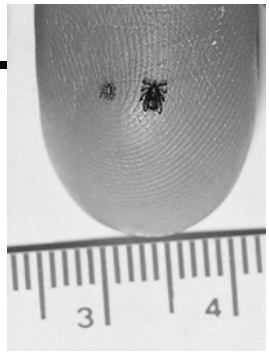
LYME DISEASE

- Epidemiology
- Clinical Manifestations
- Differential Diagnosis
- Diagnosis
- Treatment
- Prevention

EPIDEMIOLOGY

- Caused by spirochete *Borrelia burgdorferi*
- Transmitted by *Ixodes* ticks
- Nymph-stage ticks feed on humans May through July - transmit spirochete
- Endemic areas
  - Northeastern coastal states
  - Wisconsin & Minnesota
  - Coast of Oregon & northern California

Ixodes scapularis ticks



Larva, nymph, and adult female and male Ixodes dammini ticks

EPIDEMIOLOGY (cont)

- > 🖹 of dear ticks carry spirochete
- Rising frequency attributed to enlarging deer population & concurrent suburbanization
- High risk areas - wooded or brushy, unkempt grassy areas & fringe of these areas
- Lower risk on lawns that are mowed

MAJOR RISK FACTORS

- Geographical
  - Northeast, north-central (Wisconsin, Minnesota) coastal regions of California & Oregon
- Occupational
  - Landscaper, forester, outdoor
- Recreational
  - hiking, camping, fishing, hunting

CLINICAL MANIFESTATIONS

- Stage 1 - Acute, localized disease
- Stage 2 - Subacute, disseminated disease
- Stage 3 - Chronic or late persistent infection

ACUTE INFECTION

- Tick must have been feeding for at least 24-48 hrs
- Erythema migrans develops 1 to 4 weeks after bite
- Without treatment rash clears within 3 to 4 weeks
- About 50% of pts will also c/o flulike illness - fever, H/A, chills, myalgia

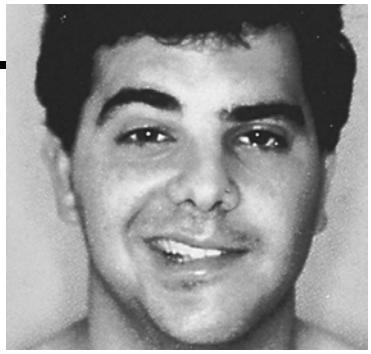
DISSEMINATED DISEASE

- May develop in wks to mos in untreated pts
- Symptoms usually involve skin, CNS, musculoskeletal system, & cardiac
- Dermatological manifestations
  - new skin lesions, smaller and less migratory than initial
  - Erythema and urticaria have been noted

DISSEMINATED (cont)

- Neurologic complications
- Occurs wks to mos later in about 15% to 20% of untreated
- Symptoms
  - Lyme meningitis
  - mild encephalopathy
  - unilateral or bilateral Bell's palsy
  - peripheral neuritis

Left facial palsy (Bell's palsy) in early Lyme disease



DISSEMINATED (cont)

- Musculoskeletal symptoms
- Symptoms evolve into frank arthritis in up to 60% of untreated pts
- Onset averages 6 mos from initial infection
- Symptoms
  - migratory joint, muscle, & tendon pain
  - knee most common site
  - no more than 3 joints involved during course
  - lasts several days to few weeks then joint returns to normal

DISSEMINATED (cont)

- Cardiac involvement
- Noted in about 5% to 10% beginning several wks after infection
- Transient heart block may be consequence
- Range from asymptomatic to first-degree heart block to complete
- Cardiac phase lasts from 3 to 6 wks

CHRONIC - LATE PERSISTENT

- Follows latent period of several mos to a yr after initial infection
- 60% to 80% will have musculoskeletal complaints
- Most common; arthritis of knee - may also occur in ankle, elbow, hip, shoulder

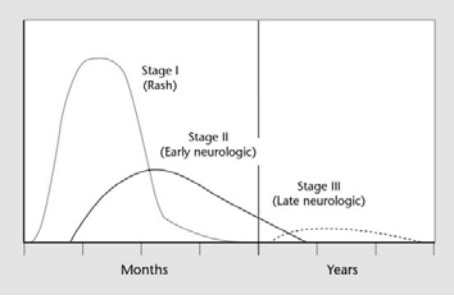
CHRONIC (cont)

- Neurologic impairment
  - distal paresthesias
  - radicular pain
  - memory loss
  - fatigue

NATURAL HISTORY

- Without treatment will see disseminated disease in about 80% of pts
- Oligoarthritis - 60% to 80%
- Chronic neurologic & persistent joint symptoms - 5% to 10%

Clinical stages of Lyme disease



CONCURRENT INFECTIONS

- Human *babesiosis*
  - fever, chills, sweats, arthralgias, headache, lassitude
  - pts with both appear to have more severe Lyme disease
- Ehrlichiosis
  - described as "rashless Lyme disease"
  - high fever & chills & may become prostrate in day or two

DIFFERENTIAL DIAGNOSIS

- Acute & early disseminated stages
  - Rocky Mountain spotted fever
  - human babiosis
  - summertime viral illnesses
  - viral encephalitis
  - bacterial meningitis

DIFFERENTIAL (cont)

- Late disseminated & chronic stages
  - gout
  - pseudogout
  - Reiter's syndrome, psoriatic arthritis, ankylosing spondylitis
  - rheumatoid arthritis
  - depression
  - fibromyalgia
  - chronic fatigue syndrome

DIAGNOSIS

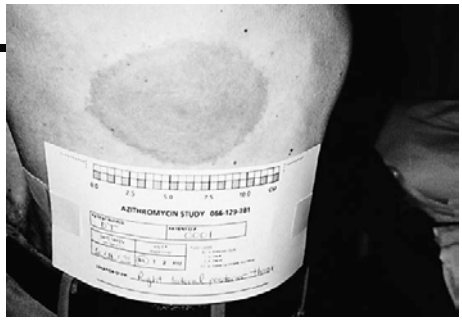
- Clues to early disease
  - EPIDEMIOLOGIC
    - travel or residence in endemic area within past month
    - h/o tick bite (especially within past 2 weeks)
    - late spring or early summer (June, July, August)

EARLY DISEASE (cont)

- RASH
  - expanding lesion over days (rather than hours or stable over months)
  - central clearing or target appearance
  - minimal pruritis or tenderness
  - central papular erythema, pigmentation, or scaling at sit of tick bite
  - lack of scaling
  - location at sites unusual for bacterial cellulitis (usually axillae, popliteal fossae, groin, waist

Erythema (chronicum) migrans

Single erythema migrans



EARLY DISEASE (cont)

- ASSOCIATED SYMPTOMS
  - fatigue
  - myalgia/arthralgia
  - headache
  - fever and/or chills
  - stiff neck
  - respiratory & GI complaints are infrequent

EARLY DISEASE (cont)

- PHYSICAL EXAM
  - Regional lymphadenopathy
  - Multiple erythema migrans lesion
  - Fever

DISSEMINATED DISEASE

- Clinical presentation can make diagnosis
  - epidemiological inquiry
  - review of key historic features
  - physical findings
  - serum for antibody testing
  - spinal tap

LATE DISEASE

- Careful attention to musculoskeletal & neurologic symptoms
- Differentiating Lyme from fibromyalgia & CFS
  - oligoarticular musculoskeletal complaints that include signs of joint inflammation
  - limited & specific neuro deficits
  - abnormalities of CFS
  - absence of disturbed sleep, chronic H/A, depression, tender points

ANTIBODY TESTING

- Testing with ELISA is not required to confirm diagnosis
- Pts with objective clinical signs have high pretest probability of disease
- Tests are not sensitive in very early disease
- Should not use is pt without subjective symptoms of Lyme

TESTING(cont)

- A + test in person with low probability of disease risks false + rather than true +
- Test when pts fall between these two extremes
  - pt with lesion or symptoms without known endemic exposure (new area)
  - pretest probability now has high sensitivity & specificity

TESTING (cont)

- For a positive or equivocal ELISA or IFA CDC recommends Western blot
- Testing cannot determine cure as pt remains antibody +
- PCR is being developed - still considered investigational

TREATMENT

- Early Lyme disease
  - doxycycline, 100 mg BID for 21 to 18 days
  - amoxicillin, 500 mg TID for 21 to 28 days
  - cefuroxime, 500 mg BID for 21 days

PREVENTION

- Wear light-colored clothes - easier to spot tick
- Wear long pants, long sleeves
- Use tick repellent, such as permethrin, on clothes
- Use DEET on skin
- Check for ticks after being outside
- Remove ticks immediately by head

VACCINATION

NO LONGER AVAILABLE

WEST NILE VIRUS

- Summer 1999 - first detected in NYC & Western hemisphere
- 59 hospitalized - epicenter Queens - 7 died
- Summer 2000 - epicenter Staten Island - 19 hospitalized - 2 died
- For 2002 - 39 states, 3737 confirmed cases, 214 deaths

INFECTIOUS AGENT

- Member of family Filaviviridae
- Belongs to Japanese encephalitis complex
- Before 1999 outbreaks seen only in Africa, Asia, Middle East, rarely Europe
- Reservoir & Mode of transmission
  - wild birds primary reservoir & *Culex* spp. major mosquito vector

INCUBATION PERIOD/SYMPTOMS

- Incubation usually 6 days (range 3-15)
- Symptoms
  - milder: fever, headache, myalgias, arthralgias, lymphadenopathy, maculopapular or roseolar rash affecting trunk & extremities
  - occasionally reported: pancreatitis, hepatitis, myocarditis
  - CNS involvement rare & usually in elderly

TREATMENT

- No known effective antiviral therapy or vaccine
- Intensive supportive in more severe cases

DIFFERENTIAL DIAGNOSIS

- Enteroviruses
- Herpes simplex virus
- Varicella

TESTING

- Lab conformation based on following criteria:
  - isolating West Nile virus from or demonstrating viral antigen or genomic sequences in tissue, blood, CSF, or other body fluid
  - demonstrating IgM antibody to West Nile virus in CSF by ELISA
  - demonstrating 4-fold serial change in plaque reduction neutralization test (PRNT) antibody to West Nile virus in paired, acute & convalescent serum samples
  - demonstrating both West Nile virus-specific IgM & IgG antibody in single serum specimen using ELISA & PRNT

Must report suspected cases of West Nile to the NYC Department of Health

During business hours call Communicable Disease Program (212) 788-9830

At all other times call Poison Control Center - (212) 764-7667

INFECTIOUS MONONUCLEOSIS

- Infectious mononucleosis - designates the clinical syndrome of prolonged fever, pharyngitis, lymphadenopathy
- Epstein-Barr virus-associated infectious mononucleosis (EBV-IM)
- non Epstein-Barr virus-associated infectious mononucleosis (non-EBV-IM)
  - approximately 10-20% have

EPIDEMIOLOGY

- >90% of adults have serologic evidence of prior EBV infection
- Mean age of infection varies
- In US 50% of 5-year-old children & 50-70% of first-year college students have evidence of prior infection
- Infection in children most prevalent amongst lower socioeconomic
- 15-19 - peak rate of EBV-IM

- Chance of acute EBV infection leading to IM ↑ with age
- Good sanitation & uncrowded living conditions ↑ risk of EBV-IM

OTHER CAUSES OF IM

- CMV
- Human herpesvirus 6
- HIV
- Adenovirus
- Toxo
- Corynebacterium diptheriae
- Hep A
- Rubella
- Coxiella burnetii

CLINICAL MANIFESTIONS

- Classic triad - fever, pharyngitis, lymphadenopathy
- Prodrome- malaise, anorexia, fatigue, headache, fever
- Symptoms usually peak 7 days after onset & ↓ over next 1-3 wks
- Splenic enlargement - 41-100%

- Less common clinical features
  - upper airway compromise
  - abdominal pain
  - rash (ampicillin ↑ risk of)
  - hepatomegaly
  - jaundice
  - eyelid edema

DIAGNOSTIC TESTING

- Serologic test for heterophil antibodies
- Percentage with antibodies higher > 4yrs old
- % of persons who are + at 1 week varies with test (1 study - 69% + at 1 wk; 80% + by 3 wks)
- False +s rare

- If heterophil antibody continues neg & still suspect;
  - serum for viral capsis antigen (VCA) IgG & IgM & for EBV nuclear antigen (EBNA) IgG
  - VCA antibodies + in many at onset

LABORATORY ABNORMALITIES

- Total leukocyte count ↑
- usually > 50% of total leukocytes consist of lymphocytes
- possible mild thrombocytopenia
- ↑ LFTs - 2-3-fold
- abnormalities on UA

IM IN OLDER ADULTS

- 3-10% of persons >40 are susceptible
- Presenting S & S different
- Fever present but few have pharyngitis & lymphadenopathy
- Jaundice in >20%
- R/O; hepatobiliary disease, neoplasms, collagen vascular diseases, bacterial infections

MANAGEMENT

- Supportive
- NSAIDs or tylenol - no ASA
- Bedrest during febrile stage
- If have splenomegaly avoid vigorous activity for 3-4 wks
- No evidence that steroids or antivirals are of benefit

CHRONIC FATIGUE SYNDROME

- Has been called: chronic EBV syndrome, postviral fatigue syndrome, "yuppie flu"
- 1988 CDC convened researchers & clinicians to define & classify CFS
- 1994 international group proposed guidelines for CFS
- CDC reported prevalence of 4-11 cases/100,000 population
- In US most cases occur in young to middle-aged white women

ETIOLOGY

- No cause identified
- Postulated
  - infective
  - neuromuscular
  - immunologic
  - neurologic
  - psychiatric

DIAGNOSTIC CRITERIA (PER CDC)

Fatigue criteria

- Must not be lifelong
- Must be persistent, relapsing & unexplained
- Must not be result of ongoing exertion & cannot be relieved by rest

Symptom Criteria

- Sore throat
- Short-term memory or concentration impairment
- Tender cervical or axillary lymph nodes
- Headaches of a new type, pattern, or severity
- Unrefreshing sleep
- Postexertional malaise lasting > 24 hrs
- Multijoint pain without joint swelling or inflammation
- Muscle pain

Exclusion Criteria

- Past or current diagnosis of major depression with psychotic or melancholic features, bipolar disorder, schizophrenia, delusional disorders, dementia, bulimia nervosa, anorexia nervosa
- Active medical conditions
- Previously diagnosed conditions with unclear resolution (malignancies, hepatitis B or C)
- Alcohol or substance abuse within 2 yrs of onset of fatigue
- Severe obesity (BMI $\geq$ 45)

- Detailed medical history
- Complete physical
- Labs
  - CBC
  - ESR
  - TSH
  - UA
  - Serum chem for electrolytes, BUN, cr, glucose, calcium, phosphorus, alk phos, total protein, albumen, globulin, LFTs

MANAGEMENT

Goal: Restore pts occupational & social functioning & prevent further disability.

- Guidelines
  - Establish diagnosis
  - Prevent further disability
  - If indicated, start medication ASAP
  - Warn about unproven therapies
  - Initiate psychological intervention

PHARMACOTHERAPY

- Antivirals
- Immunomodulators
- Psychotropic agents
- Pain medications
- Antiallergy medications
- Acetylcholinesterase inhibitors
- Agents used in alternative medicine

NONPHARMACOLOGIC TREATMENT

- Exercise
- Cognitive behavior therapy
- Self-help groups
- Work as therapeutic modality

DIFFERENTIAL

- Fibromyalgia
- Endocrine
- Chronic viral infections
- Malignancy
- Sleep disorders causing fatigue
- Connective tissue diseases
- Body weight changes
- Side effects of medications
- Other illnesses

PSYCHIATRIC CONDITIONS EXCLUDING CFS DIAGNOSIS

- Major depressive episodes
- Anxiety disorders
- Delusional disorders
- Bipolar disorder
- Schizophrenia
- Eating disorders
- Dementias
- Sleep disorders
- Substance use disorders

HERPES ZOSTER

- Represents reactivation of varicell-zoster virus
- Latently resides in a dorsal root or cranial nervie ganglia
- Multiple erythematous plaques with clustered vesicles
- Vesicles begin to dry & crust in 7-10 days, clear within 2-3 wks, new may continue to appear for up to 1 wk

COMMON DISTRIBUTION

- Thoracic dermatome 50%
- Cervical dermatome 20%
- Trigeminal dermatome 15%
- Lumbosacral dermatome 10%

PRESENTATION/DIAGNOSIS

- Prodrome
- Vesicular rash
- Diagnosis - presentation

Herpes zoster

Acute herpes zoster ophthalmicus

POTENTIAL COMPLICATIONS

- Trigeminal dermatome
  - may affect second branch associated with involvement of eye
    - keratitis, uveitis, secondary glaucoma, iridocyclitis
- Ramsay-Hunt syndrome
  - affects facial & auditory nerves
  - facial palsy with cutaneous zoster of external ear or TM, with associated tinnitus, vertigo, &/or hearing loss

TREATMENT

- Early treatment
  - within 48-72 hrs
- Acyclovir (Zovirax)
  - 800mg 3x/day
- Valacyclovir (Valtrex)
  - 1,000mg 3x/day
- Famciclovir (Famvir)
  - 500mg 3x/day

POSTHERPETIC NEURALGIA

- Famvir and Valtrex ↓ incidence
- Capsaicin cream (Zostrix 0.025% & Zostrix HP 0.075%) 4x/day
- Amitriptyline
- Gabapentin
- Often remits spontaneously after 6 months
- Pain referral