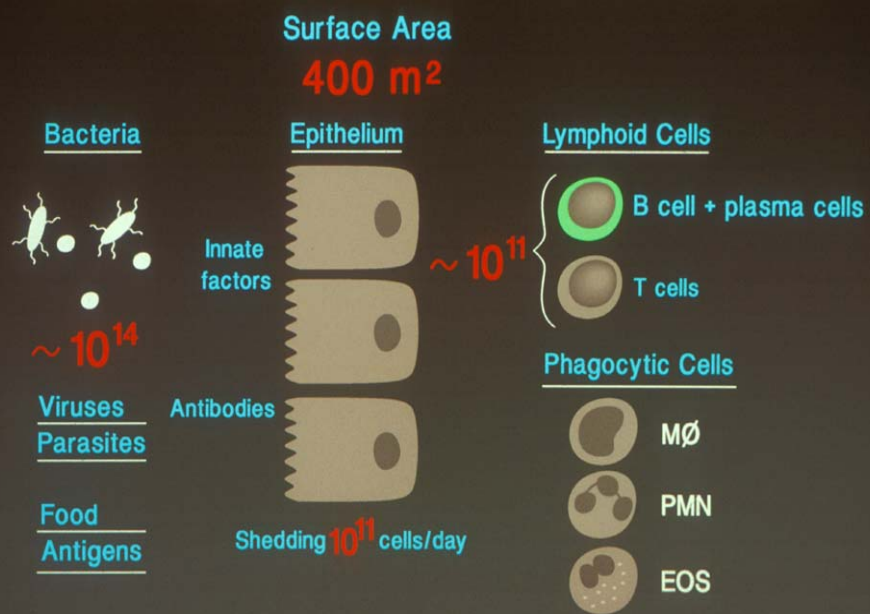


# Humoral Responses in HIV-infected Individuals

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## Immunological Battlefield of Mucosal Surfaces



## **HIV-1 and SIV Infections: Mucosal Involvement**

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**Virus entry:** genital tract  
                  intestinal              sexual contact, ingestion

**Virus replication:** intestinal tract

**Early depletion of CD4<sup>+</sup> T cells in mucosal tissues** – especially gut

**Altered mucosal immune responses:** decreased Ab responses to neoantigens  
                                                          decreased IgA responses to HIV-1 / SIV  
                                                          cell-mediated immune responses (?)

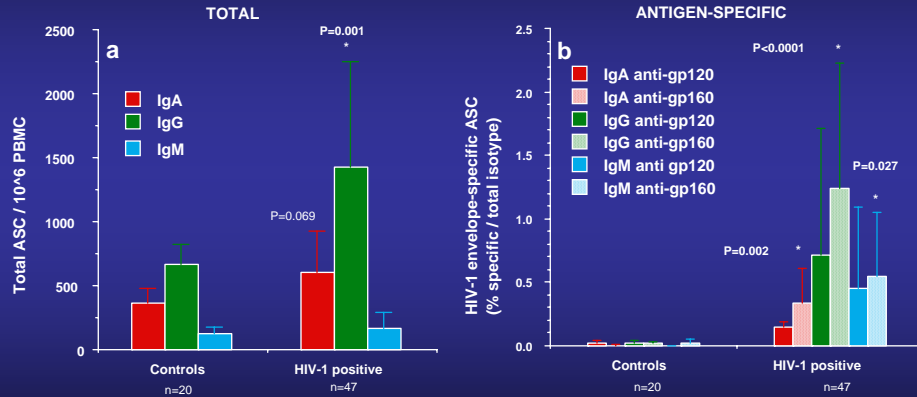
**Infections with mucosal pathogens**

## **Antibody-secreting Cells (ASC)**

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- **Plasma Ab are produced in the bone marrow >>> spleen, lymph nodes by resident plasma cells**
- **Mucosal Ab are produced locally with a variable but usually very low (<1%) contribution from plasma**  
**Exception - genital tract, urine, bile, lungs**
- **Peripheral blood ASC - cells on their way to mucosal tissues and spleen and lymph nodes (homing receptors)**  
**transient (1-2 wks) appearance of specific ASC in peripheral blood**

## IgA, IgG AND IgM-SECRETING CELLS IN PERIPHERAL BLOOD



## Paucity of HIV-1-Specific IgA Responses in HIV-1-Infected Patients

Fluid	Isotype	Total Ig level (ng/ml)	Specific antibody level (ng/ml)	Specific Ab as % of total	
				IgG	IgA
Serum (50)	IgG	15,513,000	108,000	0.7	
	IgA	2,173,000	3,290		0.15
Rectal fluid (49)	IgG	4,500	106	2.4	
	IgA	165,000	26		0.02
Cervico-vaginal fluid (26)	IgG	108,000	3,148	2.9	
	IgA	31,000	69		0.2
Seminal plasma (18)	IgG	62,000	2,895	4.7	
	IgA	47,000	68		0.15
Peripheral blood antibody-secreting cells (47)				1.2	0.3

## Immune Responses to HIV-1 in Infected Individuals

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- Increased levels of total IgG in sera and some external secretions; less evident for IgA
- HIV-1-specific IgA – present at very low levels in sera > vaginal washes > seminal plasma > urine > nasal washes.
- HIV-1-specific antibodies present in sera and the majority of secretions – DOMINANT ISOTYPE - IgG
- Urine, vaginal washes, nasal washes and seminal plasma – highly reliable (94 – 100%) for the detection of IgG HIV-1-antibodies by ELISA
- Parotid saliva and rectal washes – unreliable, frequently false positive
- Chemiluminescence-enhanced WB more reliable than ELISA
- When present, IgA HIV-1 antibodies are specific for gp160

## Selective IgA Hyporesponsiveness to HIV-1 Antigens in Sera, External Secretions and Peripheral Blood Antibody-secreting Cells

## General Conclusions

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- No significant change in total IgA levels in sera and secretions
- Antigen-specific IgA responses to HIV-1 absent or very low
- HIV-1-exposed but seronegative women have no IgG or IgA HIV-1-specific antibodies in external secretions
- Specific responses to other antigens (e.g., influenza virus) preserved in sera and secretions
- HIV-1-specific IgG responses in sera, secretions and ASC are dominant

SELECTIVE IgA HYPO- OR UN-RESPONSIVENESS TO HIV-1 IN MOST INDIVIDUALS

## HIV Infection and Aging

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- Alterations in the magnitude and Ig isotype responses in sera and external secretions
- Alterations of immune responses to chronically-encountered antigens (indigenous mucosal microbiota-exhaustion of the immune system)
- Alterations in humoral responses to systemic (e.g., pneumococcus, influenza virus) and mucosal (e.g., intranasal influenza virus) vaccines