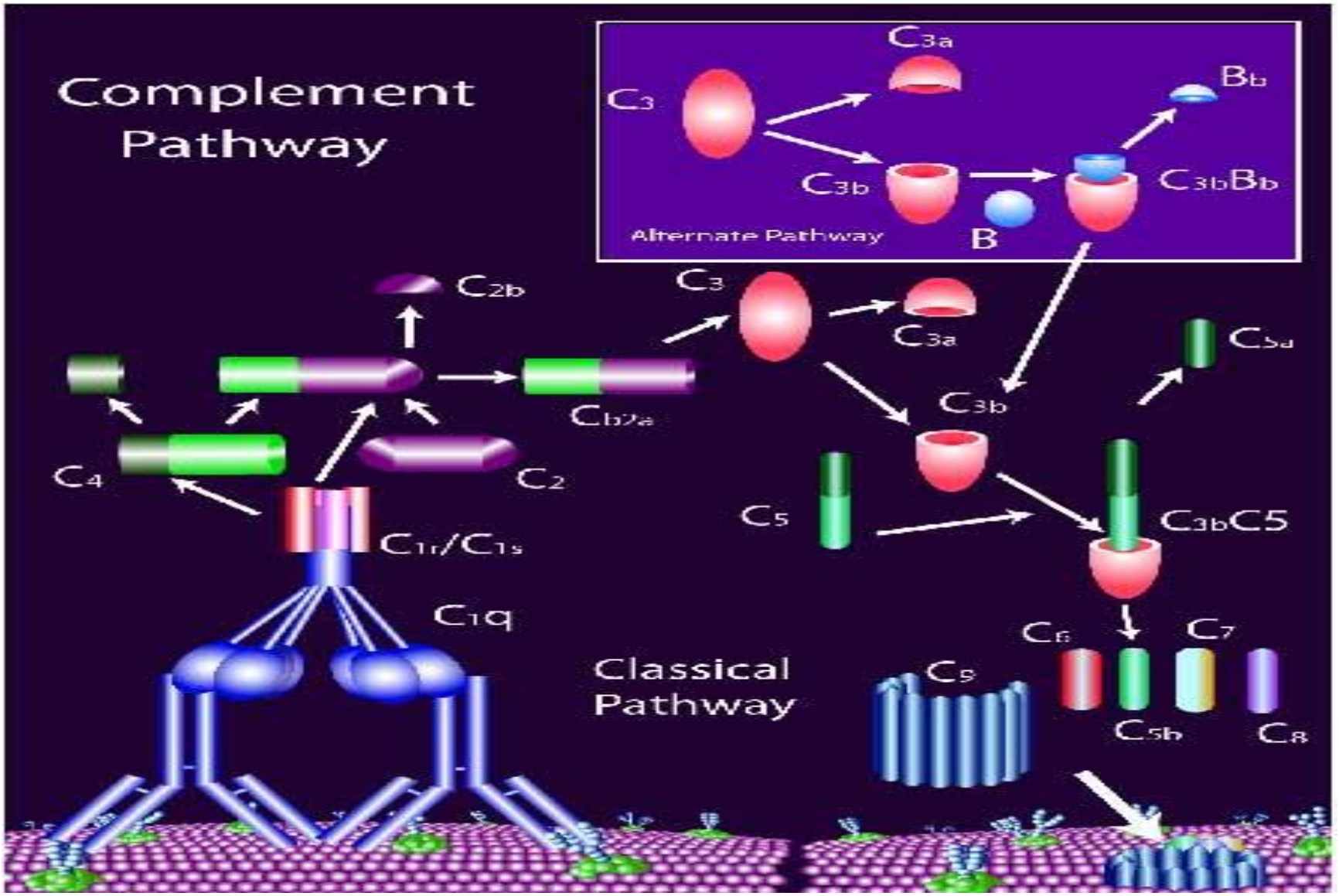
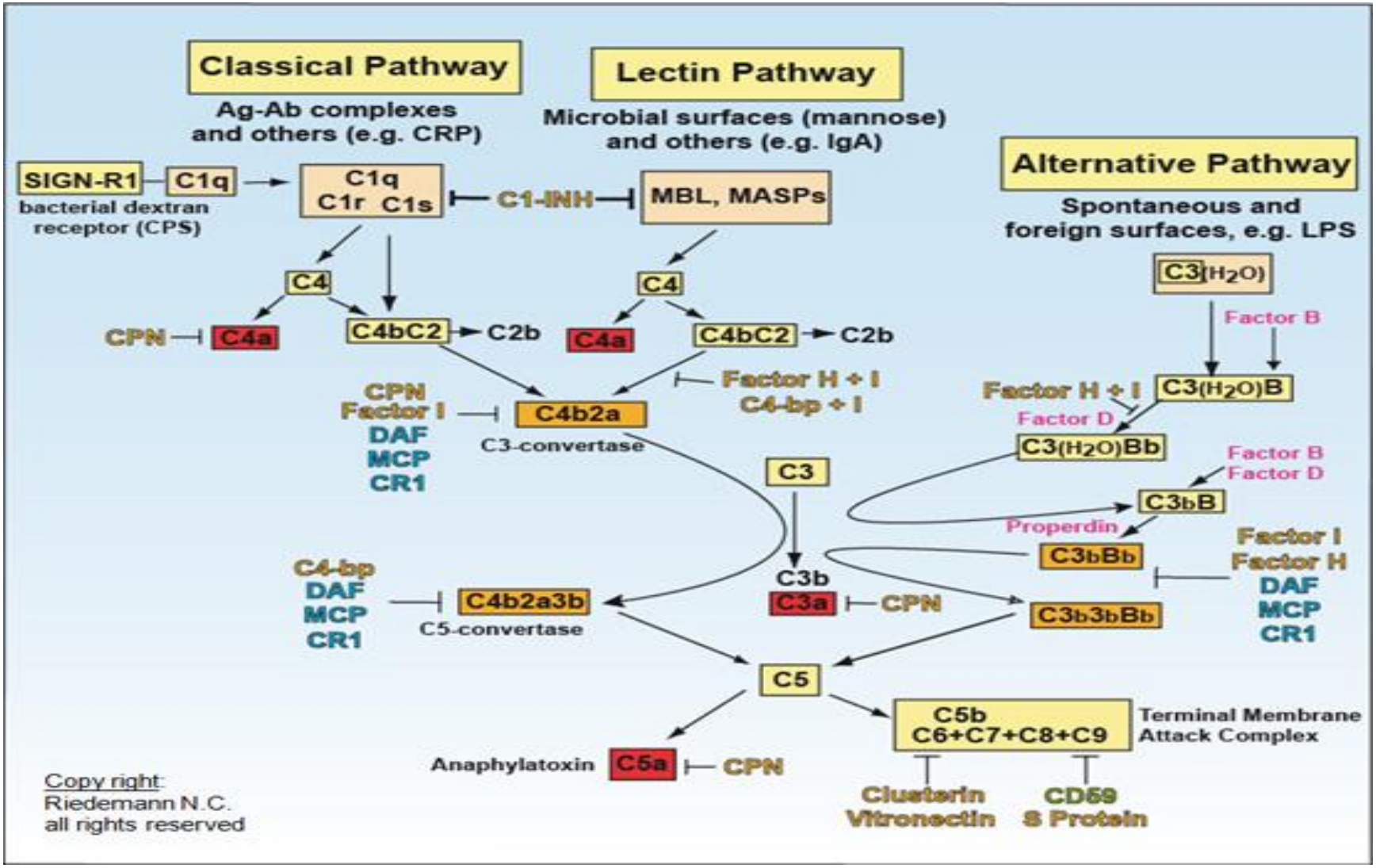
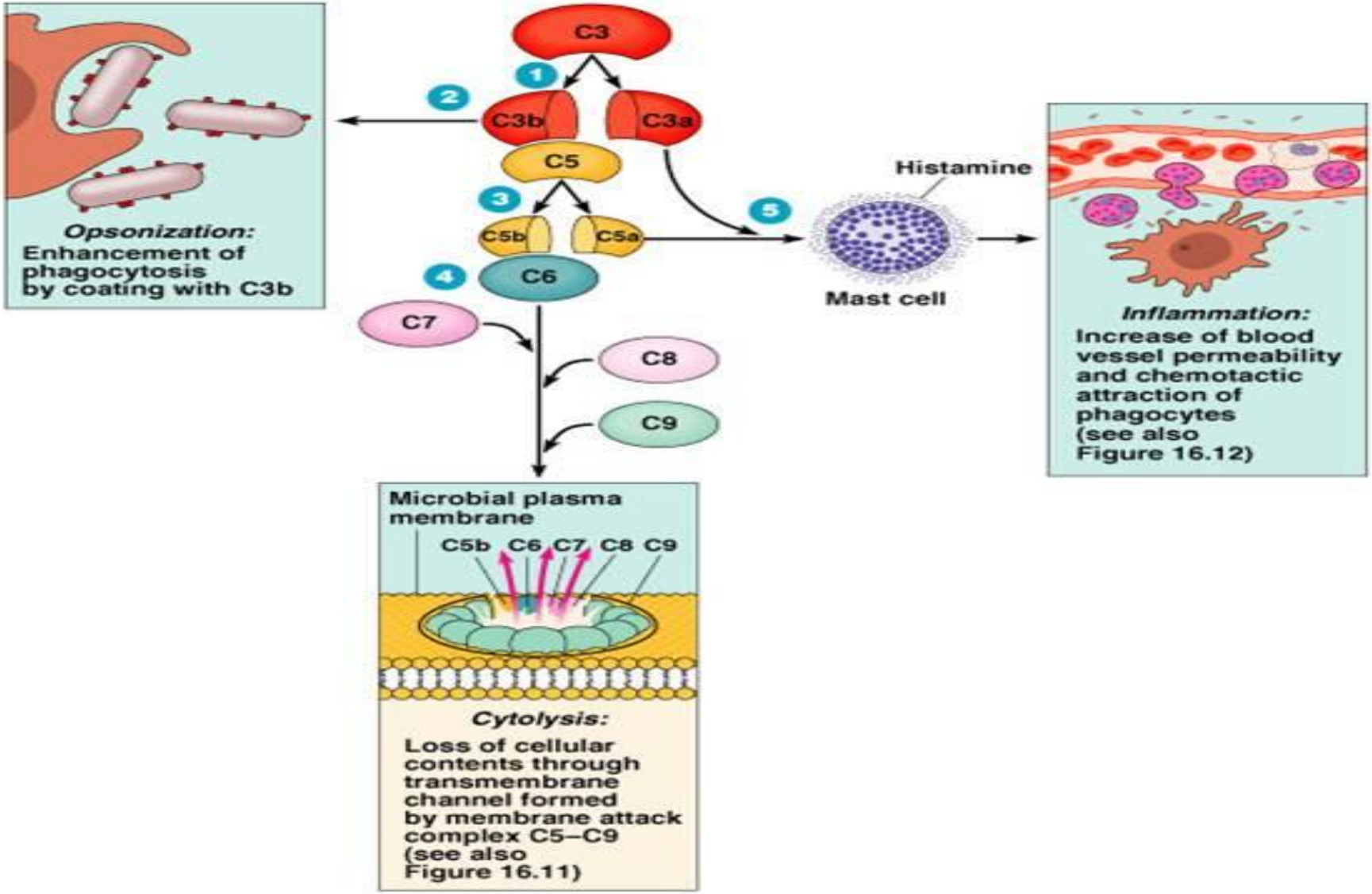
Clinical Immunology Case Studies

Timothy Craig


Complement Pathway
C3a
C3
Bb
C3b
C3bBb
B
Alternate Pathway
C2b
C3
C3a
C5a
C4b2a
C3b
C4
C2
C5
C3bC5
C1r/C1s
C1q
C6
C7
C9
Classical Pathway
C5b
C8





24 year old male with second episode of meningococcal meningitis. What complement defect would you suspect?

- A. C1
- B. C1-esterase inhibitor
- C. C3
- D. C8

- Ans-

24 year old male with second episode of meningococcal meningitis. What complement defect would you suspect?

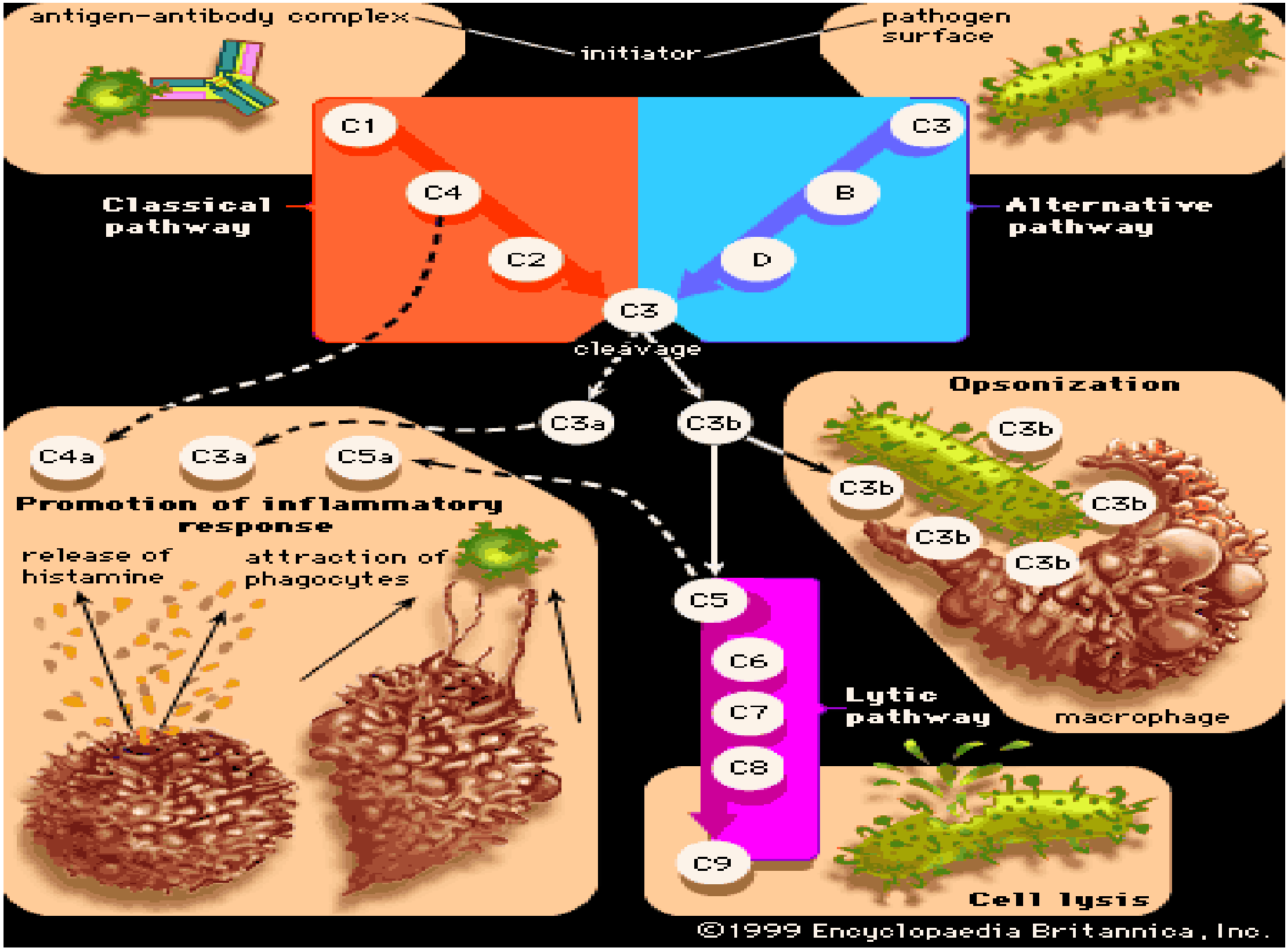
- A. C1
- B. C1-esterase inhibitor
- C. C3
- D. C8

- Ans-

24 year old male with second episode of meningococcal meningitis. What complement defect would you suspect?

- A. C1
- B. C1-esterase inhibitor
- C. C3
- D. C8

- Ans- D


antigen–antibody complex
initiator
pathogen surface
C1
C4
C2
C3
B
D
Classical pathway
Alternative pathway
C3
cleavage
C3a
C3b
C4a
C3a
C5a
Opsonization
C3b
C3b
C3b
C3b
C3b
Promotion of inflammatory response
release of histamine
attraction of phagocytes
C5
C6
C7
C8
C9
Lytic pathway
macrophage
Cell lysis
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To test this man for a possible deficiency in the complement system the best screening test would be?

- A. C3
- B. C-1-esterase inhibitor
- C. C-4
- D. CH50

- Ans-

To test this man for a possible deficiency in the complement system the best screening test would be?

- A. C3
- B. C-1-esterase inhibitor
- C. C-4
- D. CH50

- Ans- D

- To screen for complement defects the best test would be CH 50 and Alternate system-CH50.
- Levels will usually be extremely low if a C deficiency is present.

What vaccine would you suggest for your patient with a complement deficiency?

- A. MMR
- B. HPV
- C. TDPac
- D. Meningococcal

- Ans-

What vaccine would you suggest for him?

- A. MMR
- B. HPV
- C. TDPac
- D. Meningococcal

- Ans- D

The suggested vaccines are:

- HIB
- Pneumococcal (protein conjugated and polysacc followed by polysacc alone)
- Meningococcal
- Patients should have high dose of amoxicillin with clavulanic acid to take for high fevers.
- Repeat vaccines every 5 years

28 year old female with a history of occasional Abd. pain and limb swelling. She was started on BCP 3 weeks ago. What complement would you test for?

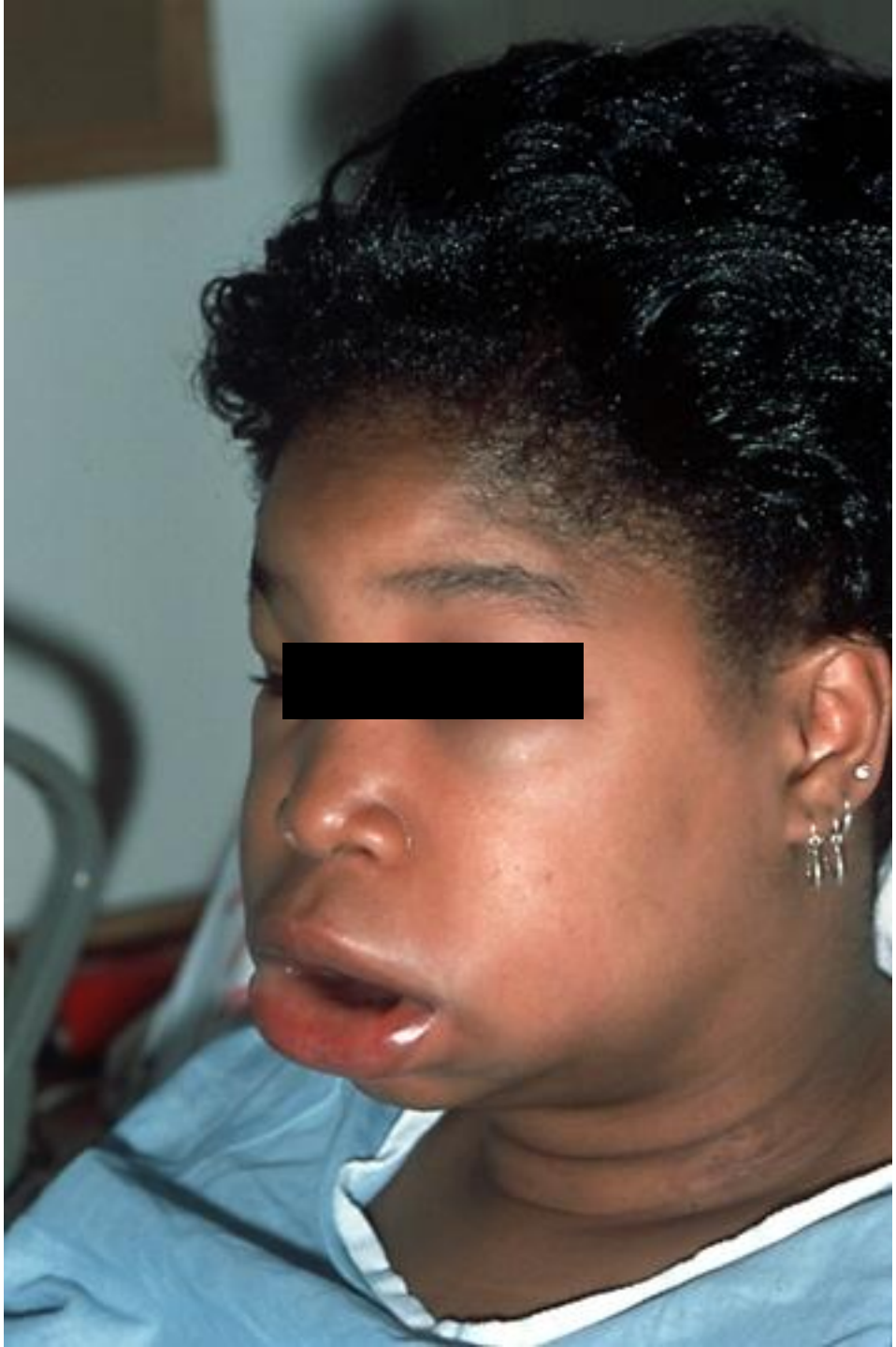
- A. C1
- B. C4
- C. C3
- D. C9

- Ans-

28 year old female with a history of occasional Abd. pain and limb swelling presents with severe facial swelling. She was started on BCP 3 weeks ago. What complement would you test for?

- A. C1
- B. C4
- C. C3
- D. C9

- Ans- B



The edema associated with HAE is due to?

- 1. histamine
- 2. bradykinin
- 3. Factor 12
- 4. Plasmin
- 5. Complement

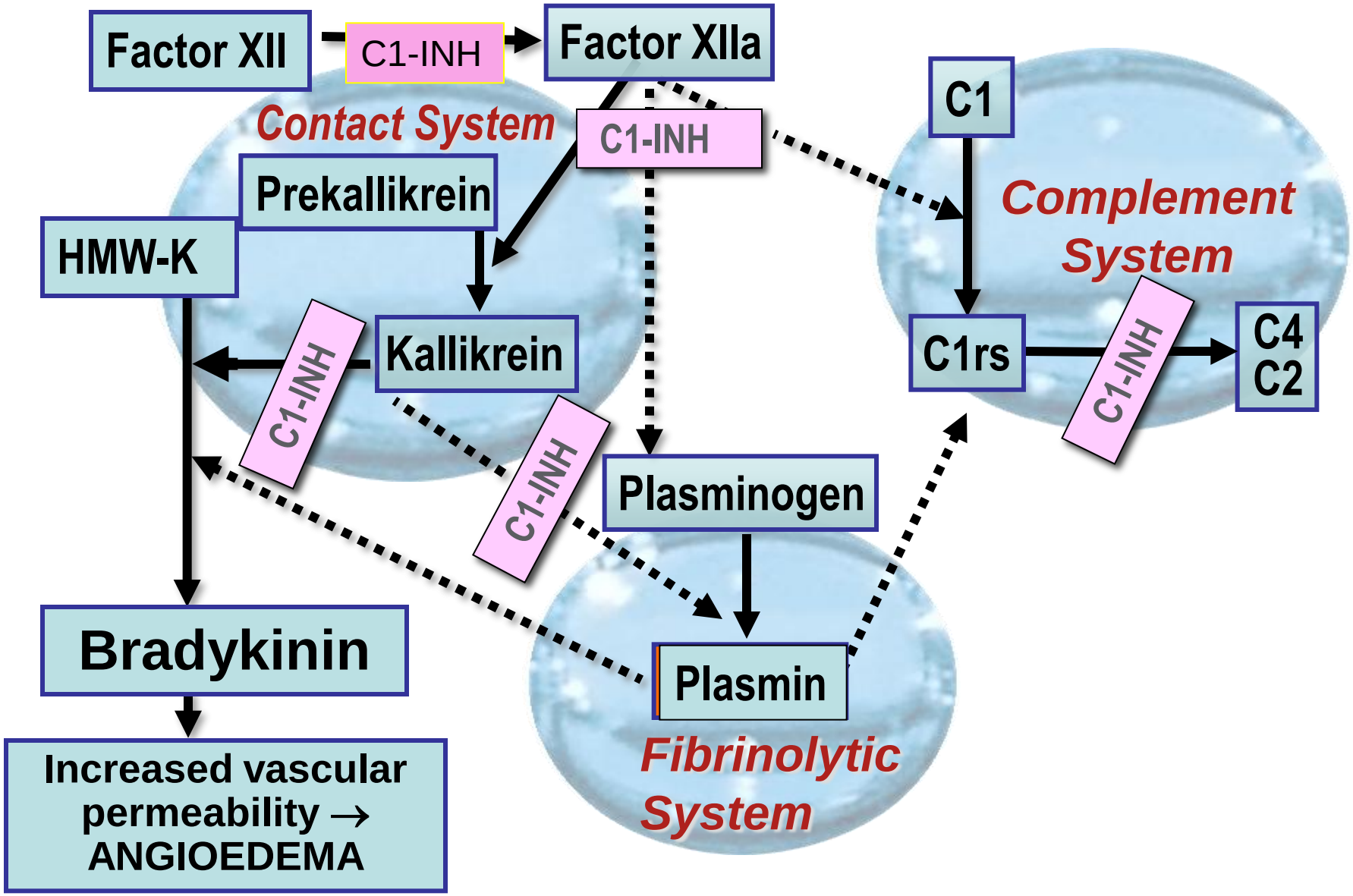
- Answer-

The edema associated with HAE is due to?

- 1. histamine
- 2. bradykinin
- 3. Factor 12
- 4. Plasmin
- 5. Complement

- Answer- 2

C1-INH involved in 3 systems → C1-INH depletion



Therapy

HAE responds to?

- 1. corticosteroids
- 2. androgens
- 3. epinephrine
- 4. antihistamines
- 5. H-2 blockers

Ans:

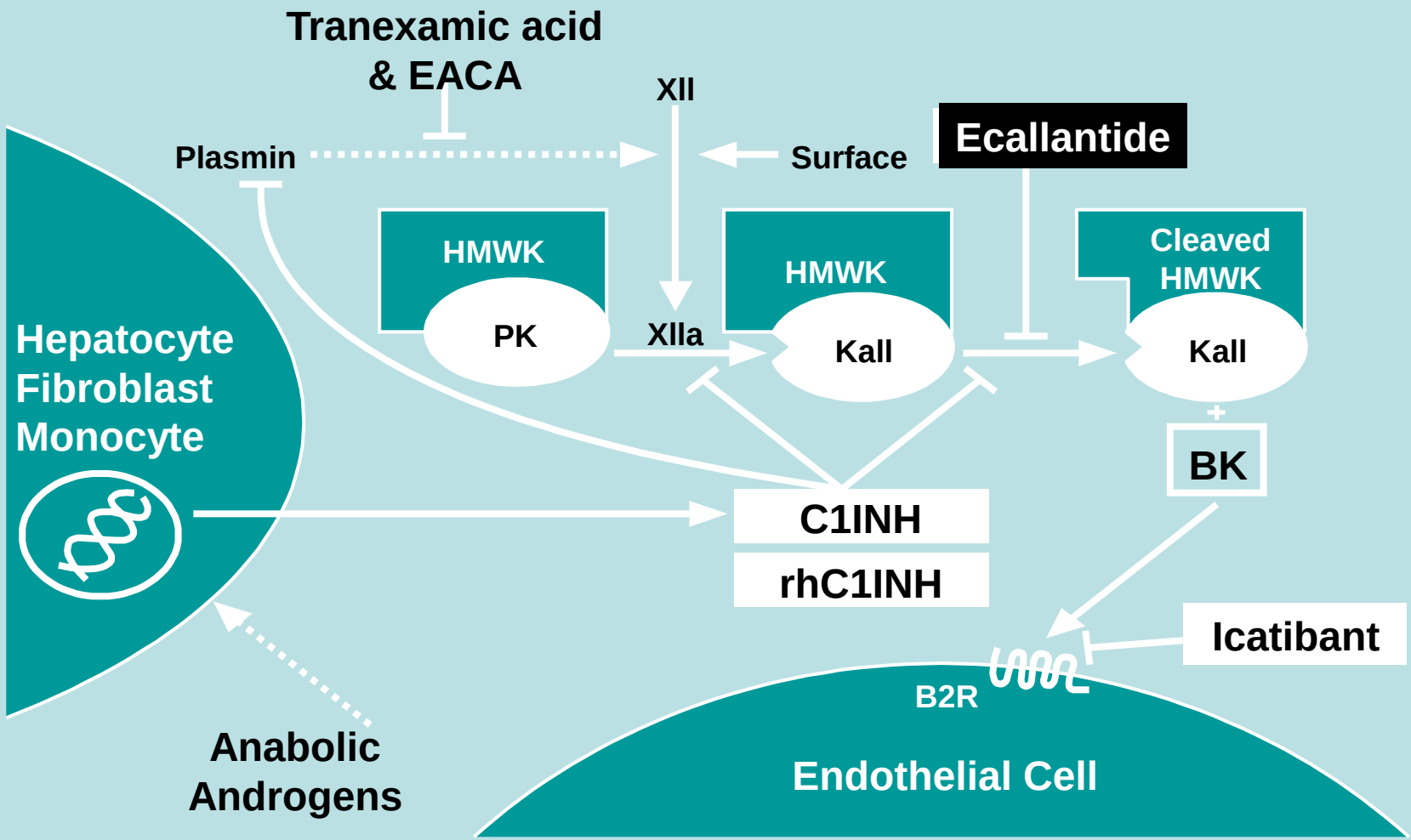
Therapy

HAE responds to?

- 1. corticosteroids
- 2. androgens
- 3. epinephrine
- 4. antihistamines
- 5. H-2 blockers

Ans: 2

Mechanisms of HAE Drugs in Development



Zuraw B. *Immuno Allergy Clin North Am*. 2006; 26(4):691-708.

Differentiating Features of Angioedema

	HAE	AAE	Histamine induced	ACE-I induced
Angioedema	Yes	Yes	Yes	yes
Urticaria	No	No	Usually	No
Age at onset	6-20 years	>50 years	Anytime	anytime
Family History	Usually	No	No	No
Underlying disease	No	Yes	No	Htn, CAD, CHF
Location of swelling	All	All	Especially face/lip	face
Precipitated by trauma	Yes	Yes	No	No
Duration of swelling, hours	48-72	48-72	2-48	72
Response to treatment with epi, antihistamines, steroids	No	No	Yes	No

Zuraw, Ann Allergy Asthma Immunol 2008

58 year old male with recurrent Abd. pain and swelling. His symptoms started 3 months ago and he has no family history of HAE. The test that would help to help differentiate this from HAE would be?

- A. C1 esterase inhibitor
- B. C4
- C. C1q quantitative
- D. C2 quantitative

- Ans-

58 year old male with recurrent Abd. pain and swelling. His symptoms started 3 months ago and he has no family history of HAE. The test that would help to help differentiate this from HAE would be?

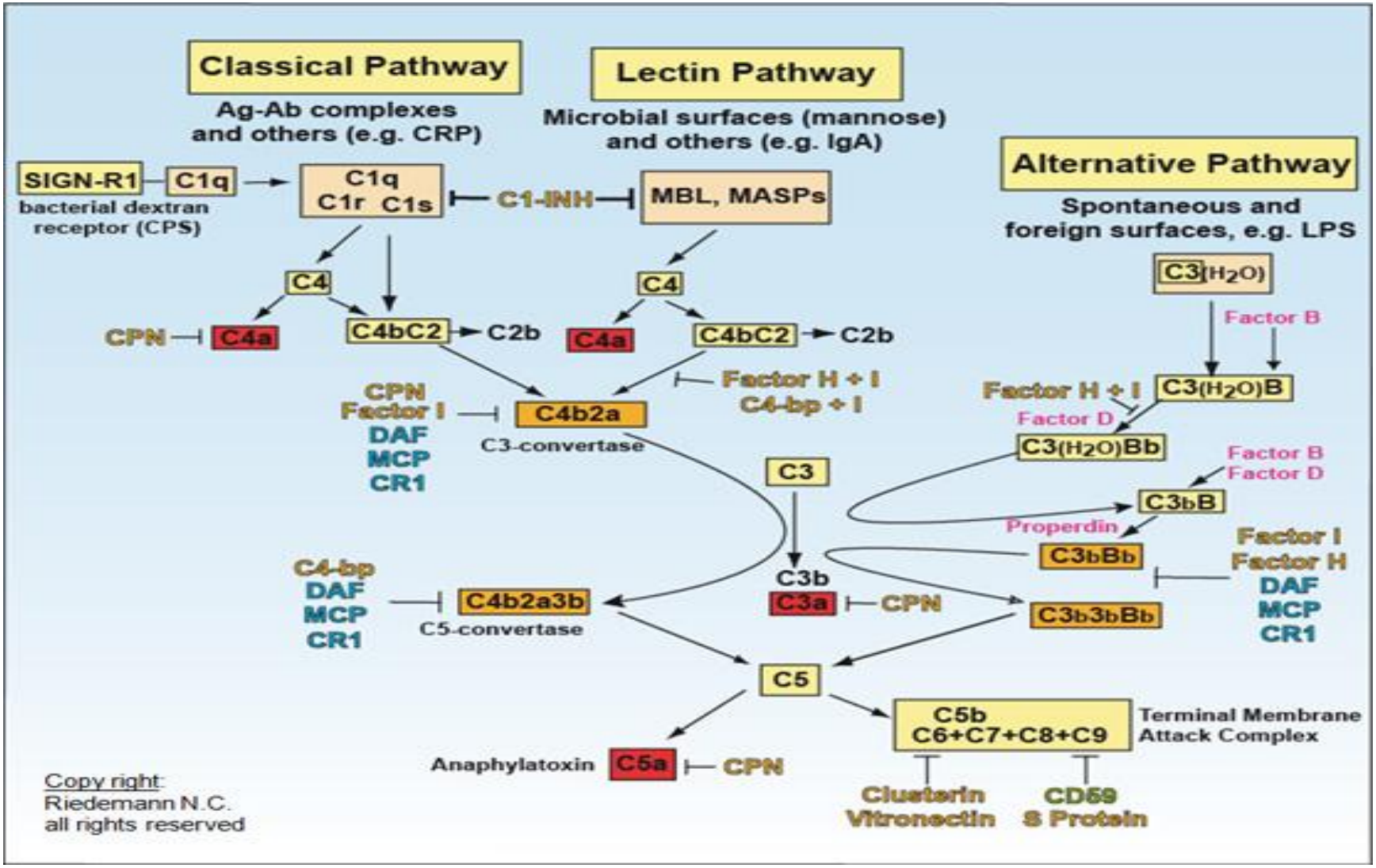
- A. C1 esterase inhibitor
- B. C4
- C. C1q quantitative
- D. C2 quantitative

- Ans- C

HAE Summary

	HAE-1	HAE-2	AA-1	AA-2
C1	N	N	L	L
C4	L	L	L	L
C2	+/-	+/-	L	L
C1-I	L	N	L	L
CI-Fu	L	L	L	L
%	85	15	lymphoma	SLE

- Best screening test for HAE is ___?___.
- Best test to diagnosis AA is _____?_____

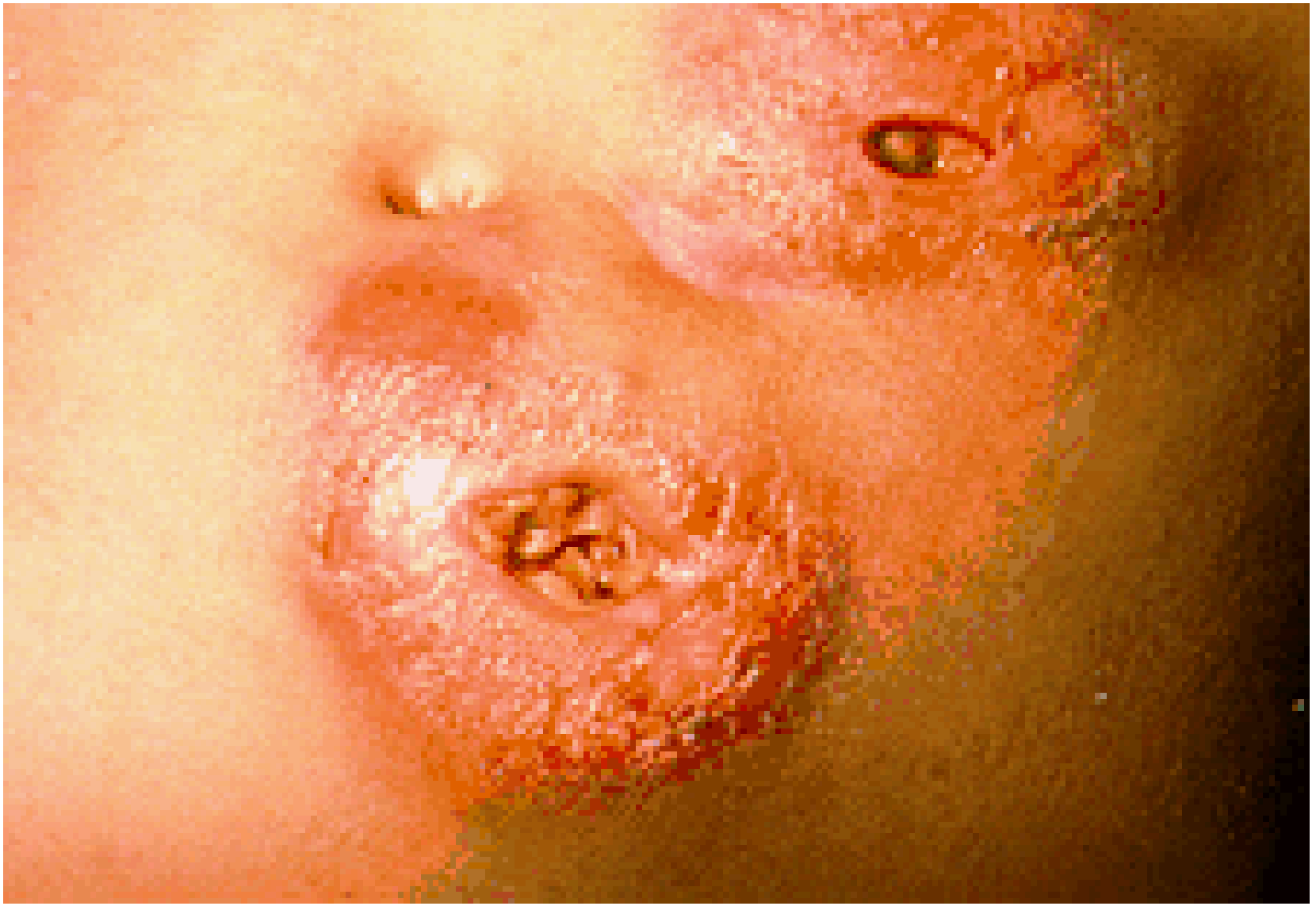


Summary of the complement system

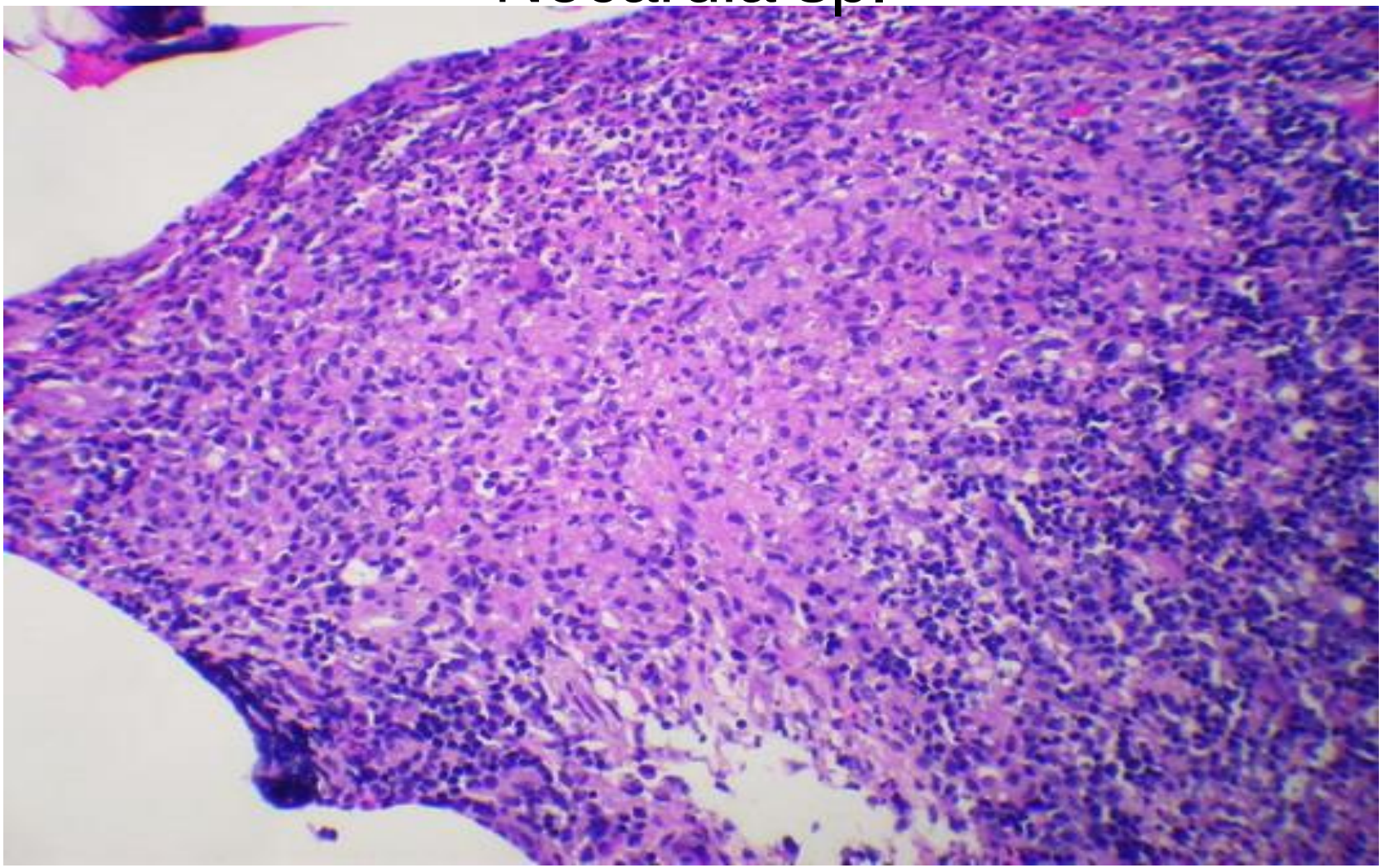
- Early defects predispose to ICX disease.
- Late defects predispose to Neisseria
- Defects in C3 predispose to sepsis.
- Depressed C3 is seen in active SLE
- Depressed C4 is seen in HAE
- Depressed C1 is seen in Acquired AE
- Depressed alternative pathway predisposes to sepsis
- CH 50 is the best test for assessing C deficiency

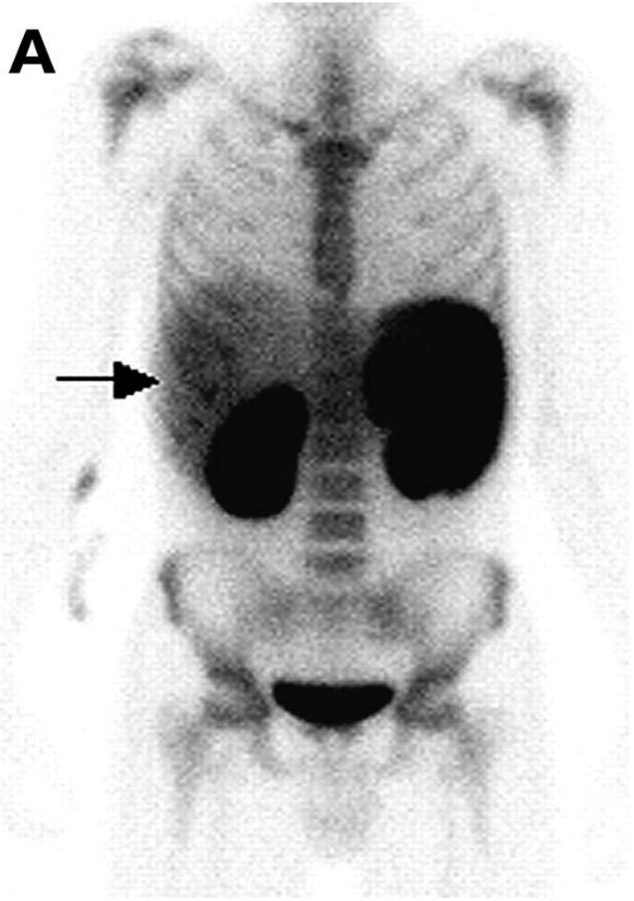
Phagocyte Defects

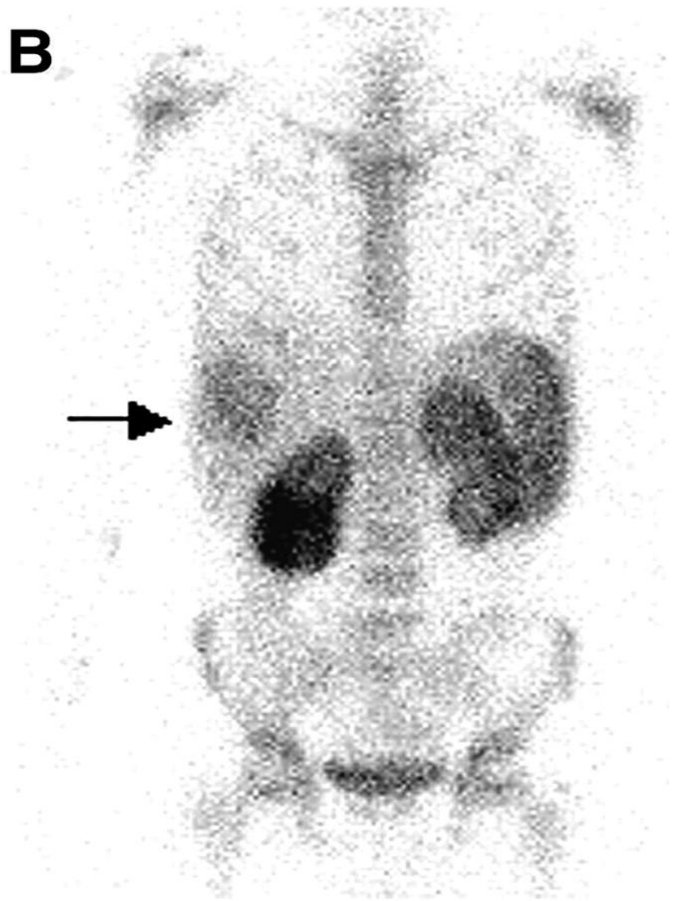
- 21 year old male with fever for 5 days. He has had recurrent draining lesions over the cervical nodes and inguinal nodes.
- He states he has a history of life long recurrent infections to include draining pulmonary infections.



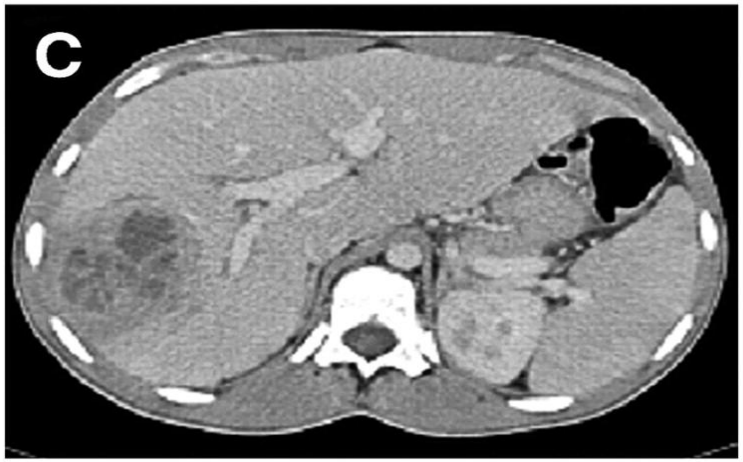
Non-specific inflammation with neutrophils, but no true defined abscess. Culture grew Nocardia sp.







Liver abscess



What disease would you suspect your patient has?

- A. Common Variable Immunodeficiency
- B. Chronic Granulomatous Disease
- C. Cystic Fibrosis
- D. Leukocyte Receptor Defect

- Ans-

What disease would you suspect your patient has?

- A. Common Variable Immunodeficiency
- B. Chronic Granulomatous Disease
- C. Cystic Fibrosis
- D. Leukocyte Receptor Defect

- Ans- B

How would you test to confirm the disease your patient has?

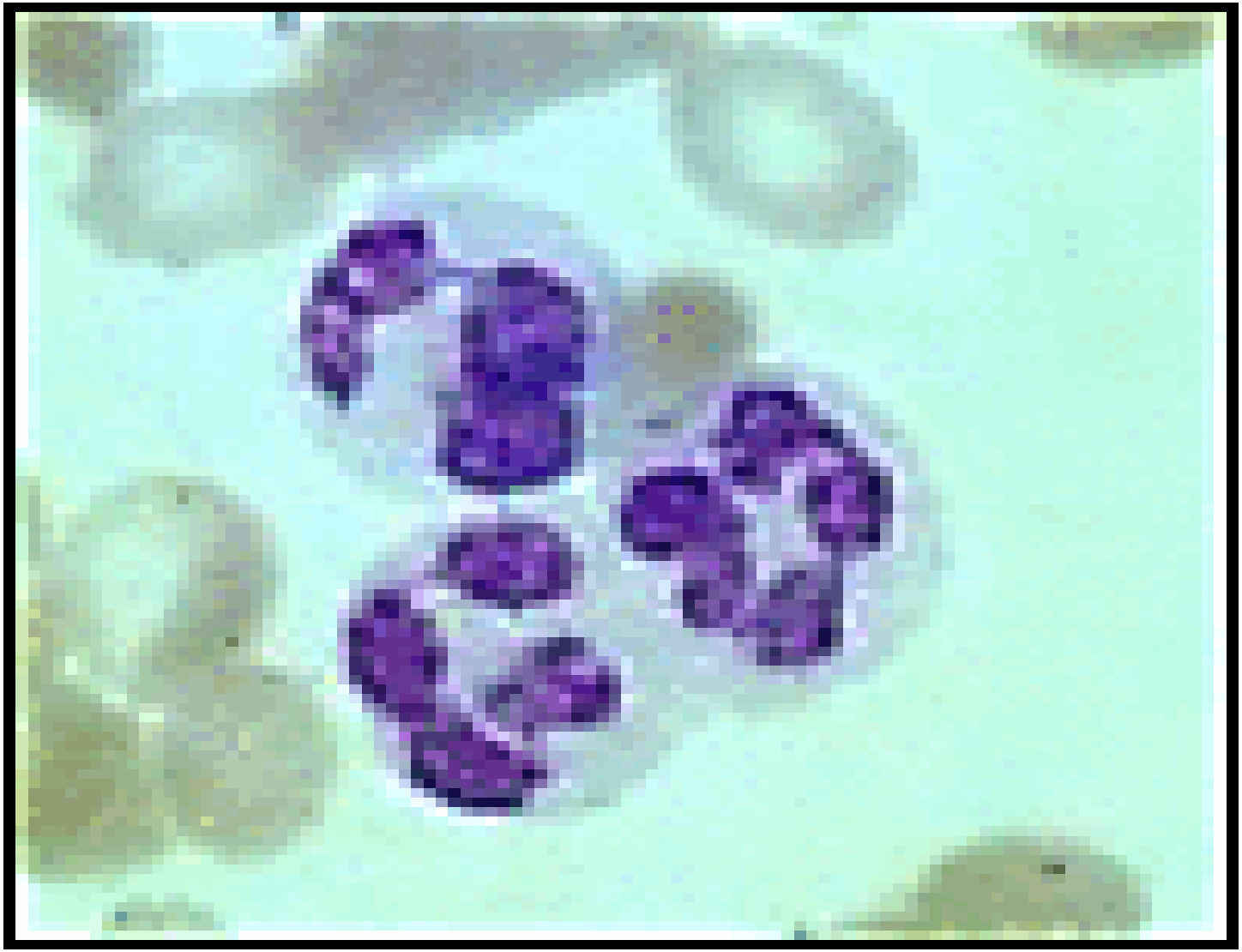
- A. CD11 and CD 18
- B. IgG levels
- C. Dihydrorhodamine (DHR)
- D. CD 19 and CD 20

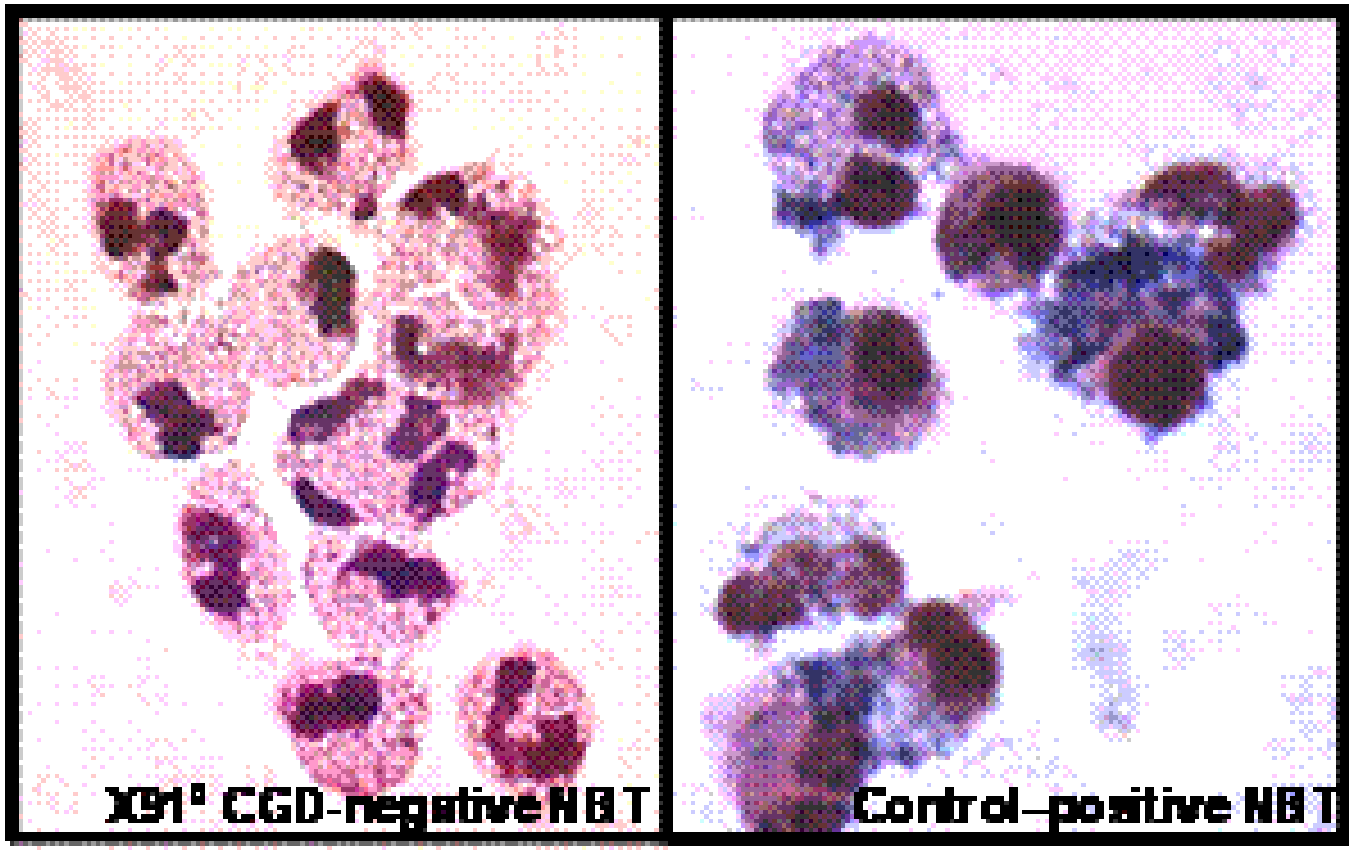
- Ans-

How would you test to confirm the disease your patient has?

- A. CD11 and CD 18
- B. IgG levels
- C. Dihydrorhodamine (DHR)
- D. CD 19 and CD 20

- Ans- C (in the past Nitroblue Tetrazolium)





NBT reduction test

Chronic Granulomatous Disease (CGD)

- Recurrent infections (lungs, skin, bone and liver) secondary to the inability to kill certain organisms due to NADPH oxidase subunit defect.
- Organisms (catalase positive) that suggest CGD: S aureus, Aspergillus, Chromobacterium, Burkholderia, Nocardia
- Diagnosis: NBT or DHR
- Rx- antibiotic and anti-fungal prophylaxis. Interferon can be effective.

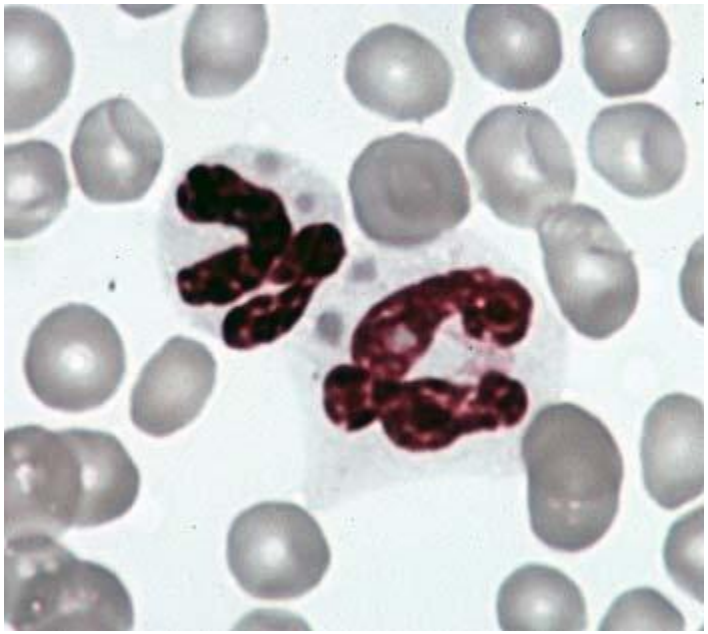
Leukocyte adhesion defect (LAD)

- Lack integrins (CD11, CD18) and can not bind endothelial cell adhesion receptors.
- Huge neutrophilia without PMN at sites of infection.
- Umbilical cord does not separate normally, severe periodontal disease, skin infections
- Diagnosis by obtaining CD18 by FAC

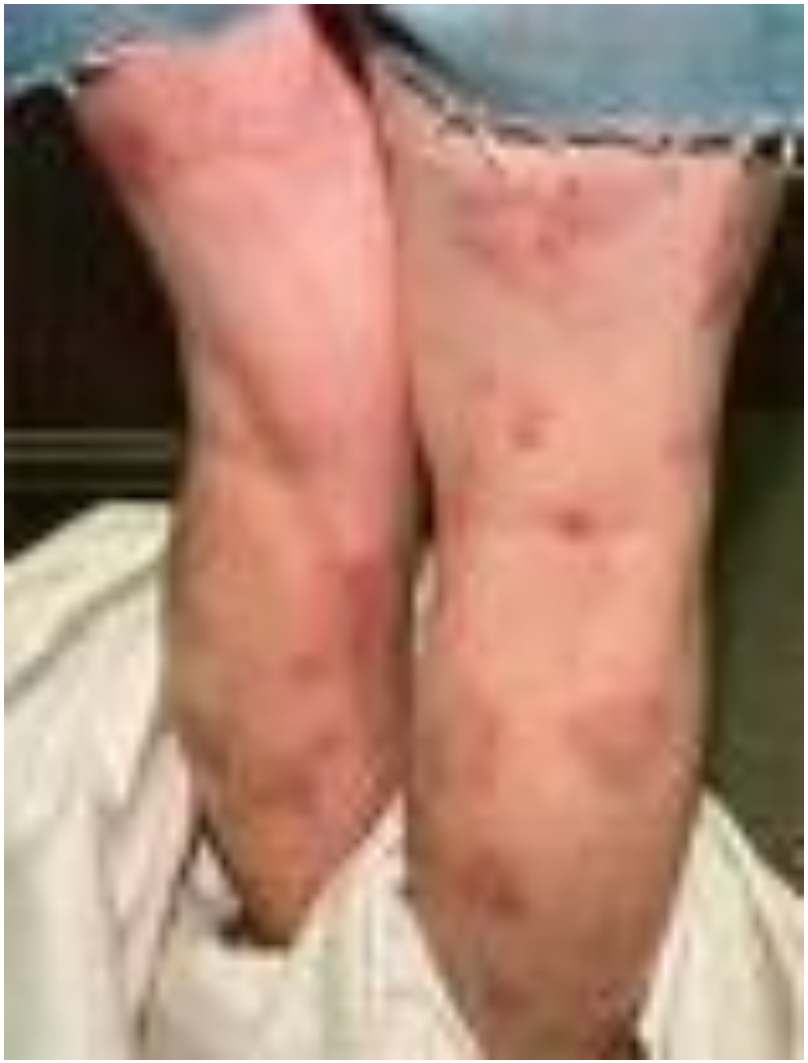
Other neutrophil defects

- Chediak-Higashi Syndrome (CHS): albinism, neuropathy, periodontal disease, recurrent Staph infections. Wright stain demonstrates giant granules in PMNs.
- Myeloperoxidase Deficiency: usually not a concern except in DM. Get recurrent candidasis and fungal infections.
- Hyper IgE (Jobs) Syndrome: High IgE levels (>2000), eczema, cold abscesses, candidiasis and staph infection, course facies, reduced PMN chemotaxis

Chediak-Higashi Syndrome



Hyper IgE (Jobs) Syndrome



Hyper IgE (Jobs) Syndrome

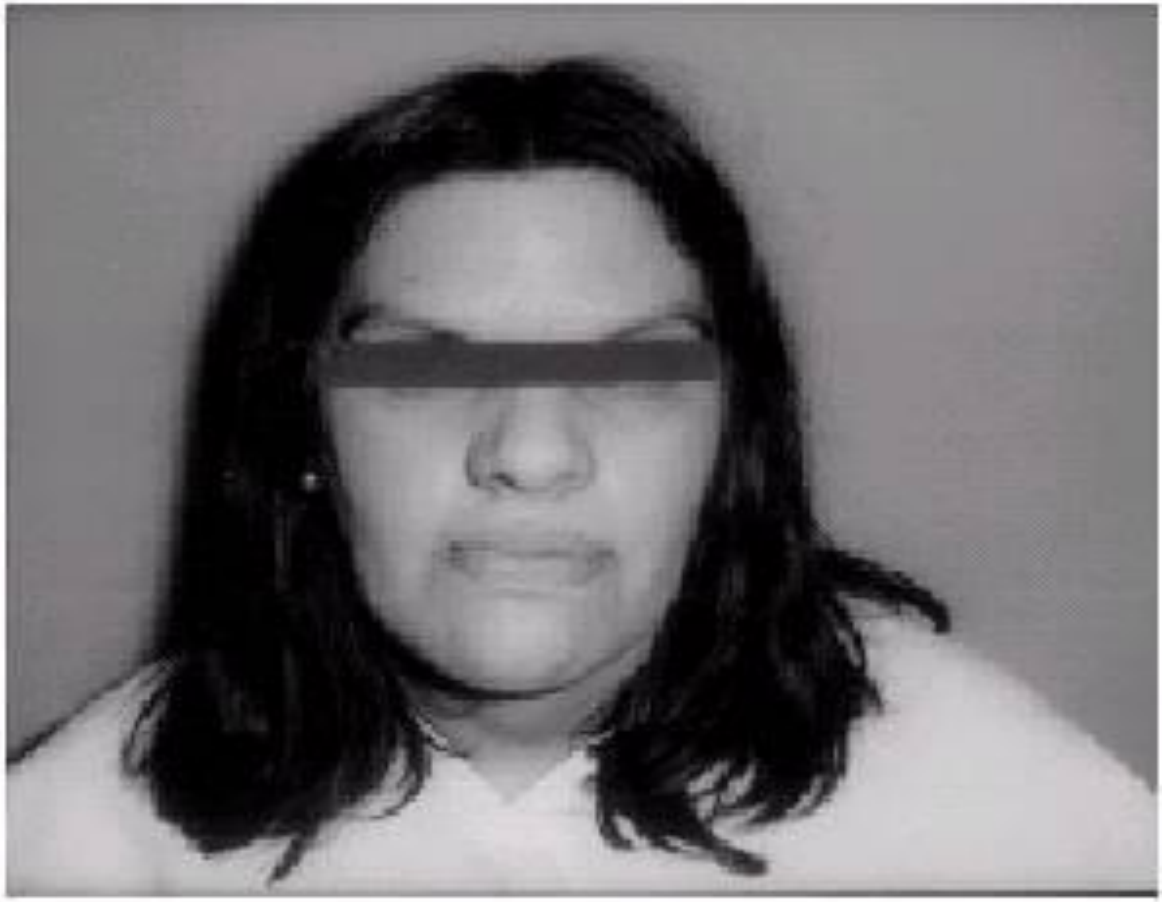
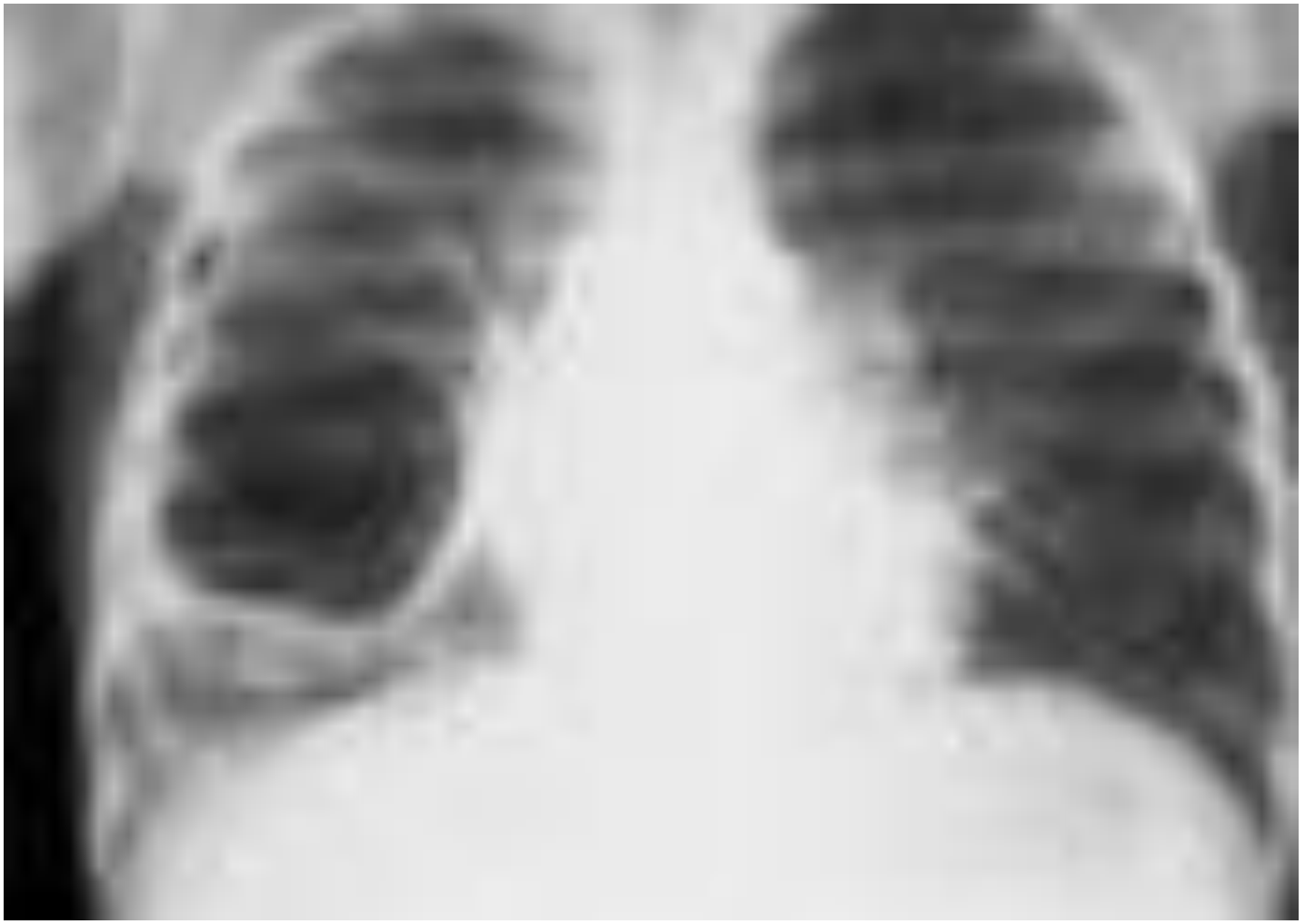


Fig. 3.– Rasgos faciales de la paciente

Hyper IgE (Jobs) Syndrome



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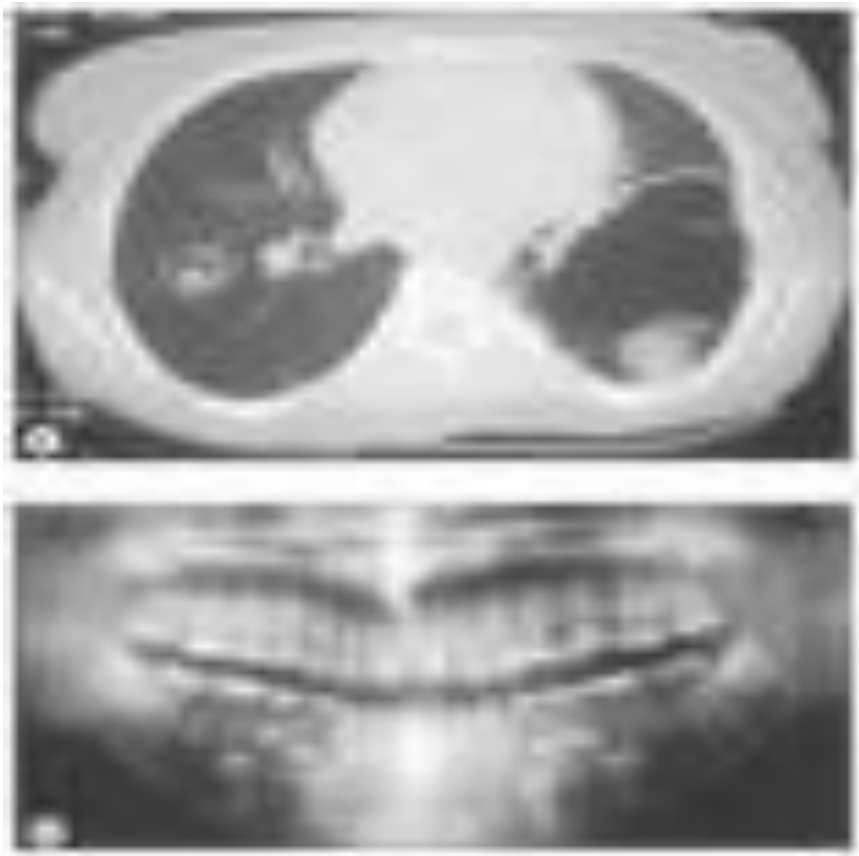

28 year old male with recurrent pneumonia, sinusitis, otitis and conjunctivitis. He was in good health until the past 2 years and since has had 3 CXR documented pneumonias, one with isolated S. pneumoniae. The most likely diagnosis is?

- A. Complement defect
- B. Neutrophil defect
- C. T cell defect
- D. B cell defect

- Ans-

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- A. Complement defect
- B. Neutrophil defect
- C. T cell defect
- D. B cell defect

- Ans- D

B Cell or Immunoglobulin Defects

- Burtons (X-linked Agammaglobulinemia)
- Selective IgA deficiency
- Common Variable Immunodeficiency (mixed T and B)
- Selective IgG deficiency
- Hyper-IgM Syndrome (mixed T and B)

The most common immunoglobulin defect is?

- A. Hyper IgM
- B. X-linked agammaglobulinemia
- C. IgA deficiency
- D. Common Variable Immunodeficiency

- Ans-

The most common immunoglobulin defect is?

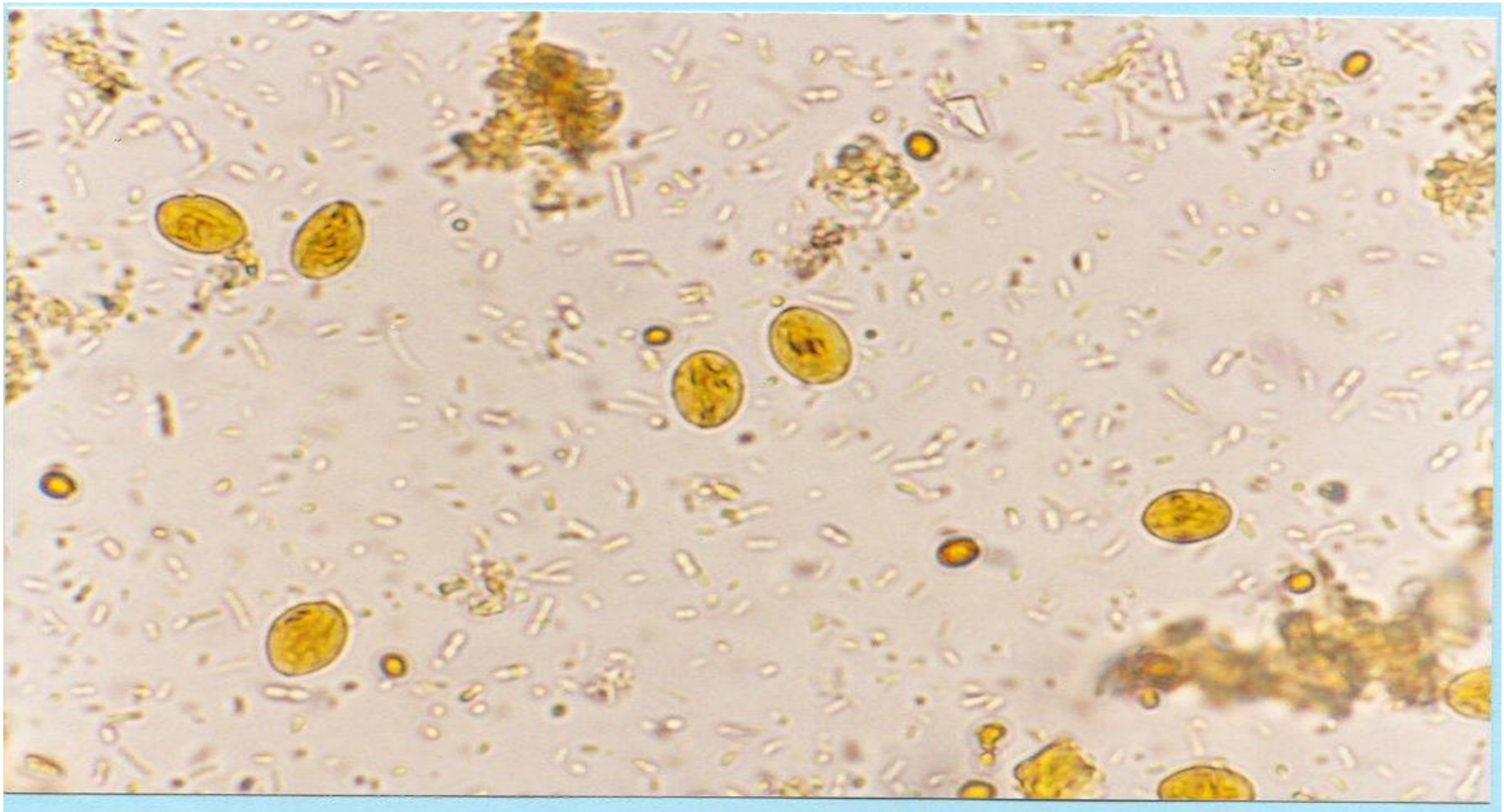
- A. Hyper IgM
- B. X-linked agammaglobulinemia
- C. IgA deficiency
- D. Common Variable Immunodeficiency

- Ans-

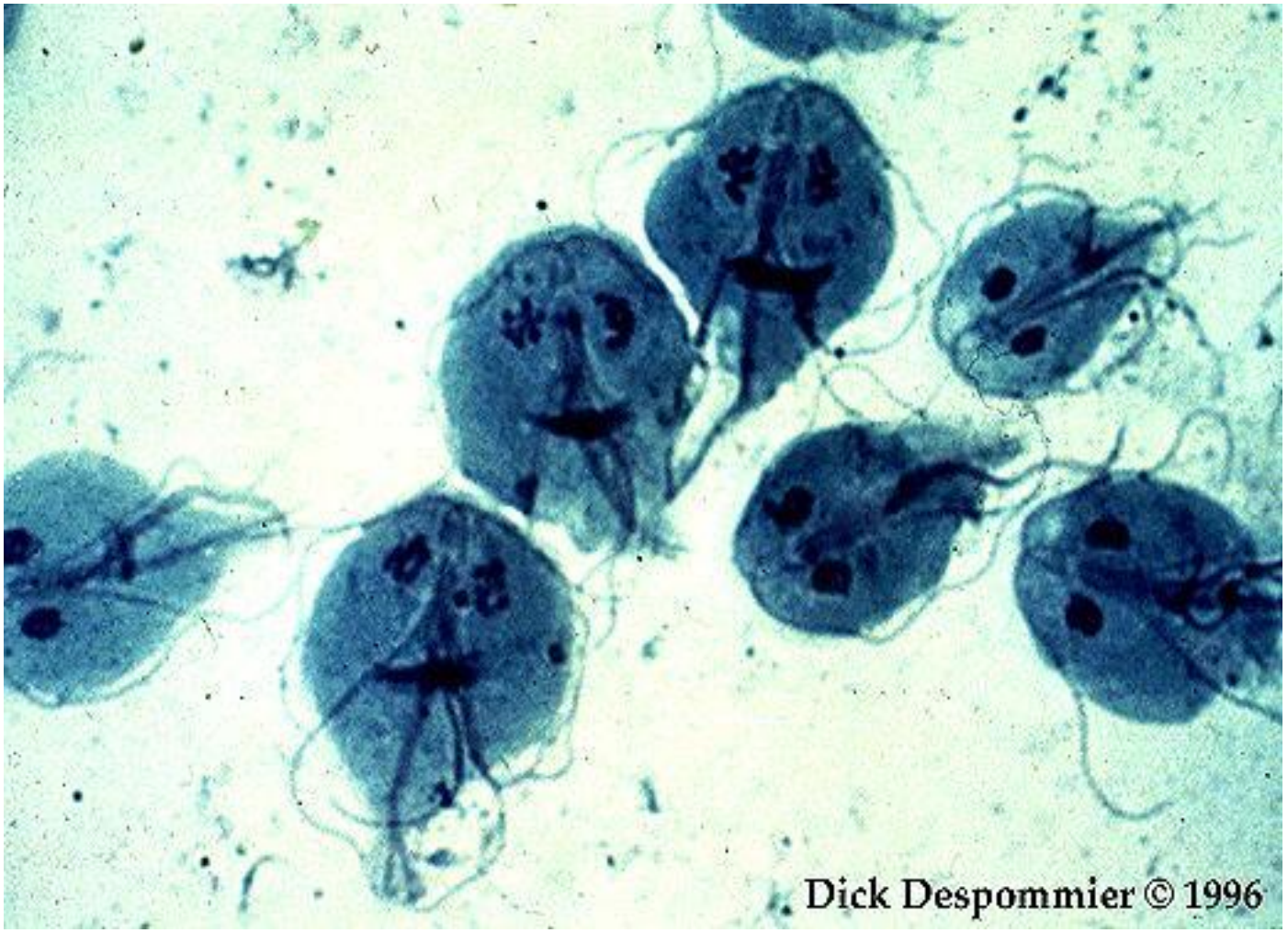
IgA deficiency

- Most are healthy
- 1:500 blood donors
- May get recurrent infections including: S pneumoniae, H influenzae, hepatitis virus and Giardia
- Also, predisposed to autoimmune disease and Common Variable Immunodeficiency.

Giardia Cysts in Stool Prep



Giardia wet prep



Mr Cocoa is a 45 yo with recurrent infections and bronchiectasis. He has been on prednisone for SOB for 2 months. He was referred to you because his FP found an IgG level of 323. What would you do?

- A. Give him a MMR and tetanus vaccine and test response with pre and post titers.
- B. Give him a pneumococcal and tetanus vaccine and test pre and post titers.
- C. Give him Prevnar and tetanus vaccine and test his pre and post titers
- D. Give him oral polio vaccine and MMR vaccine and test pre and post titers.
- Ans-

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- A. Give him a MMR and tetanus vaccine and test response with pre and post titers.
- B. Give him a pneumococcal and tetanus vaccine and test pre and post titers.
- C. Give him Prevnar and tetanus vaccine and test his pre and post titers
- D. Give him oral polio vaccine and MMR vaccine and test pre and post titers.
- Ans- B

Common Variable Immunodeficiency (CVID)

- Recurrent sino-pulmonary infections
- Especially Pneumococcal, H. flu, and rarely get PCP and CMV
- Predisposed to giardia, enteroviruses, lymphoma, gastric carcinoma, sprue and colitis.
- Lymphadenopathy and pul and liver granulomas
- Test with Ig levels and response to polysacc and protein vaccine.
- Have positive CD19 and CD 20 cells (B-cell)
- Rx- IV or SQ immunoglobulin

T cell defects

- Most often seen in acquired HIV disease or as a hereditary disease in young children
- Severe and recurrent unusual infections including viruses, fungi, bacteria and protozoan.
- Treatment is usually bone marrow transplantation early in life.

The best way to test if your patient has T-cells would be to test which CD markers?

- A. CD 19, 20 and 21
- B. CD 16 and 56
- C. CD 15
- D. CD 3, 4 and 8

- Ans-

The best way to test if your patient has T-cells would be to test which CD markers?

- A. CD 19, 20 and 21
- B. CD 16 and 56
- C. CD 15
- D. CD 3, 4 and 8

- Ans- D

The best way to test the function of T-cells in your patient is?

- A. Vaccine challenge with MMR
- B. Delayed hypersensitivity skin panel
- C. Test response to BCG vaccine
- D. Immediate hypersensitivity skin testing

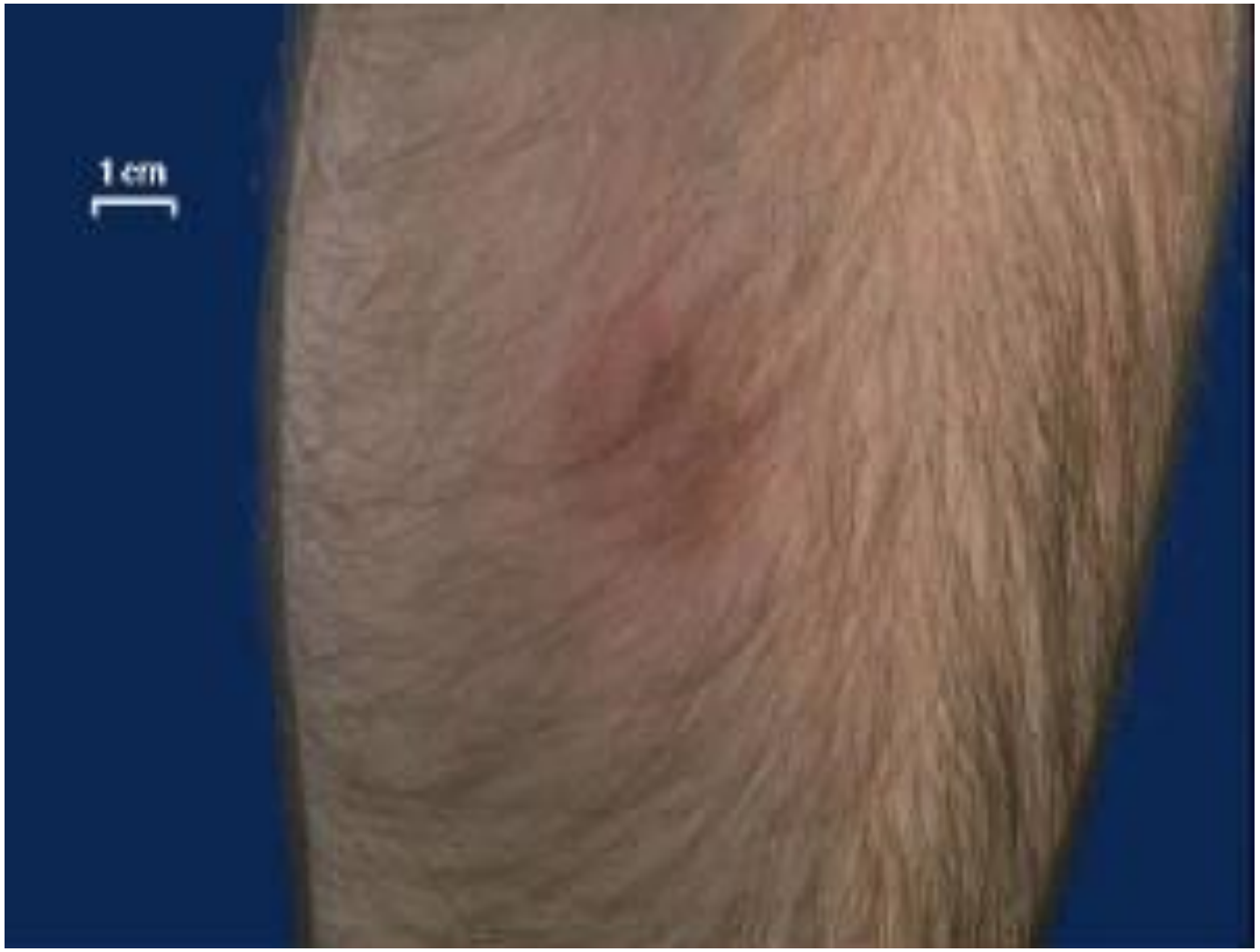
- Ans-

The best way to test the function of T-cells in your patient is?

- A. Vaccine challenge with MMR
- B. Delayed hypersensitivity skin panel
- C. Test response to BCG vaccine
- D. Immediate hypersensitivity skin testing

- Ans- B

Tetanus ID injection read in 2 to 3 days



Recurrent mycobacteria infections is seem with which cytokine defect?

- A. IL-5
- B. Interferon gamma
- C. IL-4
- D. IL 10

- Ans-

Recurrent mycobacteria infections is seem with which cytokine defect?

- A. IL-5
- B. Interferon gamma
- C. IL-4
- D. IL 10

- Ans- B (also defects in IL 12 and TNF)

Chronic Mucocutaneous Candidiasis

- Recurrent superficial candida infections
- Associated with endocrinopathies or other autoimmune diseases
- defect in cell-mediated immunity that may either be limited to *Candida* antigens or be part of a more general defect
- May have low levels of Fe++

Defects seen in Chronic Mucocutaneous Candidiasis include?

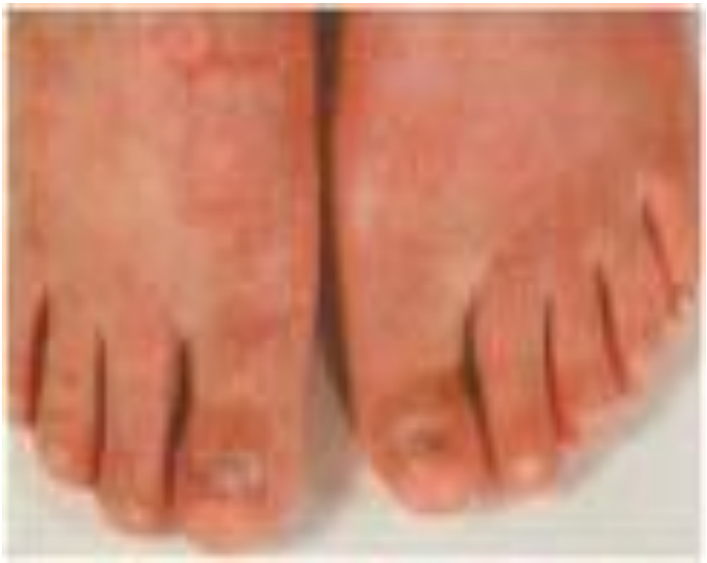
- A. High levels of IL-10
- B. High levels of IL-2
- C. High levels of IL-12
- D. High levels of IL-8

- Ans-

Defects seen in Chronic Mucocutaneous Candidiasis include?

- A. High levels of IL-10
- B. High levels of IL-2
- C. High levels of IL-12
- D. High levels of IL-8

- Ans- A (also high levels of IL-17)



Mannose binding lectin deficiency

- Still in flux
- Defined as a MBL below 500 ng/ml
- MBL binds to carbohydrate groups on bacteria and self.
- Early innate defence
- Have increase risk of autoimmune disease
- Also, increase risk of pyogenic bacteria, especially with capsules secondary to defect in opsonization

42 year old male has recurrent pancreatitis of unknown etiology. Biopsy demonstrates infiltration with plasma cells. What stain would you use to diagnose his disease?

- A. IgG4
- B. CD4
- C. Complement
- D. IgA
- E. EBV

- Answer:

42 year old male has recurrent pancreatitis of unknown etiology. Biopsy demonstrates infiltration with plasma cells. What stain would you use to diagnose his disease?

- A. IgG4
- B. CD4
- C. Complement
- D. IgA
- E. EBV

- Answer: A

IgG4 disease

- Middle age men
- Infiltration with plasma cells with IgG4
- Serum level of IgG4 is usually elevated
- Pancreatitis (type 1), sialadenitis, sclerosing cholangitis, fibrosis of the retroperitoneal space, thyroiditis, pneumonitis, periaortitis
- Rx- corticosteroids

Thank you

I hope you enjoy the rest of your day.

Sincerely,

Timothy Craig
tcraig@psu.edu