

Lecture 2. Diseases of the immune system. Principles of immunodiagnosis, immunotherapy, immunorehabilitation and immunoprophylactics.

Lecturer: professor, DM V. Babadzhan.

Immune deficiencies

Occur when one or more components of the immune system are defective.

Immune defects can be inherited or acquired.

The immune defects can involve the T cell, the B cell or both compartments of the immune system, the Complement or the APC.

Immunodeficiency

- Can involve the different parts of the immune system either alone or together
 - May involve a deficiency in cell-mediated or humoral immunity
 - May involve deficiency in phagocytosis
- Divided into
 - Primary immunodeficiency of genetic origin
 - Secondary immunodeficiency from another underlying disorder

Immunodeficiency Diseases

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graph TD; A[Immunodeficiency Diseases] --> B[Primary]; A --> C[Secondary];
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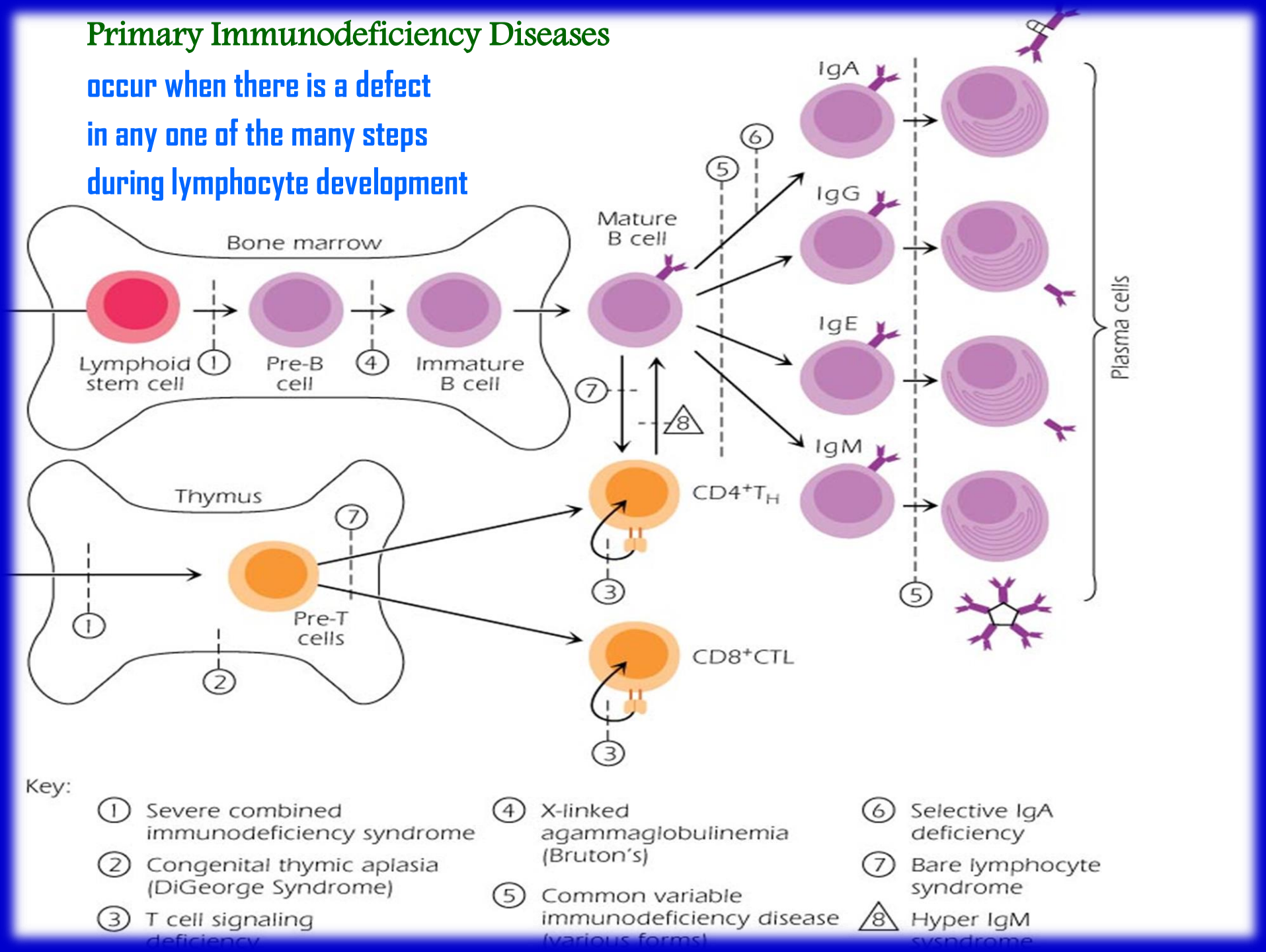
Primary: Usually congenital, resulting from genetic defects in some components of the immune system.

Secondary: (Acquired): as a result of other diseases or conditions such as:

- »HIV infection
- »malnutrition
- »immunosuppression

Primary Immunodeficiency Diseases

occur when there is a defect in any one of the many steps during lymphocyte development



Classification of Primary IDDs

- **Primary B cell immunodeficiency:**
 - X-linked Agammaglobulinaemia (Bruton,s disease)
 - Selective IgA deficiency
- **Primary T cell immunodeficiency:**
 - Di George syndrome
 - Ataxia – telangiectasia
 - Wiskott – Aldrich syndrome
 - Acquired immunodeficiency
 - Chemotaxis deficiency
 - Chronic granulomatous disease
 - Chediak – Higashi syndrome
 - Leukocyte adhesion deficiency
- **Complement system deficiency**

Primary B Cell Immunodeficiency

- Common variable immunodeficiency associated with
 - Mature B cells failure to differentiation into mature plasma secreting cells (antibody forming cells).

X-linked Agammaglobulinaemia (XLA)/Bruton's Disease:

- Deficiency of B cell tyrosine kinase causing failure in the development of pre-B cell maturation to B cells.
- Majority of XLA patients show:
 - Profound hypogammaglobulinaemia involving all immunoglobulin classes with <1% B cells in normal peripheral blood.
 - Patients suffer mainly from infectious diseases with bacteria and viruses that require antibodies for their disposal.

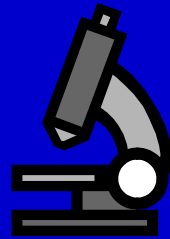
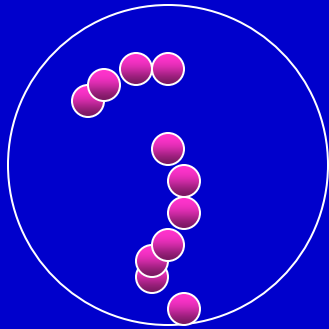
Bacterial Infections

1.Impetigo: This is typified by dermal lesions on face or extremities and often affects groins and axillae. Lesions, which may be either bullous (blisters which rupture) or non-bullous (smaller and encrusted) are highly contagious. The causative agent of bullous lesions is *Staphylococcus aureus* and of non-bullous lesions is Group A, hemolytic streptococcus. Topical or systemic antibiotics are the customary treatment.

2.Scarlet fever: Scarlet fever is an infection by group A streptococci (*Streptococcus pyogenes*) and is characterized by a bright red papular rash on the trunk. In the oral cavity “strawberry tongue” is common which is a red tongue covered by a removable coating and presence of distinctive swollen papilla. Treatment consists of systemic antibiotic regimens and complications include rheumatic fever, arthritis and glomerulonephritis.

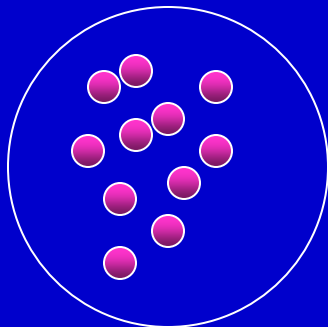
BACTERIAL INFECTIONS

Impetigo:



The ruptured blister, encrusted lesions are caused by beta hemolytic Group A streptococci.

The bullous lesions are caused by *Staphylococcus aureus*



Selective IgA deficiency (IgA D)

- **Patients with IgA deficiency have:**
 - IgA levels < 5mg/dL with normal levels of other Igs and
 - 50% have chronic otitis, sinusitis or pneumonia.
- **IgA committed B lymphocytes:**
 - Fail to mature into IgA-secreting plasma cells caused by intrinsic B cell defect.
- **Patients of IgA deficiency are susceptible to:**
 - Allergic conjunctivitis, urticaria and asthma.
 - Autoimmune and neurological disorders.
 - Various gastrointestinal diseases (food allergy).
 - recurrent sinopulmonary infections.

Severe Combined Immunodeficiency Disease (SCID)

Disorder characterized by:

- Deficiency in both B and T lymphocyte functions with markedly low IgG, IgA and IgE levels.
- SCID associated with:
 - Children failure to thrive.
 - chronic respiratory infections.
 - Gastrointestinal and/or cutaneous infections particularly recurrent viral, bacterial, fungal and protozoan infections in 6 months' infants.

- SCID manifests early with:
 - Persistent and recurrent diarrhoea, otitis, thrush and respiratory infections in the first few months of life.
- T cell defects associated with:
 - Candidiasis, CMV infection, measles and varicella leading to life threatening pneumonia, meningitis and sepsis.
- **SCID managed through Ig infusion, stem cell transplantation and gene replacement.**

T Cell Immunodeficiency Diseases

- **T cell congenital disorders display:**
 - Little or no cell mediated immunity and may involve B cell deficiencies.
- **Patients particularly susceptible to:**
 - Repeated fungal (*Candida*) infection.
 - Protozoan and viral infections.

Primary T cell immunodeficiency includes:

- **Di-George syndrome**
- **Wiskott-Aldrich syndrome**
- **Cartilage hair hypoplasia,**
- **Ataxia - telangiectasia**
- **Defective expression of class II MHC molecules**
- **Defective expression of CD3-T cell receptor (TCR) complex**

Di George Syndrome (Thymic Aplasia)

Congenital disorder characterized by:

- Lack of embryonic development or underdevelopment of the 3rd and 4th pharyngeal pouches.
- Thymic hypoplasia, hypothyroidism and congenital heart disease.
- Patients susceptible to uncontrolled opportunistic infections.
 - Impaired in cellular mechanisms.
 - Profound lymphopenia (T cell $<1200\mu\text{L}$).

Ataxia Telangiectasia (AT)

Autosomal recessive progressive neurodegenerative childhood disorder associated with:

- Lack of coordination (cerebella ataxia) and dilation of facial blood vessels (telangiectasis) and slurred speech.
-
- Patients have defective mechanisms of DNA repair and are predisposed to leukaemias and lymphomas.
- Extremely sensitive to radiation exposure and susceptible to chronic respiratory infections.

Wiskott–Aldrich Syndrome (WAS)

An X-linked recessive disorder associated with thrombocytopenia and eczema.

- Patients have
 - Elevated IgA and IgE
 - Low IgM

Variable T cell dysfunction
T cell dysfunction manifested by:

- Severe herpes virus and *Pneumocystis carinii* infections
- Increased lymphomas and autoimmune diseases.
- Recurrent pyogenic bacterial infections.
- Usually affecting ears, sinuses and lungs.

Mixed Immunodeficiencies

Inherited defects of phagocytic function.

Inherited defects of complement: Loss of specific complement components. Inability to form the MAC and/or to produce anaphylatoxins.

Viral Infections

1.Acute herpetic gingivo-stomatitis (primary herpes infection): Primary herpes is a viral infection of the oral mucosa caused by Type I herpes simplex virus (HSV-1). It affects young children (usually under 5 years) who have not developed resistance to the virus. Clinically, patients present with multiple painful ulcers, 1 to 2mm in diameter surrounded by erythematous tissue on all mucosal surfaces of the oral cavity. Pain upon eating, especially salty or acidic foods, is common and tooth-brushing is painful if ulcers appear on gingivae. Low fever and malaise also are present and patients often become under-nourished or dehydrated from insufficient food or liquids. The infection which sheds viruses from ulcers, is highly contagious and can spread to other mucous membranes such as eye tissue. The condition is self-limiting and will subside within 10 to 14 days.

VIRAL INFECTIONS

Primary herpes infection:

Symptoms:

1. **Painful generalized ulcers on oral mucosa. Sometimes it appears extra-orally.**
2. **Low fever and malaise. Patients often are undernourished due to pain upon eating.**
3. **Self-limiting. Will last 10 to 14 days.**
4. **Differential diagnosis must rule out candidiasis (thrush) which is not painful and produces a white membranous patches on mucosal surfaces.**



Occurs frequently in young children

VIRAL INFECTIONS

Primary herpes infection:

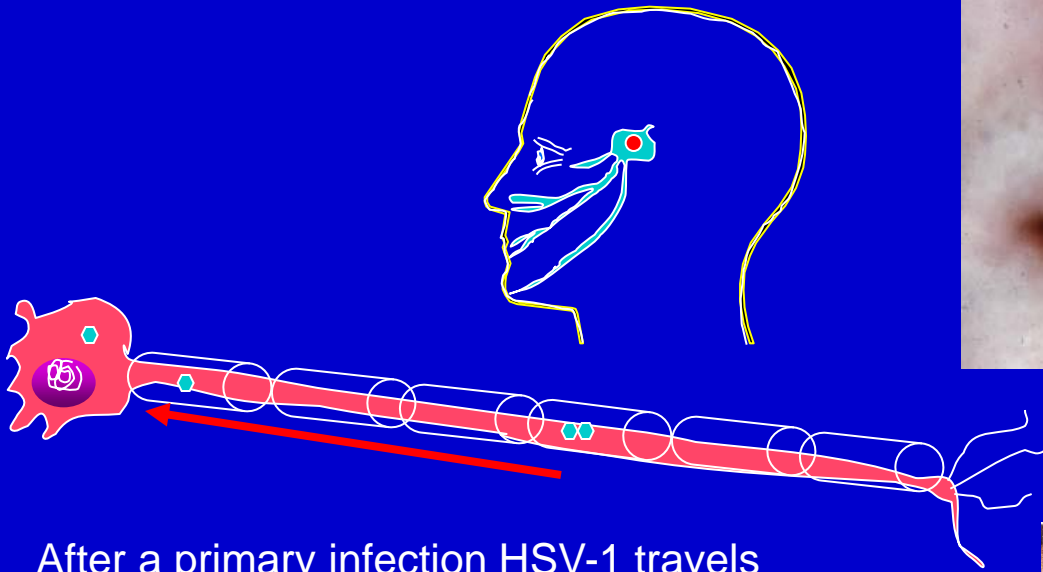
Treatment:

- 1. Palliative treatment**
- 2. Viscous topical anesthetic xylocaine or benadryl elixir plus kaopectate (to relieve for pain, especially upon eating) and Pedelite.**
- 3. A balanced nutrient drink to compensate for insufficient diets.**
- 4. Anti-viral agent Acyclovir (Zovirax; 400mg q3h for 10 days) may be administered in extreme cases to inhibit the virus.**
- 5. (Note: steroids should not be used as the inflammatory reaction constitutes the first line of defense against the virus.)**



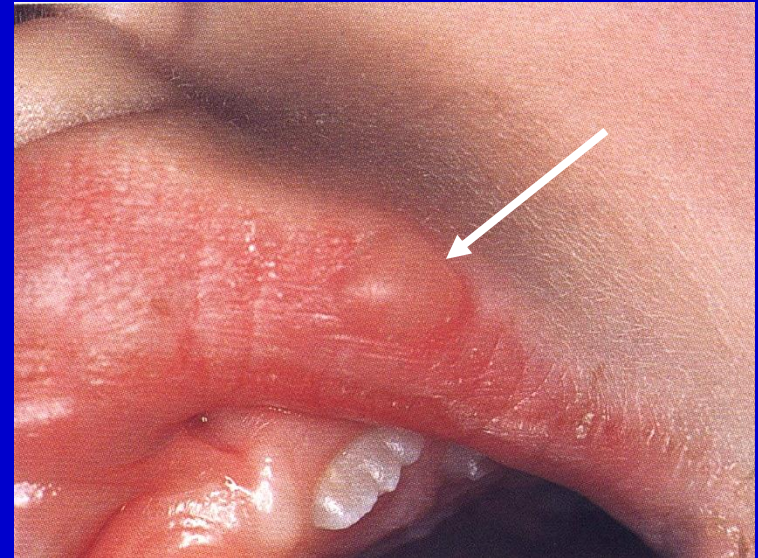
VIRAL INFECTIONS

Recurrent herpes labialis:



After a primary infection HSV-1 travels up a sensory nerve and remains dormant in a ganglion (trigeminal).

It can revert to the lytic form upon certain stimulation and usually erupts at the vermillion border of the lips.



Viral Infections

2.Recurrent herpes labialis (cold sore): This is a HSV-1 infection which occurs in individuals who previously experienced a primary herpes infection. The virus remains dormant in sensory nerve ganglia after the first infection, but can erupt following episodes of emotional stress, excessive exposure to sunlight, trauma, dental procedures or intake of certain foods to form single ulcerated lesions on the vermilion border of the lips and mouth (usually). The common occurrence during “cold seasons” when resistance is often compromised accounts for the name (cold sore). In addition, foods containing high levels of arginine such as cereals, nuts and chocolate can activate the virus. The limited manifestation, versus primary herpes, is due to immunity developed after the first exposure to the virus. The condition is self-limiting, lasting 10 to 14 days. Remedies which may enhance resolution of the ulcer are aloe or acyclovir which inhibit HSV-1. Foods high in lysine such dairy products and yeast may alleviate the condition by counteracting the effect of arginine.

Viral Infections

3.Herpangina: This is caused by the cocksackie A virus and is evidenced by multiple painful ulcers on oral mucosa similar to primary herpes infections. The susceptible age is similar to that of primary herpes, being before age 5, but it is less common and affects mainly the distal portion of the mouth or throat.

Treatment and progress of the condition is similar to that of primary herpes.

4.Hand, foot and mouth disease: The causative agent is cocksackie A virus and clinical appearance is herpetic-like multiple ulcers on the hard palate, tongue and buccal mucosa. The susceptible ages are 1 to 10 years and the condition is less common than primary herpes. In addition, characteristic ulcerative lesions appear on soles of feet and plams. Treatment and course of the disease are similar to primary herpes.

5.Herpes zoster infection (varicella zoster virus, Type 3 Herpes Simplex virus): This is commonly known as chicken pox when it affects school age children and first appears as papular lesions on the skin which form encrusted ulcers. If the virus infects adults, shingles, a painful dermal condition, will develop. In chicken pox oral lesions appear on oral mucosa secondarily to skin lesions and resemble herpetic ulcers, but are not painful (usually). The disease confers immunity and is self-limiting within 14 days.

VIRAL INFECTIONS

Varicella (chicken pox) – zoster (shingles). Human Herpes Virus-3; HHV-3:



chickenpox



shingles

Coxsackie A virus:



Herpangina



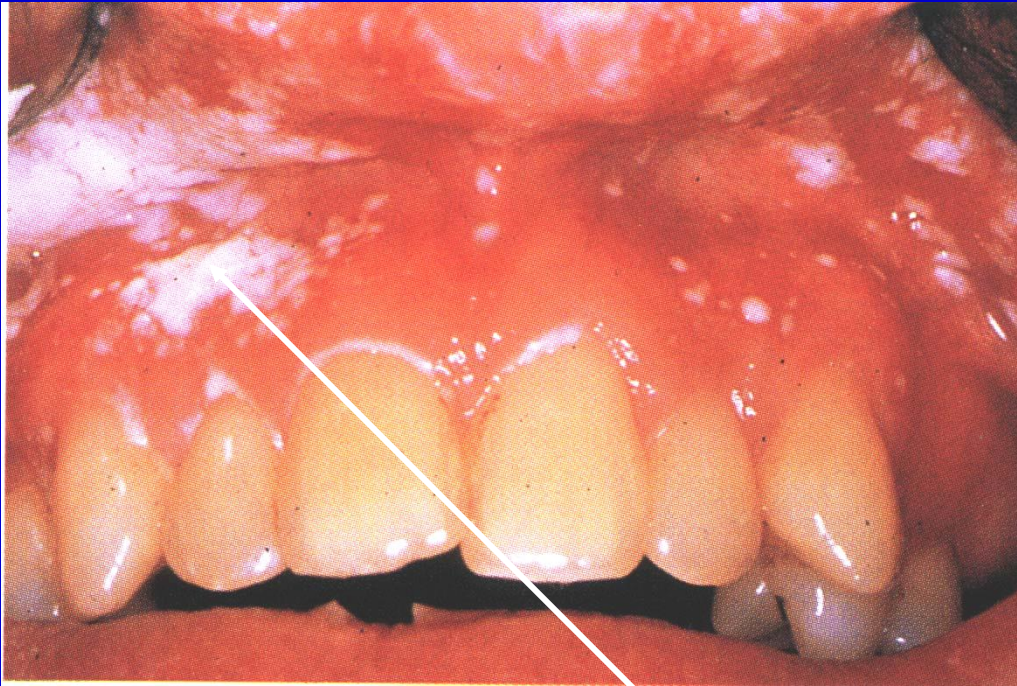
Hand foot and mouth disease

Fungal Infections

Candidosis (thrush) is the most common oral fungal infection and frequently affects young children. It appears as white patchy lesions on the oral mucosa. When the white patches are removed a bright red tissue surface is seen which is usually non-painful. Sometimes a distinctive yeasty oral odor is present. Occurrence frequently follows broad spectrum antibiotics, but it may also be transmitted from vaginal yeast infections. Diagnosis may be confirmed by identification of *Candida albicans* in mucosal specimens and treatment consists of topical anti-fungal ointment such as Nystatin.

FUNGAL INFECTIONS

Candidosis (Thrush):



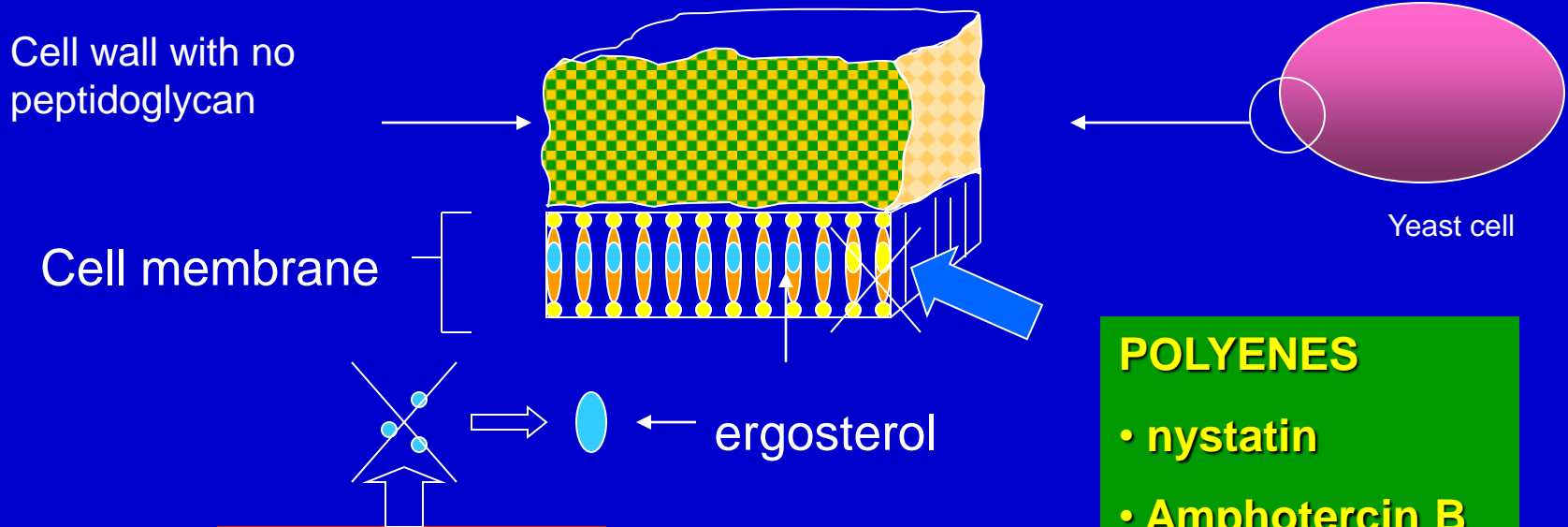
Oral thrush



adam.com

“thrush”, “acute pseudomembraneous”

TREATMENT



AZOLES

- miconazole
- fluconazole
- ketoconazole

These inhibit
synthesis of
ergosterols

POLYENES

- nystatin
- Amphotercin B

These adsorb to
cell membranes
and disrupt
ergosterols

Recurrent Aphthous Ulcer (canker sore)

This appears as single (usually) painful erythematous ulcers on oral mucous membranes which are slightly larger than herpetic lesions. The condition is self-limiting within 14 days, but contains no virus. The etiology has not been definitively established, but may involve autoimmune reactions to antigens from *Streptococcus sanguis*. Several palliative non-prescription remedies are available including kenalog in orabase (a steroid anti-inflammatory agent; Note: steroids may be used since viral etiology is not suspected.)

RECURRENT APHTHOUS ULCER (CANKER SORE)



The condition is self-limiting and is treated by palliative measures.

A definitive cause is not known.

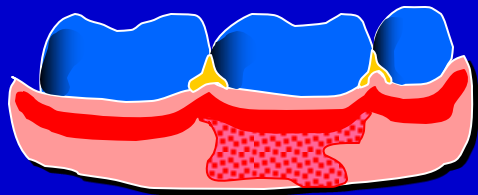


SYSTEMIC DISORDERS WITH ORAL MANIFESTATIONS

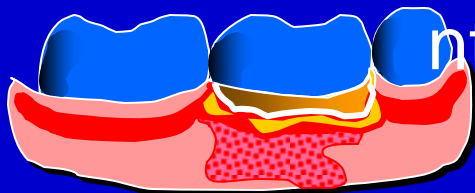
AID



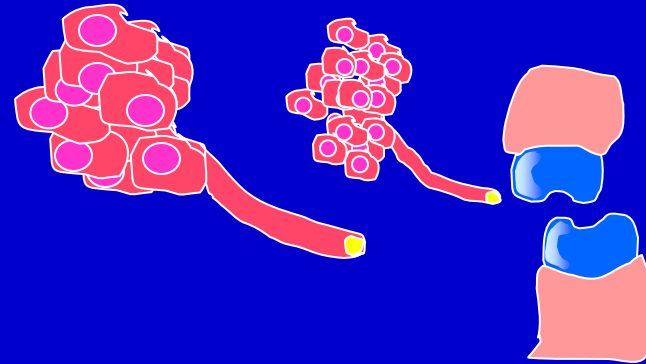
thrush



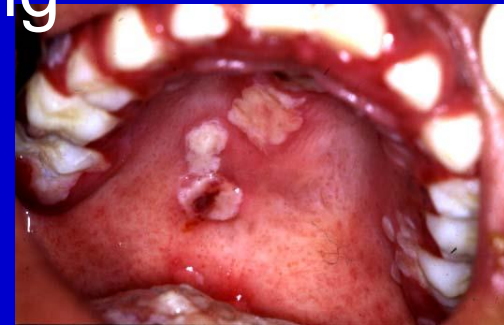
gingivitis



periodo
ntitis



Parotid
swelling



Herpetic
ulceration

SIGNS, ALLOWING TO SUSPECT IMMUNODEFICIENCY

- **Recidivic bacterial-viral infections which are characterized:**
 - a) **chronic course;**
 - b) **incomplete reconvalescence;**
 - c) **unsteady remissions;**
 - d) **unusual microflora (opportunistic infection, with multiresistence stability to the antibiotics).**
- **Unusual reactions on vaccines.**
- **Information of physical investigation:**
 - **delay of development; decline of body mass; subfebril tempereture; increase, excalation or complete absence of lymphatic knots, amygdales, thymus; dermatitises, skin abscesses; candidosis of mucous membrane of mouth cavity.**
- **Haematological changes: leukocitopenia, thrombocitopenia, anaemia.**
- **Paratherapeutic interferences:**
 - **chemotherapy; splenectomy; irradiation.**
- **Protracted stress.**
- **Autoimmune diseases.**
- **Tumour.**

Acquired immune deficiency is violation of the immune system, developing in a postneonatal period (in adults) and not subsequent upon genetic defects.

Acquired immune deficiency is dysimmunity, which arise up as a result of somatic and other diseases, and also other factors and have clinical symptoms.

Acquired immune deficiency

- a) develops on a background before normally functioning immune system;
- b) characterized the proof decline of quantitative and functional indexes of immune status;
- c) it is the area of risk development of chronic infectious diseases, autoimmune pathology, allergic diseases and tumor formations.

Forms of acquired (secondary) immunodeficiency

The acquired secondary immunodeficiency is a syndrome of AIDS, developing as a result of defeat of the immune system the human immunodeficiency virus (HIV).

The inducing (specified) secondary immunodeficiency (ICD-10, code D.84.8) arises up as a result of concrete reasons, causing its appearance: x-ray radiation, cytostatic therapy, application of corticosteroids, traumas and surgical intervention, dysimmunities, developing the secondary in relation to a basic disease (diabetes, disease of liver, kinds, malignant tumors).

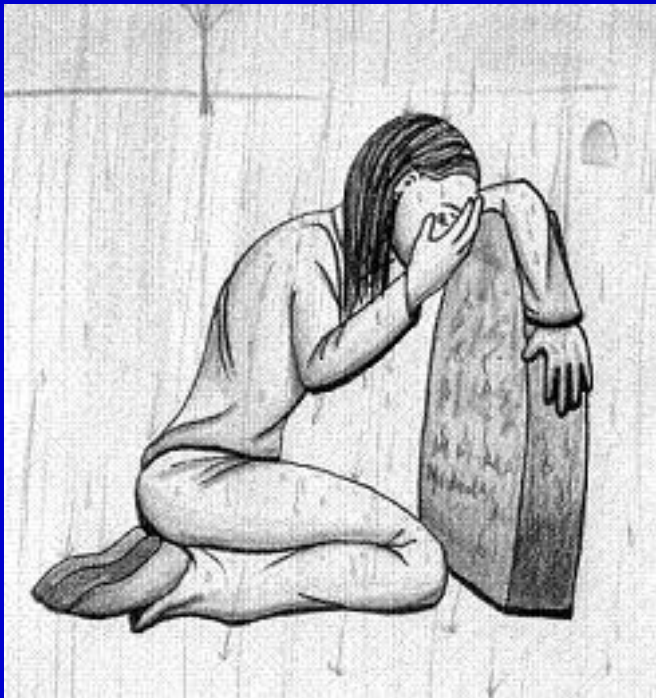
The spontaneous (unspecified) secondary immunodeficiency (ICD-10, code D.84.9) is characterized absence of reason, causing violation of immune reactivity. Clinically shows up as chronic, recidivate infectious-inflammatory processes of bronchial tree, additional lesions of nose, urogenital and gastroenteric system, eyes, skin, soft tissues, caused opportunistic microorganisms.

CLASSIFICATION OF SECONDARY IMMUNODEFICITES

- By the rates of development:
 - Acute immunodeficiency (conditioned an acute infectious disease, trauma, intoxication and other).
 - Chronic immunodeficiency (develops on a background of chronic festering-inflammatory diseases, autoimmunity, tumors, persistent viral infection).
- II. By the level of breakage:
 - Violation of cellular (T-cells) immunity.
 - Violation of humeral (B-cells) immunity.
 - Violation of phagocytes.
 - Violation of complement system.
 - Combined defects.
- III. By prevalence:
 - «Local» immunodeficiency.
 - Systemic immunodeficiency.
- IV. By the degree of severity:
 - Compensated (mild).
 - Subcompensated (moderate).
 - Decompensated (severe).

Psychological aspects

- beta-endorphins
- during exams
 - lymphopenia
 - activity of NK cells
 - ↓ production of IFN-gamma
 - ↓



Secondary Immunodeficiencies

Examples of Drugs That Can Cause Immunosuppression

Name	Use
Azathioprine	Prevention of rejection of renal transplants Treatment of rheumatoid arthritis
Cyclosporine	Prevention of rejection of renal transplants
Cyclophosphamide	Cancer chemotherapy
Methotrexate	Cancer chemotherapy
Prednisone	Treatment of autoimmune diseases (such as rheumatoid arthritis, pemphigus vulgaris, Behçet syndrome, lupus erythematosus)

Secondary Immunodeficiencies

- Occur as the result of an underlying disorder
 - May be malnutrition, viral infection, cancer, renal disease and Hodgkin's disease
 - May occur with immunosuppressive drugs, drugs used along with radiation, chemotherapy

Oral Manifestations of Therapy for Oral Cancer

- Radiation Therapy
- Chemotherapy

Consequences of immunodeficiencies in dental patients

Increased incidence of infections in the oral cavity (Herpes virus), even with organisms that are usually non-pathogenic such as *Candida* species (candidiasis):

In AIDS patients

In cancer patients undergoing chemotherapy, and in immunosuppressed transplant recipients:

Increased plaque formation

Ulcerations

Xerostomia

Sialadenitis

Periodontal disease, bone loss

Osteomyelitis

Papillary atrophy of the tongue

Radiation Therapy

- The patient often experiences mucositis during radiation therapy.
 - Mucositis begins about the second week of therapy and subsides a few weeks after its completion.
 - It is painful and appears as an erythematous and ulcerated mucosa.
 - The patients may have difficulty eating, pain on swallowing, and loss of taste.



Radiation Therapy (cont.)

- Destruction of major salivary glands may result in xerostomia
 - The patient is prone to rampant caries and oral candidiasis.
 - They also are prone to osteoradionecrosis.



Radiation Therapy (cont.)

- Patients should have an oral evaluation before radiation therapy of the head and neck.
 - Potential sources for oral infection and teeth with a questionable prognosis should be removed.
- The hygienist can help with
 - Fluoride application
 - Patient education
 - Frequent follow-up appointments

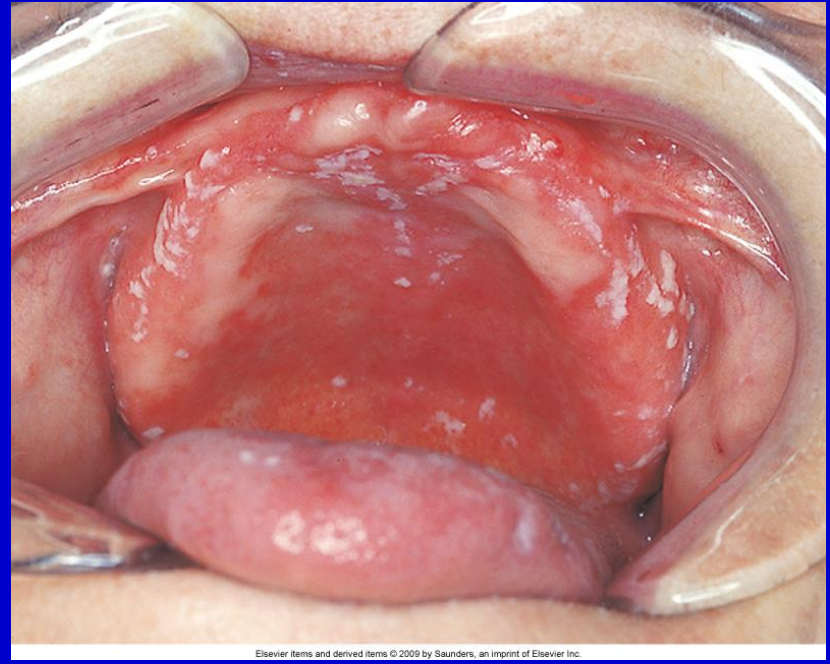
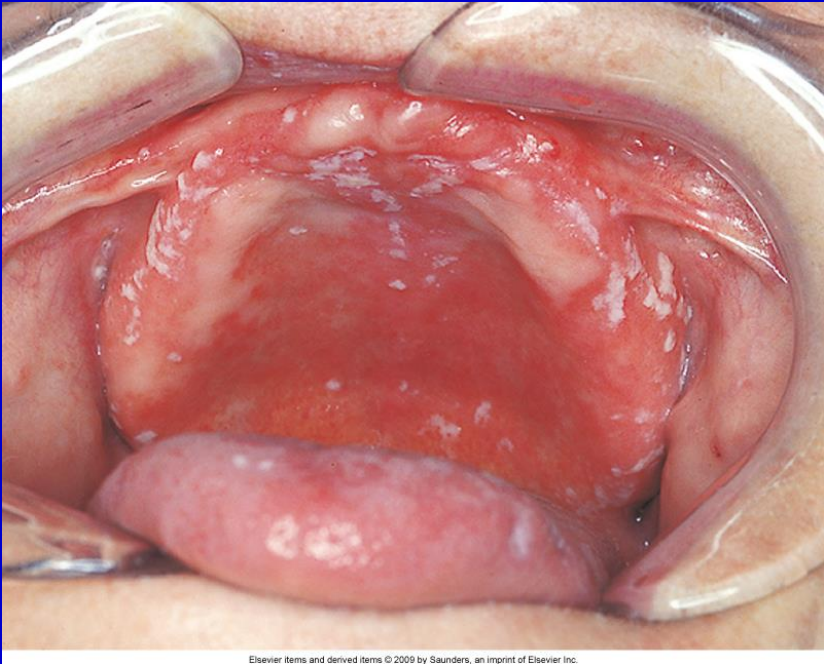
Chemotherapy

- Drugs used for cancer chemotherapy affect basal cells of the epithelium.
 - Mucositis and oral ulceration are common complications.
- A decrease in all blood cells may occur
 - Lowered RBC counts can lead to anemia.
 - Lowered WBC counts can lead to infections.
 - Lowered platelets can lead to bleeding problems.

Effects of Drugs on the Oral Cavity

- Blood pressure drugs, antianxiety medications, antipsychotic medications, and antihistamines can cause xerostomia.
- Prednisone suppresses the immune system and can lead to candidiasis and oral infections.
- Antibiotics may increase risk of candidiasis.

Effects of Drugs on the Oral Cavity (cont.)



Effects of Drugs on the Oral Cavity (cont.)

- Tetracycline can cause tooth discoloration.
- Phenytoin and nifedipine can cause gingival enlargement.
- Cyclosporine may cause gingival enlargement.

Immunotropic preparations

- **Immunostimulators (immunomodulators)**
- Biological (human, animal origin):
 - - Immunoglobulins
 - - Erbisol
 - - Thymalin
 - - Tactivin

- **Immunosuppressive**
- Glucocorticosteroids
- Citostatics
- Monoclonal antibodies
- Ciclosporin A

Immunoprophilactic and immunorehabilitation preparations

- Vegetable
- Bacterial
- Mycotic
- Antiviral vaccines
- Allergovaccination

Immunostimulators

Clinical criteria: chronic infection, low efficiency of treatment of inflammatory process; treatment of cytostatics, glucocorticosteroids, antibacterial and radial therapy.

Immunological criterias: decrease of amount and functional activity of lymphocytes, decline level of immunoglobulines, complement, phagocytic activity (uncompleted phagocytosis) no less what on 30-50%.

Immunosuppressive therapy

Clinical criteria: heavy forms of allergy with the defeat of kinds, transplantation of organs and tissues, connecting system diseases.

Immunological criteria: appearance high titles of autoantibodyes in blood.

Classification of immune drugs at the point of application

Affecting primarily on a cellular link (NK-cells, T-killer cells)	Affecting mainly on humoral (B-lymphocytes, Ig)	Affecting predominantly macrophage-monocytic link	influencing on interferon status
<ul style="list-style-type: none"> • timalin • Imunofan • immunomaks • Galavit ® (100 mg) 	<ul style="list-style-type: none"> • immunoglobulins • Interferons (reduce the synthesis of immunoglobulins) • Bacterial Immunopreparat (ribomunil, bronhomunal) • Galavit ® (200 mg - reduced the synthesis of low avidity antibody in a dose of 100 mg - improves the specificity of the antibody) 	<ul style="list-style-type: none"> • polioksidony • sodium nucleinate • immunomaks • derinat • Galavit ® 	<ul style="list-style-type: none"> • Interferon preparations: (laferon, viferon, Laferobion, etc.) • Interferon inducers (amiksin, Lavomax, tsikloferon, Kagocel, proteflazid) • Galavit ® (100 mg - increases the synthesis of interferon)

IMMUNOCORRECTION (I)

(ID, lymphocyte type)

CRITERIA

- 1. Decline of maintenance of CD3, CD4, CD25.**
 - 2. Decline of immunoregulatory index of CD4/CD8.**
 - 3. Decline of production IL-2, gamma-INF.**
 - 4. Increase of production IL-4, 5, 6.**
- STIMULATION of SYNTHESIS ILT-2 (IZOPRINOZIN, GROPRINOZIN)**
 - THYMIC PEPTIDS:**
 - old are THYMALIN, TAKTIVIN, THYMOPTIN**
 - new are ZADAKSIN, IMMUNOFAN**
 - METABOLIC ROW - GALAVIT.**

The patient 37 years old. Diagnosis: chronic recurrent herpes viral infection in the area of the face and lips. Oropharyngeal candidiasis. Immune deficiency in T-

Показник		Результат		Норма				
Гемоглобін		112		Ж – 115 – 145, М – 132 – 164 г/л			Виражений анізоцитоз, анізохромія ТЗН=45%	
Еритроцити		3,4		Ж - 3,7 – 4,7, М – 4,0 – 5,1x10 ¹² /л				
Тромбоцити		260		150 – 320x10 ⁹ /л				
ШОЕ		18		2 – 15 мм /год.				
Лейкоцити		3,8		4 – 9x10 ⁹ /л				
Нейтр. 43 – 71 % 2000-6500	Пал.\яд. 1 – 4 % 80-400	Сегм. \яд.	Еоз. 0,5 – 5% 80-370	Баз. 0 – 1% 20-80	Мон. 3 – 9% 90-720	Лімф. 25 – 37% 1600-3000	БГЛ 1-5% 80-500	Плаз. 0 – 1% 20-80
67	3	64	4	0	8	21	0	0
2550	110	2440	150		300	800		
Імунологічні показники		Результат	Норма (Од СІ)	Імунологічні показники			Результат	Норма (Од СІ)
Т- лімф.	%	45	50 – 80	Ig G			15,1	8,0-18,0 г/л
CD-3	Абс. число	360	1000-2200					
Т- хелп.	%	27	33-46	Ig M			4,08	0,2-2,0 г/л
CD-4	Абс. число	216	309-1571					
Т- супрес.	%	39	17-30	Ig A			1,62	0,3-3,0 г/л
CD-8	Абс. число	312	282-999					
ІРІ	CD-4/CD-8	0,69	1,4-2,0	ЦІК			62	30 – 50 Од. опт. щільн.
NK-клітини CD-16	%	15	12 – 23	Поглиналина активність		ФЧ	93	60 – 80%
	Абс. число	120	72-543			ФІ	4,57	1,5 – 3,5
В-лімф. CD-22	%	28	17-31	НСТ -тест		спон.	11	до 10%
	Абс. число	224	109-532			Інд.	19	-
РБТЛ	спон.	14	до 10%	Комплемент		рез.	8	16%
	інд.	71	50-70%			СН-50	74	30 – 60 гем. Од/мл

Causal and Immunotropic therapy:
 1) Zovirax (acyclovir) 400 mg is inside the 4 times a day for 1 month ; Gerpevir (ointment) lubricate the affected skin and mucous membranes of the lips 4 times a day 7 days;
 3) viferon 500 thousand IU 1 per day in candlelight for 1 month ; virohel - lubricate the affected skin and mucous membranes of the lips , 2 times a day, 5 - 7 days;
 - Interferon inductor - cyclopheron - 12.5 % injection - 2 ml , dose of 0.25 g / m at 1, 2, 4, 6, 8, 11, 14, 17, 20 , 23, 26, 29 days. After interferon ;
 4) imunofan 1 ml / m in a day , № 10;
 5) Polyoxidonium 12 mg (suppository) 1 every 3 days , № 10;
 6) amiksin 125 mg (1 cap.) Day after breakfast , № 20;
 7) intrakonazol (intrunhar) 100 mg 1 time a day for 2 weeks .

IMMUNOCORRECCION (II)

(ID, interferonone type)

CRITERIA

1. Decline of alfa- and gamma-INF production.
2. Decline of CD4 and CD16 levels .
3. Decline of immunoregulatory index of CD4/CD8.
4. Increase of IL-4, 5, 6 production.

- INTERFERONS (VIFERON, LAFERON);
- INDUCTORS of ENDOGENOUS INTERFERON and NK-CRLLS:
- NEOVIR, CYCLOFERON);
- AMIXIN;
- Antiagregants (CURANTYL);
- NEW (with the protracted effect) - KAGOCEL⁵⁴.

PRINCIPLES of INTERFERON THERAPY

in the syndrome of chronic fatigue and immunodeficits

- 1. Local and systemic application of viferon (laferon).**
- 2. High or middle doses of viferon (laferon) from the beginning of treatment, since 2-3 millions, rarer - with 4-6 million - during 1,5-2 months, further, -**
- 3. The doses of Viferon go down «step by step» in 1,5-time each 2-3 weeks, rarer, - each month.**
- 4. In the relapse of infection to return to former, more high dose on 2-3 weeks, further, is an attempt of decline of dose.**
- 5. Duration of course treatment of viferon (laferon) - no less than 3,5-4,5 months.**
- 6. If necessary courses repeat in critical periods.**

IMMUNOCORRECTION (III)

(ID, humoral type)

CRITERIA

- **Diminishing of amount of CD19.**
- **Decline levels of immunoglobulins classes A, M, G.**
- **Seronegativ forms of infection (specific IGM-, IGG-, DNA+)**

SPECIFIC IMMUNOGLOBULINS:

- **antistaphylococcal (3 ml IM, 3 - 5 inj. 1 time per 3 days).**
- **antiherpetic (1 or 2 types) (amp. for 1,5 ml, use for 4,5 ml IM 1 time per 3 days of 5 inj.);**
- **anticitomegalovirus;**
- **IG against the virus of Ebshtain-Barr;**
- **antichamidial (1,5 ml one time per 3 days IM of 6 inj.),**

The patient 58 years old. Diagnosis: chronic obstructive pulmonary disease, II c., Exacerbation. Diffuse fibrosis. Emphysema. LW II c. Immunodeficiency by B-cell type (D

Показник		Результат		Норма				
Гемоглобін		122		Ж – 115 – 145, М – 132 - 164 г/л			Виражений анізоцитоз, анізохромія ТЗН=45%	
Еритроцити		3,8		Ж - 3,7 – 4,7, М – 4,0 – 5,1x10 ¹² /л				
Тромбоцити		220		150 – 320x10 ⁹ /л				
ШОЕ		11		2 – 15 мм /год.				
Лейкоцити		6,6		4 – 9x10 ⁹ /л				
Нейтр. 43 – 71 % 2000-6500	Пал.\яд. 1 – 4 % 80-400	Сегм. \яд.	Еоз. 0,5 – 5% 80-370	Баз. 0 – 1% 20-80	Мон. 3 – 9% 90-720	Лімф. 25 – 37% 1600-3000	БГЛ 1-5% 80-500	Плаз. 0 – 1% 20-80
66	3	63	6	1	3	23	0	0
4360	200	4160	400	70	200	1518		
Імунологічні показники		Результат	Норма (Од СІ)	Імунологічні показники			Результат	Норма (Од СІ)
Т- лімф.	%	72	50 – 80	Ig G			11,9	8,0-18,0 г\л
CD-3	Абс. число	1092	1000-2200					
Т- хелп.	%	53	33-46	Ig M			0,18	0,2-2,0 г\л
CD-4	Абс. число	804	309-1571					
Т- супрес.	%	21	17-30	Ig A			4,8	0,3-3,0 г\л
CD-8	Абс. число	319	282-999					
ІРІ	CD-4/CD-8	2,5	1,4-2,0	ЦІК			59	30 – 50 Од. опт. щільн.
NK-клітини CD-16	%	23	12 – 23	Поглиналина активність	ФЧ	91	60 – 80%	
	Абс. число	349	72-543		ФІ	4,45	1,5 – 3,5	
В-лімф. CD-22	%	8	17-31	НСТ -тест	спон.	21	до 10%	
	Абс. число	121	109-532		Інд.	26	-	
РБТЛ	спон.	10	до 10%	Комплемент	рез.	5	16%	
	інд.	40	50-70%		СН-50	55	30 – 60 гем. Од/мл	

Immunotropic therapy:
1) causal antibiotic therapy - levofloxacin 500 mg / in drip- Lynn 1 time a day 7 days
dimexyd 5 ml per 200 ml of 0.9% sodium chloride in / drip 1 per day 5 days
azithromycin 500 mg 1 time a day, 3 days;
2) Polyoxidonium 6 mg / m 2 twice a week, for 10 days;
3) halavit 100 mg 1 time a day / m, 10 days;
4) laktophiltrum 2 MSA. 2 times a day for 14 days.
5) fluconazole 100 mg a day, 10 days.
immunorehabilitation:
6) IRS-1 19 inhalations once a day, 20 days;
7) timalin 1 ml subcutaneously in a day, 10 days.

INTRAVENOUS IMMUNOGLOBULINS

Intravenous immunoglobulins prescribes in day's dose 400 mg/kg IV dropes 1 ml/kg/h for premature born and 4-5 ml/kg/h for worn children.

IVG prescribes for prophylaxis of infections to the prematurely born children with mass of body less than 1500 g and by the level of IGG 3 g/l and below.

IVG use to achievement the concentration of IGG in blood not below than 4-6 g/l in immunodeficit with the low level of IGG in blood.

IVG prescribes for treatment of heavy festering-inflammatory diseases 1th daily 3-5 injections to reach the dose of IVG 1-2,5 g/kg.

IMMUNOCORRECCION (IV) (ID, phagocytic type)

CRITERIA

- Decline of phagocyte number and index.
- Decline of NBT-test.
- POLIOXSYDONIY - 6 mg of preparation before injection dissolve in 1-1,5 ml of phys. sol., dist. water or 0,25% sol. of Novocain, IM or SC injection.
- Acute inflammatory process: 6 mg daily, course is 3-5 injections;
- Chronic inflammatory process 6 mg daily, 5 injections, then 2 times per a week, course 10-15 injections.
- METHYLURACIL - prescribes in pills for 0,5 g 3 times per a day during 3-4 weeks or by more protracted courses.

The patient 28 years old. Diagnosis: chronic recurrent furunculosis. By phagocytic immunodeficiency type (D 84.9)

Показник		Результат		Норма				
Гемоглобін		117		Ж – 115 – 145, М – 132 – 164 г/л			Виражений анізоцитоз, анізохромія ТЗН=45%	
Еритроцити		3,7		Ж - 3,7 – 4,7, М – 4,0 – 5,1x10 ¹² /л				
Тромбоцити		230		150 – 320x10 ⁹ /л				
ШОЕ		14		2 – 15 мм /год.				
Лейкоцити		6,1		4 – 9x10 ⁹ /л				
Нейтр.	Пал.\яд.	Сегм.	Еоз.	Баз.	Мон.	Лімф.	БГЛ	Плаз.
43 – 71 %	1 – 4 %	\яд.	0,5 – 5%	0 – 1%	3 – 9%	25 – 37%	1-5%	0 – 1%
2000-6500	80-400		80-370	20-80	90-720	1600-3000	80-500	20-80
59	6	53	2	1	7	31	0	0
3600	370	3230	120	60	430	1890		
Імунологічні показники		Результат	Норма (Од СІ)	Імунологічні показники			Результат	Норма (Од СІ)
Т- лімф.	%	37	50 – 80	Ig G			12,6	8,0-18,0 г\л
CD-3	Абс. число	699	1000-2200					
Т- хелп.	%	17	33-46	Ig M			3,06	0,2-2,0 г\л
CD-4	Абс. число	321	309-1571					
Т- супрес.	%	18	17-30	Ig A			1,8	0,3-3,0 г\л
CD-8	Абс. число	340	282-999					
ІРІ	CD-4/CD-8	0,94	1,4-2,0	ЦІК			76	30 – 50 Од. опт. щільн.
NK-клітини CD-16	%	19	12 – 23	Поглиняльна активність		ФЧ	42	60 – 80%
	Абс. число	359	72-543			ФІ	1,2	1,5 – 3,5
В-лімф. CD-22	%	23	17-31	НСТ -тест		спон.	4	до 10%
	Абс. число	435	109-532			Інд.	8	-
РБТЛ	спон.	10	до 10%	Комплемент		рез.	4	16%
	інд.	60	50-70%			СН-50	75	30 – 60 гем. Од/мл

Immunotropic therapy:

- 1) specific antibiotic therapy (normal human immunoglobulin 4.5 ml / m in a day for 10 days);
- 2) causal antibiotic therapy - spiramycin 500 mg 2 times a day;
- 3) locally - triderm lesions in areas 2 times a day - 2 weeks;
- 4) Polyoxidonium 6 mg / m 2 twice a week, 20 days or 100 mg halavit a day / m, 20 days;
- 5) probiotic Linex 2 MSA. 3 times a day, 20 days.

immunorehabilitation:

- 6) viferon 150 thousand IU, a day in the candlelight, 10 entries;
- 7) Sodium Nucleinat 0.1 g 3 times a day 30 days

Vaccination against flu

- Autumn (better October)
- Possibly simultaneously with other vaccines (in different places)
- To utilize the exceptionally registered vaccines
- INFLUVAK subunit vaccine
 - antigen composition answers annual recommendations of WHO
- Doses:
 - children from 6 month to 3 years - 0,25 ml
 - to the children more senior than 3 years - 0,50 ml
 - adults - 1,0ml
- Patients, never before getting an inoculation from flu, must get the second dose of preparation in 4-6 weeks.
- Introduction:
 - intramuscular
 - deeply subcutaneously
- before introduction to warm a vaccine to the room temperature.

HIV/AIDS Info & History

- In 1981,¹ the first cases of AIDS were identified among gay men in the US. However, scientists later found evidence that the disease existed in the world as early as 1959.
- The first documented case of HIV was traced back to 1959 using preserved blood samples, which were analyzed in 1998.
- In first-world countries, AIDS is now a chronic disease, but this was not the case in the past.
- AIDS is 100% preventable, and yet there were 56,300 new infections in 2006 in the US alone.²

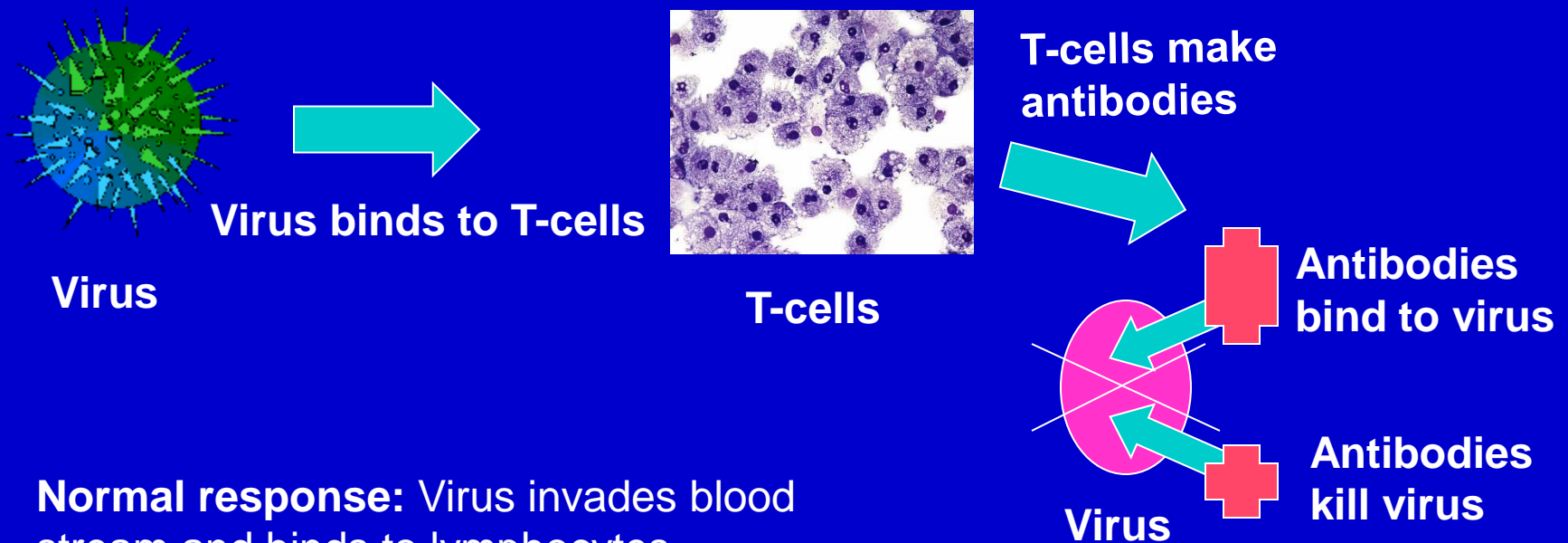
1. 1. Advert.org

2. 2. Centers for Disease Control and Prevention
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Definitions

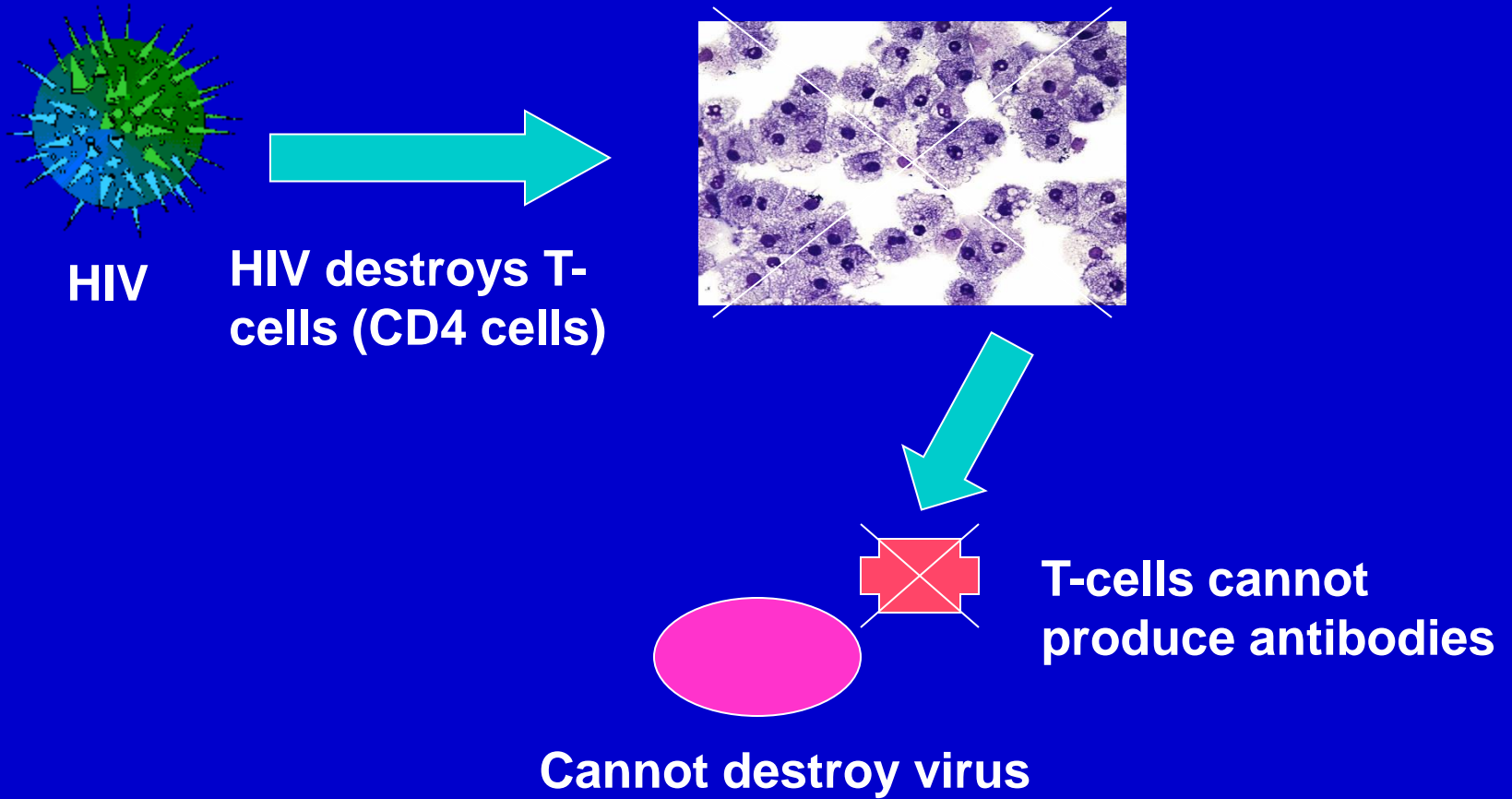
- H - Human
- I - Immunodeficiency
- V - Virus
- A - Acquired
- I - Immune
- D - Deficiency
- S - Syndrome

Normal Immune Response



Normal response: Virus invades blood stream and binds to lymphocytes. Lymphocytes make antibodies to the virus. Antibodies bind to the virus and destroy the virus.

Immune Response to HIV



Immunopathological Mechanisms of HIV infection

HIV infected patients progress to AIDS disease in three phases:

Early phase: lasts about 2 weeks accompanied by: Fever, aches and flue-like symptoms with high levels of virus in blood.

Middle phase: lasting months or several years (latent) with:

- Anti-HIV antibodies
- Continuous depletion of CD4 T cells

Late phase (AIDS): characterized by:

- Rapid decline in CD4 T cells,
- Opportunistic infections including viral (herpes simplex, herpes varicella zoster, EBV), bacterial (*M. tuberculosis*), fungi (*Candida*-thrush) and protozoan (*Microsporidia*) .
- Cancers (lymphoma; Kaposi's sarcoma).

What's the difference between HIV and AIDS?

- HIV, a virus, eventually causes AIDS, a syndrome.

Spectrum of HIV



T-Cell Count

- If 1,200 or higher, the individual has a normal immune system.
- If 800 or less, the immune system is weakened and individual is susceptible to infection.
- If 200 or less, AIDS is diagnosed.
- Once a person is diagnosed with AIDS, she or he is always categorized as having AIDS, even if her or his T-cell count increases.

Symptoms of HIV

- Recurring fever
- Night sweats
- Rapid weight loss
- Diarrhea lasting several weeks
- White, thick spots on the tongue
- Dry cough
- Shortness of breath
- Purple bumps on the skin, inside the mouth, and rectum

Criteria for Diagnosing AIDS

- A CD4 cell (type of T-cell) count of 200 or less,

or

- One opportunistic infection.
 - An opportunistic infection is an infection that typically does not affect individuals with normal immune systems.

Opportunistic Infections

- **Mycobacterium Avium Complex**
- **Salmonellosis**
- **Syphilis and Neurosyphilis**
- **Tuberculosis**
- **Bacillary angiomatosis**
- **Aspergillosis**
- **Candidiasis**
- **Coccidioidomycosis**
- **Cryptococcal Meningitis**
- **Histoplasmosis**
- **Kaposi's Sarcoma**
- **Systemic Non-Hodgkin's Lymphoma**
- **Primary CNS Lymphoma**
- **Cryptosporidiosis**
- **Isosporiasis**
- **Microsporidiosis**
- **Pneumocystis Carinii Pneumonia**
- **Toxoplasmosis**
- **Cytomegalovirus**
- **Hepatitis**
- **Herpes Simplex**
- **Herpes Zoster**
- **Human Papillomavirus**
- **Molluscum Contagiosum**
- **Oral Hairy Leukoplakia**
- **Progressive Multifocal Leukoencephalopathy**
- **AIDS Dementia Complex**
- **Peripheral Neuropathy**
- **Apthous Ulcers**
- **Malabsorption**
- **Depression**
- **Diarrhea**
- **Thrombocytopenia**
- **Wasting Syndrome**
- **Idiopathic Thrombocytopenic Purpura**
- **Listeriosis**
- **Pelvic Inflammatory Disease**
- **Burkitt's Lymphoma**
- **Immunoblastic Lymphoma**
- **Valley Fever**

HIV Infection/AIDS Staging System

Clinical Stages & Major Clinical Features:

- Stage 1:** Asymptomatic; persistent generalized lymphadenopathy (PGL) and acute retroviral infection (ARI).
- Stage 2:** Loss of weight (< 10% of body weight); minor mucocutaneous infections; herpes zoster and recurrent upper respiratory tract infections (URTI).
- Stage 3:** Loss of weight (>10% of body weight); chronic diarrhoea (> 1 month); prolonged fever; oral candidiasis; oral hairy leukoplakia; pulmonary tuberculosis; severe bacterial infections and vulvovaginal candidiasis.
- Stage 4:** HIV wasting syndrome; extrapulmonary tuberculosis; *Pneumocystis carinii* pneumoniae, Candidiasis of the oesophagus, trachea, bronchi or lungs; toxoplasmosis of the brain, cryptosporidiasis with mycobacteriosis; lymphoma; Kaposi's sarcoma (KS) and HIV encephalopathy.

Oral Candidiasis

- This is a fungal infection that occurs in nearly all patients with AIDS.
- It commonly precedes other OI's.
- Untreated, it progresses to the esophagus and stomach.

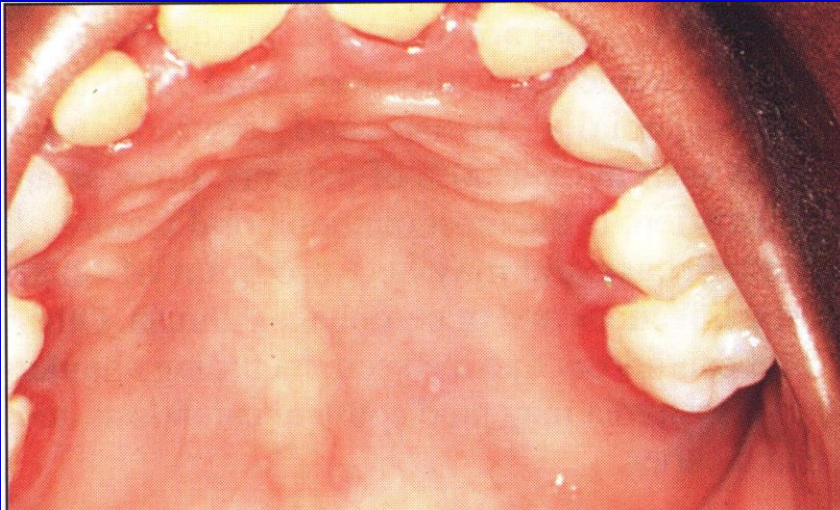


SYSTEMIC DISORDERS WITH ORAL MANIFESTATIONS

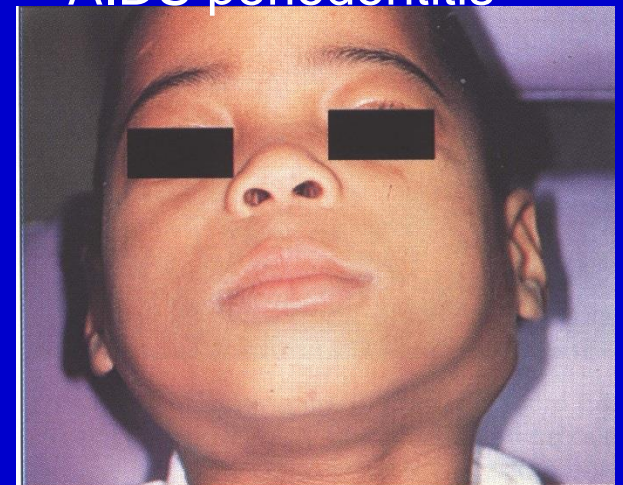
AIDS:



AIDS periodontitis



AIDS gingivitis



Parotitis

Pulmonary Infections:

M. Tuberculosis and Pneumocystis pneumonia common when CD4 T cells $<200/\mu\text{l}$.

- TB in advanced HIV infection often presents atypically with extrapulmonary diseases affecting:
 - Bone marrow, bone,
 - Urinary and gastrointestinal tracts:
 - Liver, regional nodes and the central nervous system.

Gastrointestinal illness:

- Inflammation of the lining of the oesophagus (oesophagitis).
- Fungal (candidiasis) or viral (herpes simplex or cytomegalovirus) infections.
- Chronic diarrhoea also occurs that may be caused by bacteria (*Salmonella*, *Shigella*, *Listeria* or *Escherichia coli*).

Major neurological illnesses:

- Toxoplasma encephalitis of the brain caused by *Toxoplasma gondii*, progressive multifocal leukoencephalopathy (PML), demyelinating disease.
- Cryptococcal meningitis caused by fungus *Cryptococcus neoformans*.

Malignancies:

AIDS-defining malignancies include:

- Kaposi's sarcoma presenting as purplish nodules of the skin, mouth, gastrointestinal tract and lungs.
- Hodgkin's disease, anal and rectal carcinomas.
- High grade B cell lymphomas (Burkitt's lymphoma).

Diagnosis of HIV

- Elisa test
- Western Blot test
- Oraquick test
- Home HIV tests
 - Home Access Express

Fluids that can transmit HIV

Fluids that DO
transmit HIV:

- Blood
 - Semen
 - Vaginal Fluid
 - Breast Milk
- (in order of the highest concentration of HIV)

Fluids that DO NOT
transmit HIV:

- Saliva
- Tears
- Mucus
- Urine
- Sweat
- Feces

Universal Precautions

- Wash your hands!
- Disinfect utensils and living space.
- Use barriers—preferably latex.

HIV cannot be spread through casual contact, but these are good practices for preventing opportunistic infections.

Barriers include:

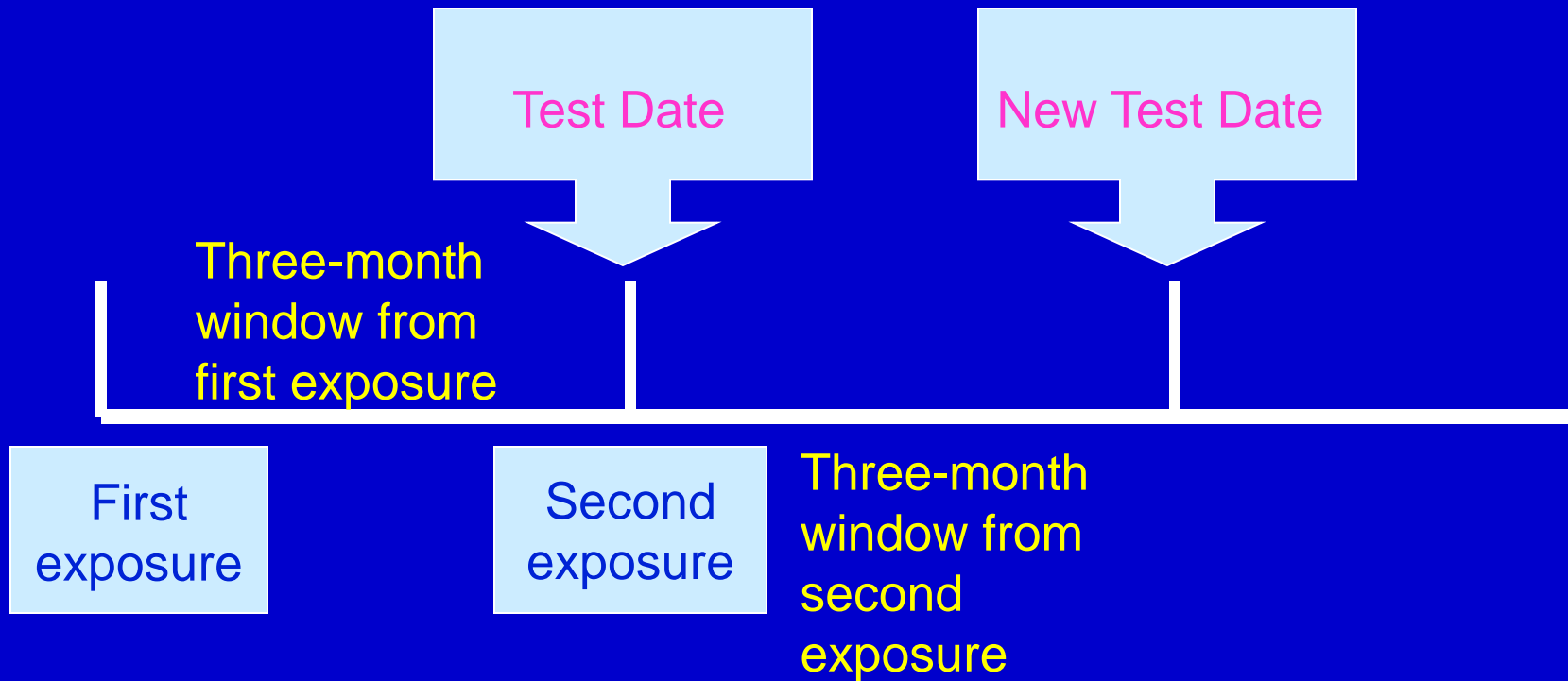
- Latex Gloves
- Latex Dental Dams
- Anything that protects your skin from a fluid



Testing

- The test is for antibodies against HIV, not for the virus itself.
- It can take up to three months for the body to produce antibodies against HIV.
- A negative test result may mean recent infection.
It is possible to infect others during this stage.
- An individual should be tested three months after possible exposure to guarantee an accurate result.

Timeline



Treatment

- Today, in the US, HIV/AIDS is a chronic disease.
- Anti-retroviral drugs are used in combination, known as Highly Active Anti-Retroviral Therapy (HAART).
- Side effects can be severe, but the risks of not being treated are more severe.
- Cornell University estimates the monthly cost of treatment as \$2,100, with a lifetime cost of treatment of \$618,900.



Thank you