

MONONUCLEOSIS AND ATHLETICS:

“DOC, WHEN CAN I PLAY?”

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Infectious Mononucleosis

“Hoagland’s Criteria”

- **Classic Triad**

- Fever
 - Rarely >104 degrees F
- Pharyngitis
 - Often exudative
- Lymphadenopathy
 - Posterior cervical

- **Laboratory**

- 50% Lymphocytes
- 10% Atypical Lymphocytes

Remember it’s a “syndrome not a disease”

Infectious Mononucleosis : Causes

- EBV 90% of acute IM
- Etiology of most EBV–negative IM : unknown
- Other Herpesviruses :
 - Cytomegalovirus (CMV)
 - herpes simplex 1 and simplex 2
 - human herpesvirus 6
- Other viruses :
 - adenovirus
 - hepatitis A, hepatitis B, or hepatitis C
 - rubella
 - primary human immunodeficiency virus in adolescents or young adults.

Infectious Mononucleosis

- No racial and sexual difference.
- The peak incidence occurs 2 years earlier in females.
- Report in middle-aged and elderly adults
 - heterophile antibody negative.
- Most clinical symptoms are a consequence of T cell proliferation and organ infiltration.

Infectious Mononucleosis: Transmission

- Incubation period : 30 – 50 days (shorter in young children)
- Oral secretions are major cause of transmission
 - “Kissing Disease”
- Blood products/Transplanted organs
 - EBV less commonly than CMV
- Intrauterine : infrequent
 - If infected, no adverse fetal outcomes and no viral transmission to the fetus.

THE MONO SYNDROME

Clinical Manifestations

Clinical manifestation of Mono By Age

Sign or symptom	Frequency (%)		
	Age < 4 yr	Age 4 – 16 yr	Adults (range)
Lymphadenopathy	94	95	93 – 100
Fever	92	100	63 – 100
Sore throat or tonsillopharyngitis	67	75	70 – 91
Exudative tonsillopharyngitis	45	59	40 – 74
Splenomegaly	82	53	32 – 51
Hepatomegaly	63	30	6 – 24
Cough or rhinitis	51	15	5 – 31
Rash	34	17	0 – 15
Abdominal pain or discomfort	17	0	2 – 14
Eyelid edema	14	14	5 – 34

Sumaya, et al. J Infect Dis.131:403-408,1975.

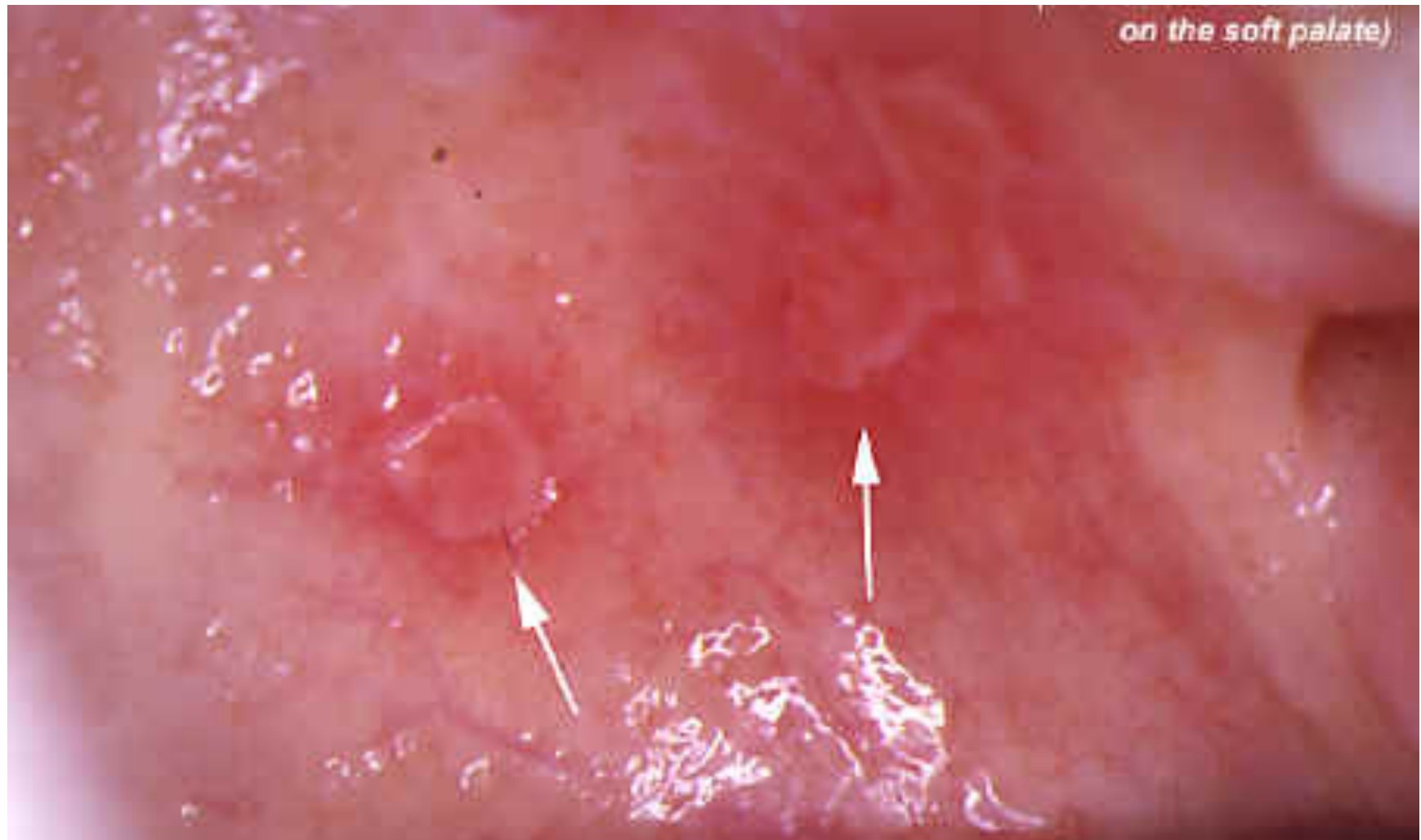
Infectious Mononucleosis

- **Acute infectious mononucleosis**
 - fatigue and malaise 1-2 wks
 - sore throat, pharyngitis
 - retro-orbital headache
 - fever
 - myalgia
 - nausea
 - abdominal pain
 - generalized lymphadenopathy
 - hepatosplenomegaly

Infectious Mononucleosis

- **Pharyngitis** is the most consistent physical finding.
 - 1/3 of patients : exudative pharyngitis.
 - 25-60% of patients : petechiae at the junction of the hard and soft palates.
 - Tonsillar enlargement can be massive, and occasionally it causes airway obstruction.

Classic Oral Petichiae



Infectious Mononucleosis



Exudative pharyngotonsillitis

Infectious Mononucleosis

- Lymphadenopathy : 90%
 - symmetrical enlargement.
 - mildly tender to palpation and not fixed
 - posterior cervical lymph nodes.
 - anterior cervical and submandibular nodes.
 - axillary and inguinal nodes.
 - Enlarged epitrochlear nodes are very suggestive of infectious mononucleosis.

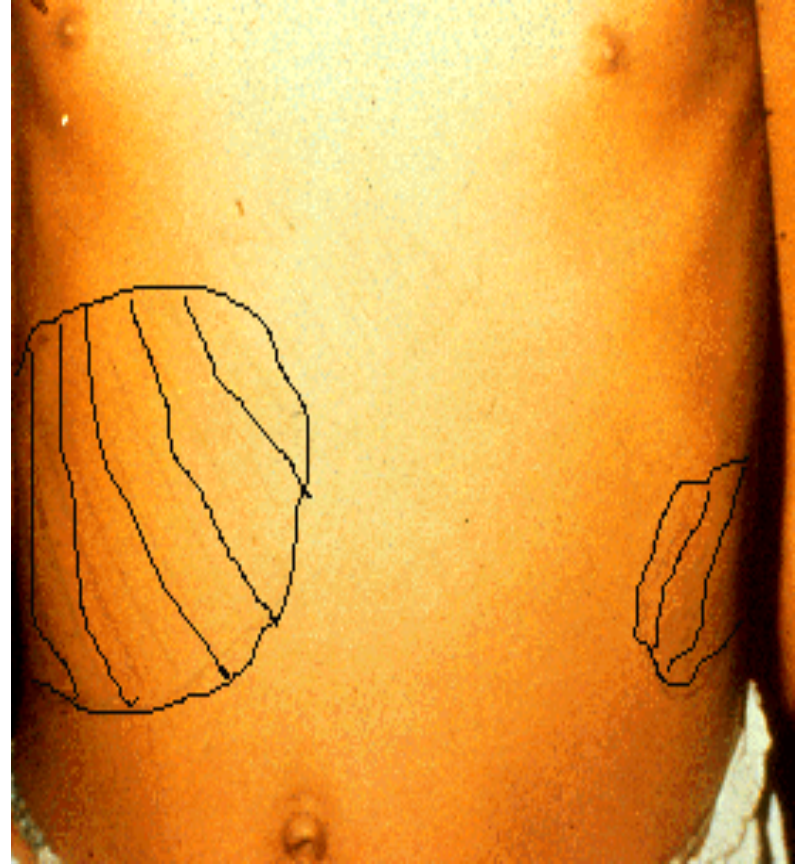
Infectious Mononucleosis

- **Hepatomegaly** : 60%
 - Jaundice is rare.
 - Percussion induced tenderness over the liver is common.
- **Splenomegaly** : 50%
 - Palpable below the left costal margin and may be tender.
 - Rapid increase in the first week of symptoms, usually decreasing in size over the next 1-2 weeks
 - Spleen can rupture from relatively minor trauma or even spontaneously.

Infectious Mononucleosis



Cervical lymphadenopathy



Hepatosplenomegaly

Infectious Mononucleosis

- Maculopapular rash : 15%
 - Usually faint, diffuse, and erythematous
 - Occurs in up to 15% of patients and is more common in young children.
 - 80% of patients, treatment with amoxicillin or ampicillin is associated with inducing the rash
 - Circulating immunoglobulin G (IgG) and immunoglobulin M (IgM) antibodies to ampicillin are demonstrable.

Infectious Mononucleosis



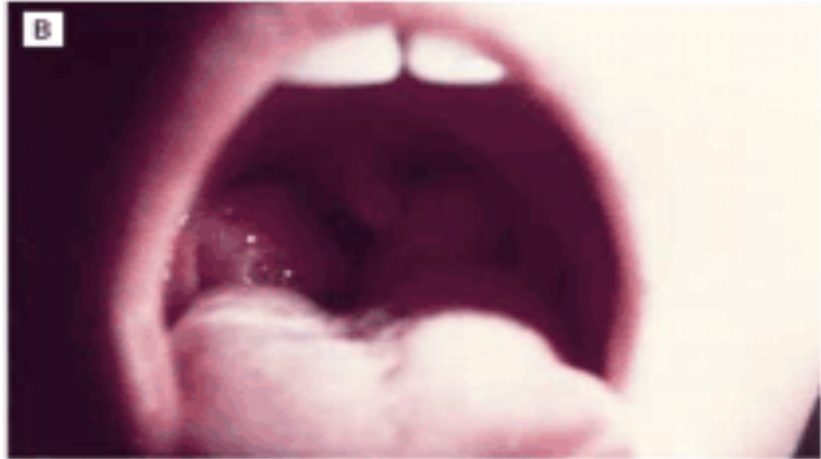
Typical mono rash

NEJM;343:481-492.

Infectious Mononucleosis

- **Eyelid edema : 15%**
 - May be present, especially in the first week
 - More common in children < 4 years of age
 - Hepatomegaly
 - Splenomegaly
 - URI symptoms

Infectious Mononucleosis



NEJM;343:481-492.

MONONUCLEOSIS

Laboratory Testing

Infectious Mononucleosis : Lab

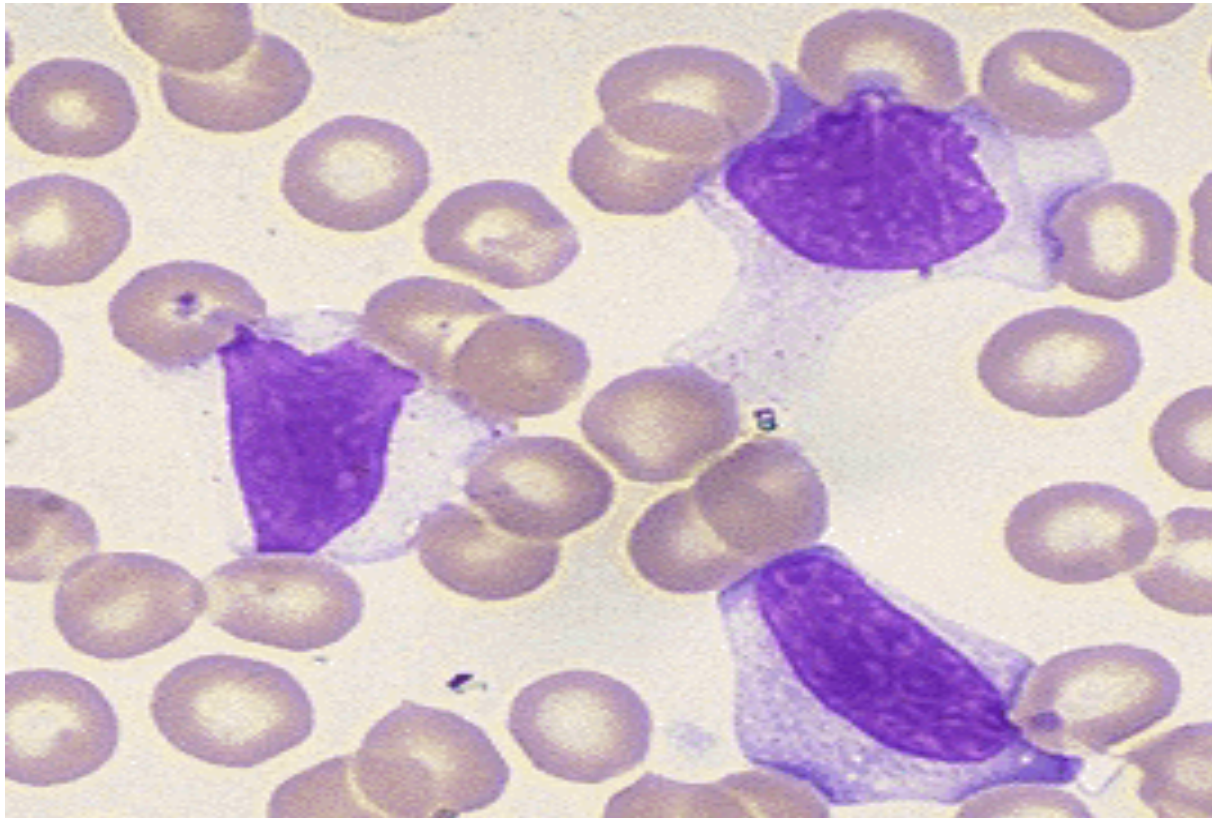
- The 3 classic criteria for laboratory confirmation
 - Lymphocytosis > 50% of cells
 - Presence of at least 10% atypical lymphocytes on peripheral smear
 - Positive serologic test for acute EBV or proof of another etiology

Infectious Mononucleosis : Lab

- **Complete Blood Count**

- 40-70%, Increased Leukocytes
- By the second week of illness, approximately 10% have a WBC count $> 25,000$ per cm^3 .
- 80-90% of patients **have lymphocytosis**, with greater than 50% lymphocytes.
- Lymphocytosis is greatest during the first 2-3 weeks of illness and lasts for 2-6 weeks.
- Atypical lymphocytes $> 10\%$; Downey types
- 25-50%, **Mild thrombocytopenia**

Infectious Mononucleosis



atypical lymphocytes : Downey types

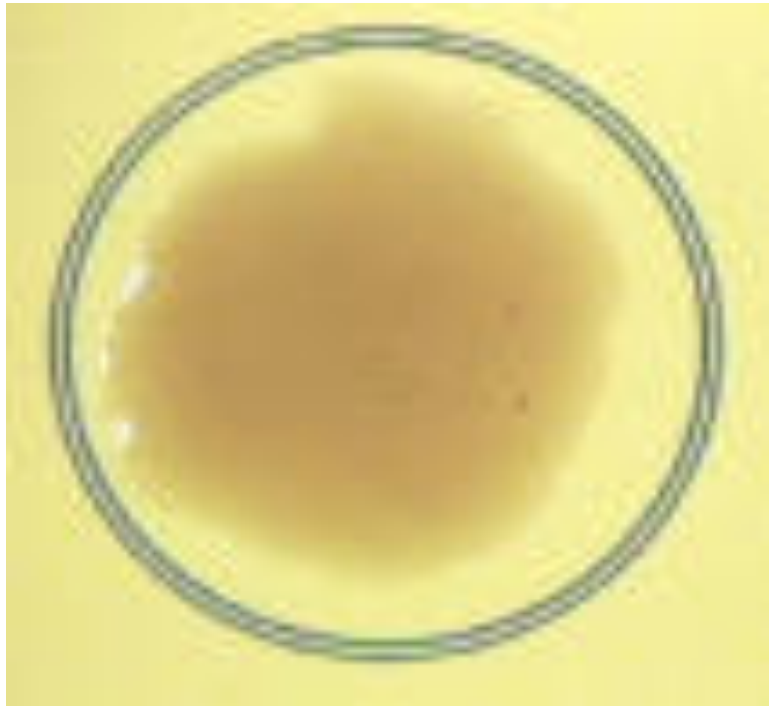
Infectious Mononucleosis : Lab

- **Liver function tests**

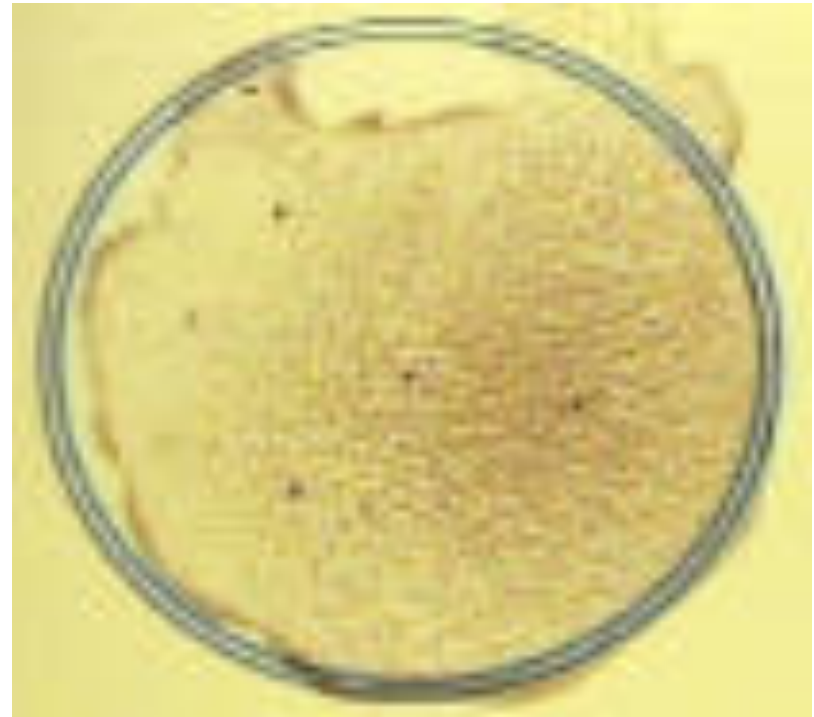
- 80-100% of patients : **elevated LFT**
- Alkaline phosphatase, AST and bilirubin typically peak 5-14 days after onset
- GGT peaks at 1-3 weeks. Occasionally, GGT remains mildly elevated for up to 12 months
- 95% of patients : **elevated LDH**
- most liver function test results are normal in about 3 months.

Infectious Mononucleosis : Lab

- Heterophile antibodies
 - 50% in first week of illness
 - 60-90% in the second or third weeks
 - begins to decline during the fourth or fifth week and often is less than 1:40 by 2-3 months after symptom onset
 - 20% of patients have positive titers 1-2 years after acquisition
 - children < 2 years : 10-30%
 - children 2-4 years : 50-75%



No clumping of the red blood cells indicates the person's serum does not contain heterophile antibodies. The few clumps that are seen are red blood cells from the test reagent that did not separate during shaking of the reagent prior to placing it on the slide.



Clumping of the red blood cells indicates the person's serum contains heterophile antibodies.

Infectious Mononucleosis : Lab

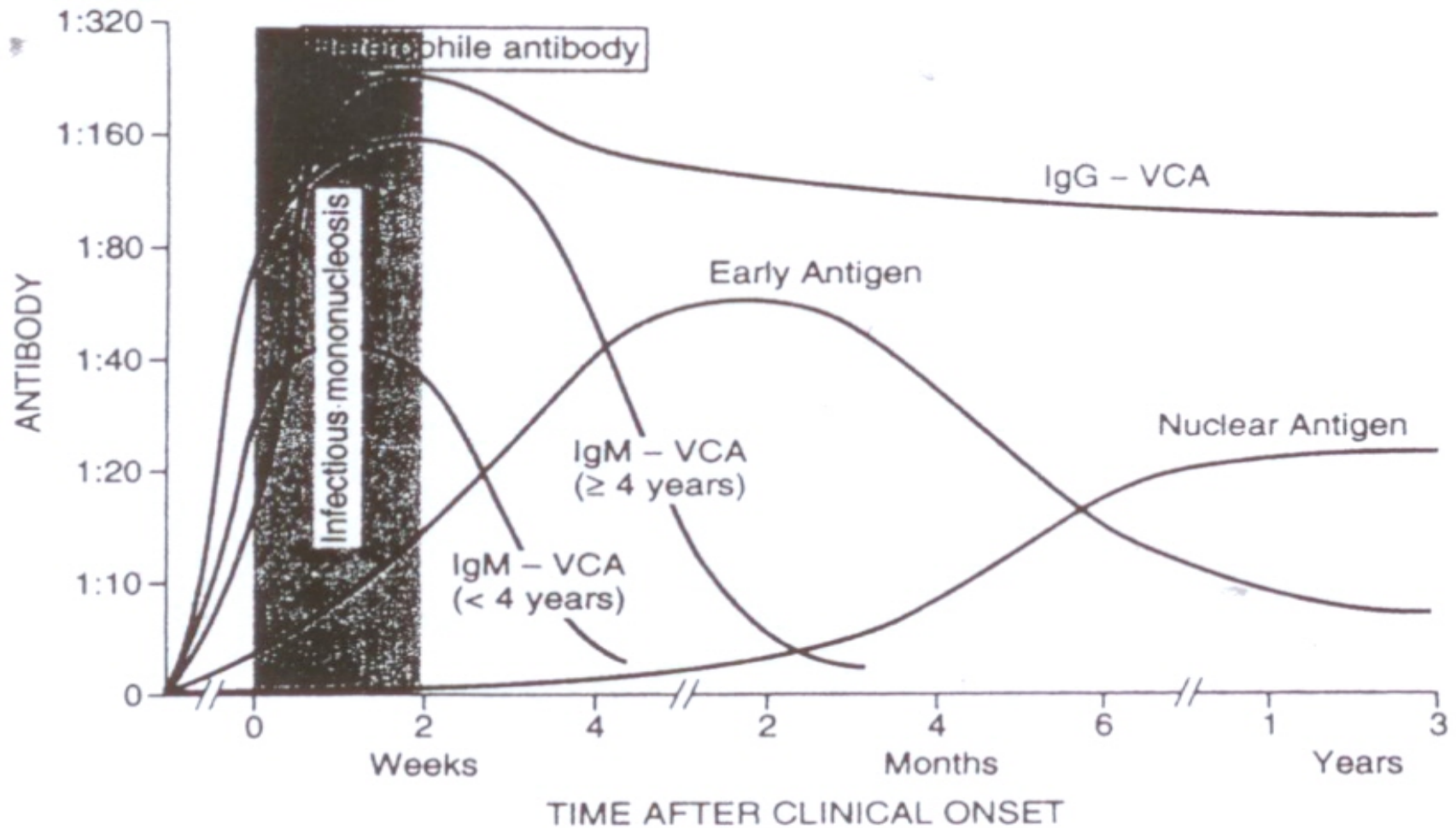
- **Time course of antibody production**

- EA is rising at symptom onset : rise for 3-4 weeks, then quickly decline to undetectable levels by 3-4 months, although low levels may be detected intermittently for years.
- VCA-IgM usually is measurable at symptom onset, peaks at 2-3 weeks, then declines and not measurable by 3-4 months.
- VCA-IgG rises shortly after symptom onset, peaks at 2-3 months, then drops slightly but persists for life.
- EBNA : convalescence and remain present for life.

PCR has changed the game

Positive PCR for EBV is DIAGNOSTIC of infection

Serum EBV antibodies



Serum Epstein-Barr Virus (EBV) Antibodies in EBV Infection

Infection	VCA IgG	VCA IgM	EA(D)	EBNA
No previous infection	-	-	-	-
Acute infection	+	+	+/-	-
Recent infection	+	+/-	+/-	+/-
Past infection	+	-	+/-	+

MONONUCLEOSIS

Complications

Mononucleosis: Complications

- **Hepatitis** :
 - Increased LFT's occur in > 90% of patients
 - LFT : < 2-3 times normal in the second and third weeks of illness
 - 45% of patients : elevated bilirubin, but jaundice occurs in only 5%.
- **Platelet count** :
 - Mild thrombocytopenia occurs in approximately 50% of patients with infectious mononucleosis.
 - Nadir approximately 1 week after symptom onset (100,000-140,000/cm³.), then gradually improves over the next 3-4 weeks.

Mononucleosis: Complications

- **Hemolytic anemia**
 - 0.5-3%, associated with cold-reactive antibodies, anti-I antibodies, and with autoantibodies to triphosphate isomerase
 - mild and is most significant during the second and third weeks of symptoms.
- **Upper airway obstruction**
 - 0.1-1%, due to hypertrophy of tonsils and other lymph nodes of Waldeyer ring
 - treatment with corticosteroids may be beneficial

Mononucleosis: Complications

- **Splenic rupture** : 0.1-0.2%
 - Spontaneous or history of some antecedent trauma.
 - Occurs most frequently during the second and third weeks.
 - mild-to-severe abdominal pain below the left costal margin, sometimes with radiation to the left shoulder and supraclavicular area.
 - Massive bleeding : Shock

Mononucleosis : Complications

- Hematologic complications
 - hemophagocytic syndrome.
 - Immune thrombocytopenic purpura occurs and may evolve to aplastic anemia.
 - accelerate hemolytic anemia in congenital spherocytosis or hereditary elliptocytosis.
 - Disseminated intravascular coagulation associated with hepatic necrosis has occurred.

Mononucleosis : Complications

- Neurologic complications : < 1%
 - during the first 2 weeks.
 - negative for the heterophile antibody.
 - severe and sometimes fatal
 - aseptic meningitis, acute viral encephalitis, coma, meningitis, and meningoencephalopathy.
 - Hypoglossal nerve palsy, Bell palsy, hearing loss, brachial plexus neuropathy, multiple cranial nerve palsies, Guillain-Barré syndrome, autonomic neuropathy, gastrointestinal dysfunction secondary to selective cholinergic dysautonomia, acute cerebellar ataxia, transverse myelitis.

MONONUCLEOSIS

Treatment

Mononucleosis: Treatment

Medical Care :

- Self-limited illness
 - Symptom relief and supportive care
- Inpatient therapy for medical and/or surgical complications rarely required
 - **Acyclovir** (10 mg/kg/dose IV q8h for 7-10 d)
 - inhibit viral shedding from the oropharynx
 - clinical course is not significantly altered
 - use of oral antivirals not indicated
 - **IVIG** (400 mg/kg/d IV for 2-5 d)
 - immune thrombocytopenia

Mononucleosis: Treatment

Indications for Steroids:

- Marked inflammation of the tonsils with impending airway obstruction
- Massive splenomegaly
- Myocarditis
- Hemolytic anemia
- Hemophagocytic syndrome
- Seizure and meningitis

Mononucleosis: Prognosis

- Immunocompetent Individuals
 - Full recovery in several months.
 - The common hematologic and hepatic complications resolve in 2-3 months.
- Neurologic complications
 - Children : resolve quickly
 - Adults : neurological deficits
- All individuals develop latent infection (EBV)
 - Asymptomatic
 - Virus can be isolated from oral secretions of 20-30% of healthy latently infected individuals at anytime.
 - 2010 study in athletes noted higher EBV loads with Lower EBV-IgG titers in asymptomatic elite athletes.

Mononucleosis: Prevention

- Isolation is not required
 - low transmission.
- Avoid contact with saliva
 - Do not kiss children on the mouth.
- Maintain clean conditions
 - day care, avoid sharing toys.
- EBV can be transmitted by blood transfusion and by bone marrow transplantation
- Vaccine development is proceeding, although the role of a vaccine is unclear.

MONONUCLEOSIS

Return to play criteria

Return To Play Guidelines

Activity :

- Depends on severity of the patient's symptoms.
- Extreme fatigue = bed rest as needed
- Malaise may persist for 2-3 months
 - EBV- PCR may assist in cases of prolonged fatigue
- Presence of “complications” will dictate return to play
 - Labs should be back to normal and fitness levels assessed
- Patients should not participate in contact sports or heavy lifting (Valsalva precautions) for at least 2-3 weeks or until clinically resolved and no SPLEEN ENLARGEMENT

Return to Play Guidelines

- Light, non-contact activities may resume 3 weeks from symptom onset.
 - Assumes avoidance of chest/abdominal trauma; significant exertion or Valsalva and that the athlete is asymptomatic and fitness level is near baseline.
- Contact activity is controversial as splenic rupture is high in first 3 weeks but can occur up to 7 weeks.
 - **EDUCATE**
 - **Splenic ultrasound may be misleading!**
 - Serial studies may be needed as ? What is “normal “ study
- **“Clinical judgment, and treatment and resolution of the individual complications, dictate resumption of activity”**

Questions?

