Zoonoses

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ZOONOSES

Infection diseases transmitted from animals to man (opposite transmission is also possible)

Causal organism:

- viruses
- bacteria
- parasites
- fungi
- prions

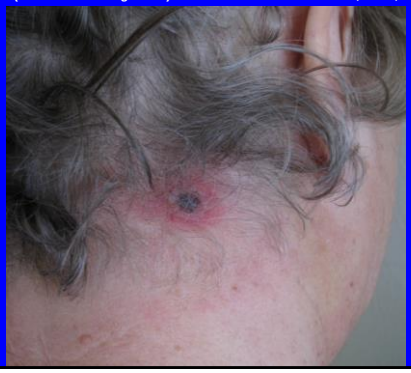
Most frequent zoonoses in CR

campylobacteriosis, salmonelosis, yersiniosis, toxoplasmosis, tularemia, EHEC,leptospirosis,listeriosis,ornithosis, toxocarosis, taeniasis, erysipeloid, cat scratch disease, Lyme disease, ehrlichiosis, tick-borne encephalitis, Q fever, hepatitis E (genotype 3)

NEW ZOONOSES

- virus Nipah (1999, Malaysia) –severe febrile encephalitis with high mortality in pig keepers
- New variant of Creutzfeldt-Jakob disease (vCJD) in human – relation to bovine spongiforme encephalopathy (BSE) in cattle (still is studied)
  The 1st case of BSE was in 1986 and the 1st case of vCJD in 1996
- Acute HE
  HEV genotypes 3 a 4 (transmission from pigs, boars, deer on man in non-endemic areas)
- TIBOLA (1996, Hungary) – new rickettsiosis, TIck-BOrne LymfAdenopathy, *Rickettsia slovaca*
- Enteroaggregative hemorrhagic E. coli (EAHEC) O104:H4 strain
  (2011, large outbreak in Germany)
- Novel coronavirus MERS-CoV (Middle East Respiratory Syndrome-Coronavirus)
  (2012, Saudi Arabia - in a patient who died of pneumonia and renal failure)
  transmission from camels
- Human infections with Highly Pathogenic Avian Influenza A (H7N9) Virus
  (since 2013 in China)

Tick-borne lymphadenopathy (TIBOLA). A 67-year old woman with an inoculation eschar with central necrosis, edematous margins and erythematous halo at the former site of the tick bite (*Dermacentor marginatus*). *BMC Infectious Diseases 2011;vol.11,art.no.167*



ZOONOSES – bioterrorism and biological weapons

- Anthrax (*Bacillus anthracis*)
- Plague (*Yersinia pestis*)
- Q fever (*Coxiella burnetti*)
- Tularemia (*Francisella tularensis*)
- Brucelosis (*Brucella abortus, B. melitensis, B. suis*)
- Glanders (*Burgholderia mallei*)
- Melioidosis (*Burgholderia pseudomallei*)
- Viral hemorrhagic fevers

Lyme disease (LD)

- Seasonal zoonosis
- Causal organism:
  Borrelia burgdorferi sensu lato
- Most often is affected:
  skin (65%)
  musculoskeletal system (17%)
  nervous system (12%)
  less other organs – heart (Lyme carditis)
  eye, or any other tissue in the body

B. burgdorferi sensu lato

Three main species:

- ***B. burgdorferi sensu stricto*** (mainly in America, in Europe has other antigens) – causes mainly affections of joints
- ***B. garinii*** (in Europe and Asia) – causes mainly affections of nervous system
- ***B. afzelii*** (in Europe and Asia) – causes mainly affections of the skin

Other species:

B. bavariensis – neurotropic as ***B. garinii,***
B. spielmanii, B. valaisiana, B. lusitanie

History of LD I.

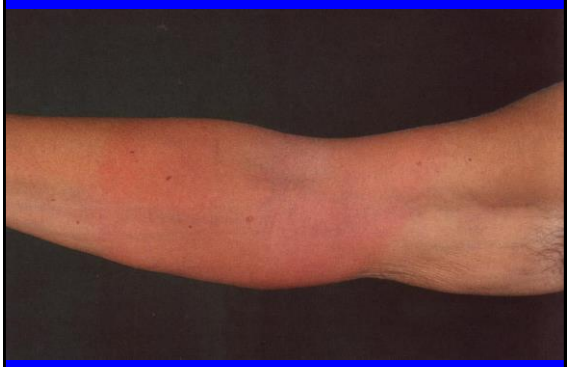
- 1883 Buchwald – acrodermatitis chronica atrophicans
- 1909 Artvid Afzelius – erythema migrans
- 1922 Garin and Bujadoux „paralyse par les tiques“
- 1941 Bannwarth – syndrome of meningopolyradiculoneuritis
- 1943 Bäferstedt – lymphadenosis benigna cutis

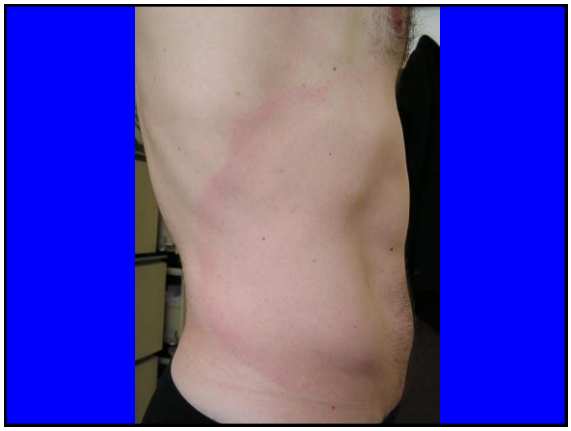
History of LD II.

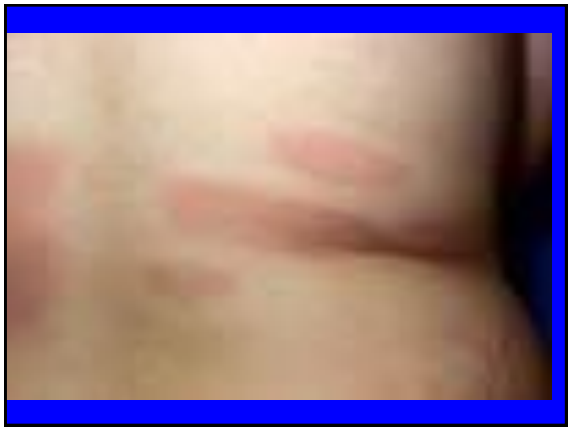
- 1947 Lehnhof – microscopic detection of spirochetes from skin biopsy of periphery of erythema migrans
- 1951 Hellström – PNC administration was effective on above-mentioned affections
- 1975 Steere – endemic arthrities in children in the area of the city Old Lyme (Connecticut, US)
- 1982 Burgdorfer – isolation of spirochaete from the gut of the tick *Ixodex dammini*
- 1984 *Borrelia burgdorferi* was marked as etiological agent of Lyme disease

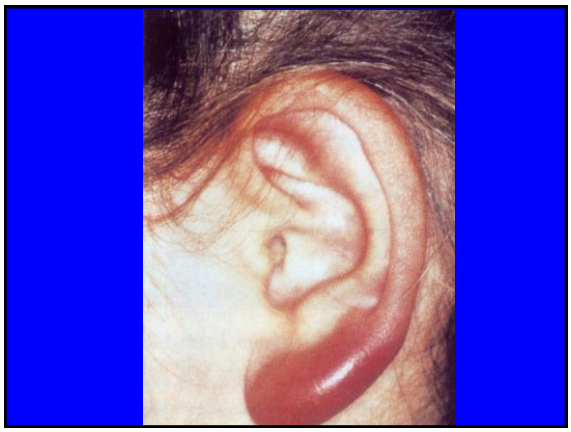
Clinical characteristics of LD

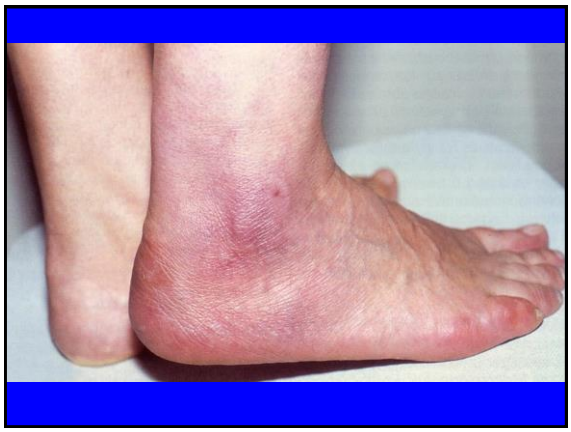
Stage	Incub. per.	Clinical manifestations
Early infection:		
1. Localized Infection	3-30 days (max. 8 weeks)	Erythema migrans
2. Disseminated Infection	Weeks-months	Erythema migrans multiplex Lymphadenosis benigna cutis Bannwarth syndrome (meningopolyradiculoneuritis) Lyme carditis (A-V blocades, myocarditis, pericarditis) Arthritis of small joints, tendovaginitis, myositis, bursitis
Late infection:	Months-years	Acrodermatitis chronica atrophicans
3. Persistent Infection		Neurological involvement (chron. encephalitis, chron. polyneuritis) Arthritis of large joint (e.g. gonitis)

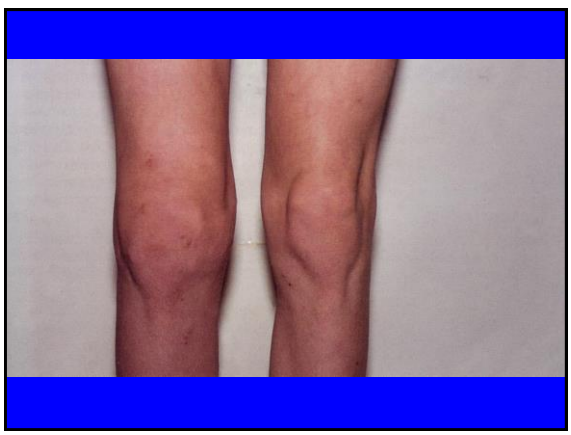




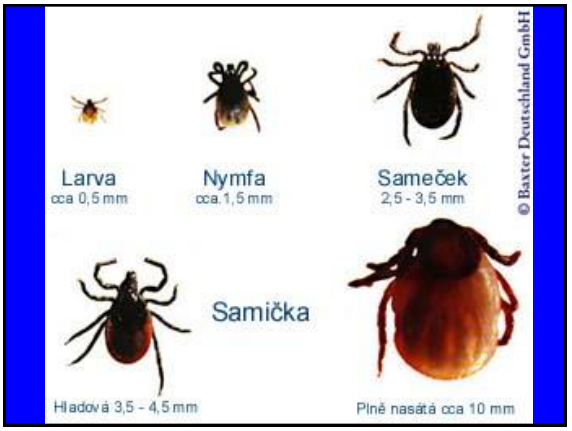








Tick *Ixodes ricinus*: larva – nymph – male – female (photo: Fedor Gassner)



Epidemiology of LD I.

- Reservoir of *B. burgdorferi:* small terrestrial mammals
- Transmission on human is by the ticks:
  in Europe *Ixodes ricinus*
  in America *I. scapularis* (*I. dammini*) and *I.pacificus*
- Risk of transmission increases with duration of sucking – 48 hours is enough time for transmission of infection from the infected tick

Epidemiology of LD II.

- Seroconversion (appearance of antibodies) after infected tick is only in 5-10% of persons. Not all of them have some clinical manifestations of LD
- Positive LD antibodies are detected in CR population cca in 10% (in forest workers more than 20%)
- Transmission from mother to foetus is possible
- Blood transfusion can transfer infection in case of borreliaemia in blood donor

LD and coinfection

- Contemporary occurrence of other disseases transmitted by ticks was registered in 10% of cases in the CR
- First of all human granulocytic anaplasmosis (ehrlichiosis) and other rickettsioses can be transferred simultaneously

Medicína po promoci 2005;6(8):20-27

Infections with possible transmission by the ticks in Europe

Etiological agent	Disease
TBE virus	Tick-borne encephalitis
B. burgdorferi sensu lato	Lyme disease
Rickettsia conori	Marseilles fever
Coxiella burneti	Q fever
Rickettsia slovaca	TIBOLA (tick-borne lymfadenopathy)
Anaplasma phagocytophilum	human granulocytic anaplasmosis (ehrlichiosis)
Bartonella henselae	Cat scratch disease
Francisella tularensis	Tularemia
Babesia microti	Babesiosis
Crimean-Congo hemorrhagic fever virus	Crimean-Congo hemorrhagic fever (cases in the last 10 years: Albania, Kosovo, Turkey, Greece, Ukraine, SW Russia, Bulgaria)

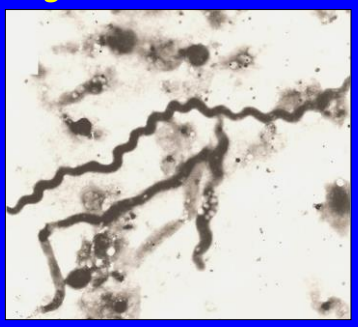
Diagnosis of LD I.

- ELISA and Western blot (WB) – detection of antibodies against antigen components of *B. burgdorferi*
- Production of IgM antibodies starts in the 3rd or 4th week after the primoinfection
- At the time of erythema migrans IgM antibodies are not usually produced
- IgM persists sometimes very long time and their detection has not to be a marker of the activity of infection
- It is always important to correlate laboratory and clinical findings!!
- Antibodies could be also negative and clinical finding is clear!!

Diagnostic of LD II.

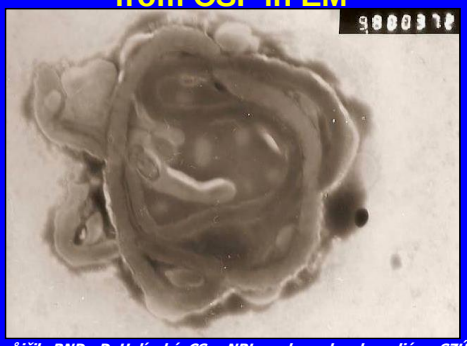
- PCR from CSF, urine, synovial liquid, sample from placenta, or from other medium
- Intrathecal production of antibodies from CSF
- Electronmicroscopy detection of *B. burgdorferi* mostly from CSF (not in routine practice in the CR)
- DNA microarrays = method of the future

B. burgdorferi from CSF in EM



Zapůjčila RNDr. D. Hulínská, CSc., NRL pro lymeskou borreliózu, SZÚ

Cyst (L-form) of *B. burgdorferi* from CSF in EM



Zapůjčila RNDr. D. Hulínská, CSc., NRL pro lymeskou borreliózu, SZÚ

Therapy of LD

Therapy is indicated only when clear clinical symptomatology is present and we are glad, if also laboratory findings are possitive

- Causal therapy = ATB
- Symptomatic treatment = analgetics, antiedematous therapy, vitamins, anxiolytics, antidepresives

Therapy of LD (Czech Guidelines 2018)

Antibioticum	Diagnosis	Duration of treatment (days)	Adults	Children
Administration per os				
Doxycycline[1]	Skin LD, NB, LA, LC	10-14	2x 100 mg nebo 1x 200 mg/d	4 mg/kg/d[1])
Amoxicillin[2]	Skin LD, LA, LC	10-14	3x 500-1000 mg/d	50 mg/kg/d
Fenoxymethylpenicillin[2]	EM, EMM, LBC	10-14	3x 1-1,5 mil. IU/d	80-100 000 IU/kg/d
Cefuroxim-axetil	EM,EMM,LBC,LA,LC	10-14	2x 500 mg/d	30 mg/kg/d
Azithromycin[3]	EM, EMM, LBC	5	1. day: 2x 500 mg 2.-5. day: 1x 500 mg	1. day: 20 mg/kg 2.-5.day: 10 mg/kg
Clarithromycin[3]	EM, EMM, LBC	10-14	2x 500 mg/d	15 mg/kg/d
Administration i.v.				
Ceftriaxon	NB, LA, ACA, LC	14-28	1x 2 g/d	50-75 mg/kg/d
Cefotaxim	NB, LA, ACA, LC	14-28	3x 1 g/d	150-200 mg/kg/d
Benzylpenicillin (penicillin G)	NB	14-28	4-5 mil. IU à 4-6 hod.	200-400 000 IU/kg/d

LD = Lyme disease, EM = erythema migrans, EMM = erythema migrans multiplex, LBC = lymphadenosis benigna cutis, LA = lyme arthritis, LC = lyme carditis, NB = neuroborreliosis
[1] doxycycline not in children younger than 8 years, not in pregnancy
[2] penicillin and amoxicillin not during nursing
[3] azithromycin and clarithromycin –prolongation of QT interval is possible and ventricular arrhythmia and ventricular tachycardia (type of torsade de pointes); azithromycin not in pregnancy

Repetition of the therapy

1. Reinfection
2. Relaps
3. Insufficient answer to the therapy

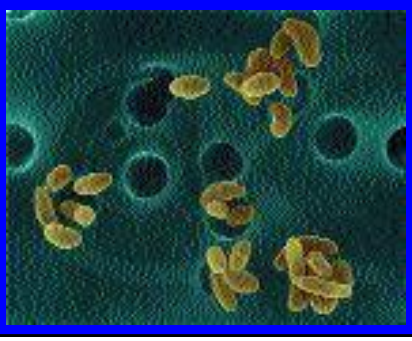
Repeat the therapy during 3 months is not indicated

Not more than 3x ATB treatment in one patient with LD!!!

Tularemia

- 1910 etiological agent was identified by Mc Coy as the agent of disease in sisels in the surroundings of the town Tulare in California
- 1914 Whery and Lamb – isolation this microbe from hares and possibility of transmission to human was pronounced
- 1921 E. Francis in USA - isolation the same microbe from blood and pus from the patients with „deer-fly-fever“ and the disease was named tularemia
- Etiological agent was named *Francisella tularensis*

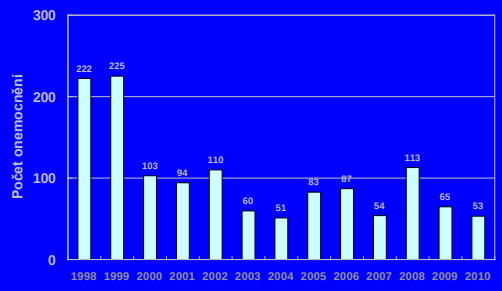
F.tularensis is G- cocobacillus, Francis agar is used for cultivation



Occurrence of tularemia in animals in CR – year 2009

New occurrence - red

A21 Tularémie



EPIDAT, SZÚ, Praha

Clinical manifestation of tularemia

- ***External manifestation***
  - **ulceroglandular**
  - **glandular**
  - **oroglandular (pharyngeal)**
  - **oculoglandular**
- ***Internal manifestation***
  - **pulmonal**
  - **abdominal**
- ***Sepsis* (generalization of infection)**
- **Combinations of external or internal manifestations**

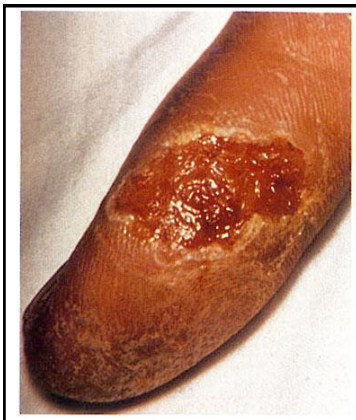
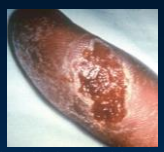


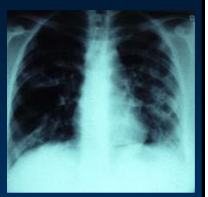
Fig. 165 Tularaemia. Irregular ulcer at the site of the initial lesion. In the common ulceroglandular form of tularaemia, caused by *Francisella tularensis*, there is an infected nodule at the site of inoculation which later ulcerates, with local lymph node enlargement. Courtesy of Dr T. F. Sellers, Jr.

Clinical Syndromes of Tularemia



atient with ulceroglandular tularemia

Cervical lymphadenitis in patient with pharyngeal tularemia



Chest radiograph of patient with pulmonary tularemia
(Radiograph shows bilateral pneumonitis and left pleural effusion)

CDC

Diagnostic of tularemia

- **We must evaluate:**
  epidemiologic case-history
  clinical picture
  and
  the results of serological examinations (aglutination, KFR)
- **Detection of specific antibodies is possible most often in the 3rd week of this disease**

Therapy of tularemia

- **ATB – most often doxycyclin + gentamicin**
- **Other ATB – spiramycin, fluofochinolons and rifampicin**
- **Duration of ATB treatment is 10 - 14 days**
- **Early treatment is very important**
- **Don´t wait for the results of serological examination!**
- **Extirpation of enlarged lymph nodes when ATB treatment is without effect**
- **Punction of enlarged lymph nodes is KI – danger of fistulas!!!**

Ulceroglandular form of tularemia

(extirpation of enlarged lymph nodes was done)

Toxoplasmosis

- Etiological agent *Toxoplasma gondii*
- Incubation period 5-20 days
- Definitiv host is cat and some other felidae.
- Sexual stage of the development of this parazite is in the the cat
- Human is inficated by the oocysts, that are in the excrements of cats
- Duration of excretion of oocysts is 2-3 weeks and is present only when the cat is inficated with *T. gondii* for the first time.

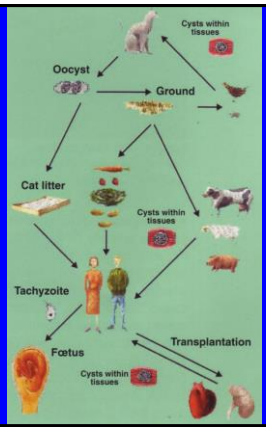
Toxoplasmosis

3 life forms of *T. gondii*:

- Tachyzoit – vegetative form
- Bradyzoit – this form ramains in the body for the whole life as tissue cysts
- Oocysts – they are very resistant and they are in the stool of the cat

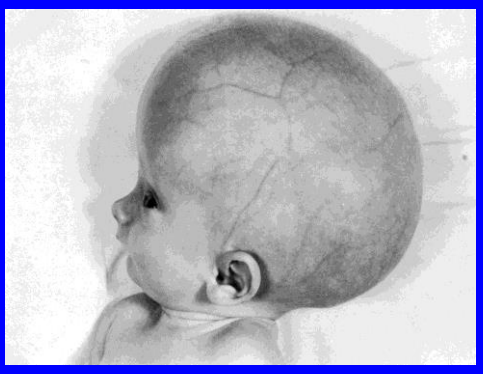
Toxoplasmosis – transmission of infection

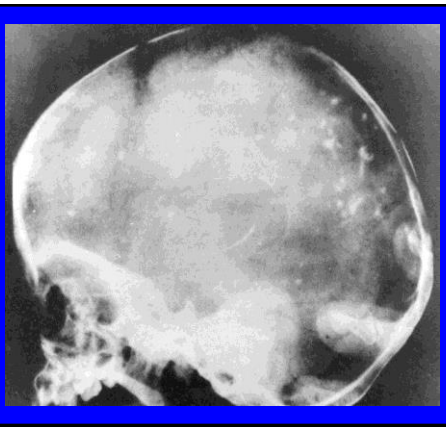
- Alimentary – consumation of raw or not good cooked meat, contaminated foodstuff or water
- Also is possible – geophagia, contact with contaminated soil or with animals
- Very rare – through the mucous of respiratory tract, urogenital tract, conjunctiva or damaged skin.
- Other modes: with blood transfusion, transplanted tissue, or in laboratory
- Transplacentar transmission leads to endouterine (congenital) infection. Danger of involvement the foetus is only when the primoinfection is in pregnancy or not longer than 6 months before the pregnancy



Toxoplasmosis clinical manifestations

- About 90% of infections are inaparent
- Implications of primoinfection in pregnancy: abortus, premature birth, birth of lifeless foetus. Typical changes in congenital toxoplasmosis = *Sabin trias* (hydrocephalus, calcifications in brain and chorioretinitis). *Sabin tetrade* = convulsions are present also
  Also is possible: microcephalia, microophthalmus, icterus, hepatosplenomegaly, atrophia n. optici, cataracta, strabismus, myocarditis, purpura, psychomotoric retardation, disorders with hearing or vision
- Most danger is primoinfection in pregnancy, not reactivation of chronic toxoplasmosis





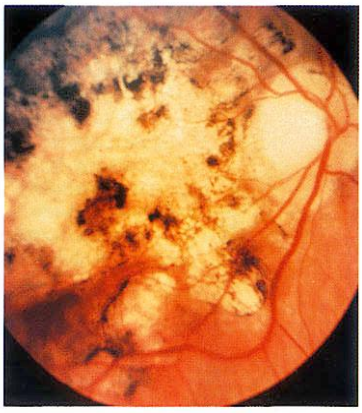
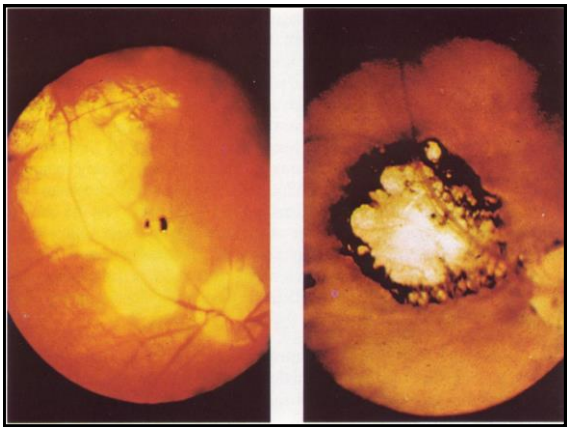


Fig. 158 Toxoplasmosis. Fundus photograph showing large areas of chorioretinitis with irregular scarring and pigmentation. Ocular toxoplasmosis is usually the result of congenital infection; infected infants may appear normal at birth but reactivation of the disease can produce chorioretinitis in later childhood or early adult life. The appearance is diagnostic, with a focal destructive chorioretinitis which leaves well-defined, heavily pigmented scars.



Toxoplasmosis – clinical manifestations

- **Only 10-20% infections are symptomatic and the most often manifestation is enlargement of lymph nodes. Toxoplasmosis is also the most often cause of the enlargement of lymph nodes in the CR. We do not treat it in immunocompetent patients.**
- **Involvement of eyes – it is acute chorioretinitis, most often only on one side**
- **Involvement of other organs (rarely) - hepatitis, myocarditis, pneumonitis**
- **Septic form with the involvement of different organs including CNS in the patients with immunosuppression or immunodeficiency**

Toxoplasmosis - diagnostics

- **Serological detection of antibodies using at least two methods: KFR and ELISA (IgG, IgM, IgA and IgE)**
- **Avidity of IgG antibodies (low values – primoinfection)**
- **Detection of DNA of *Toxoplasma gondii* from amniotic fluid using PCR method**
- **Western blot**

Toxoplasmosis - therapy

We treat:

- Pregnant women with acute infection
- Children with congenital infection
- Patients with organ involvement (eyes or other)
- Acute toxoplasmosis in immunocompromised persons
- Children until 5 years of the age

We don´t treat asymptomatic infection in immunocompetent adults

Therapy of toxoplasmosis

- Duration of the therapy: 3-4 weeks
- We use:
  pyrimethamin + sulfadiazin
  or
  pyrimethamin + clindamycin
- Patients with involvement of eyes:
  moreover corticosteroids
- KI of pyrimethamin: to 16.-18. week of gravidity
- We combine pyrimethamin with acidum folinicum (Leucovorin) to reduce myelotoxicity of pyrimethamin

Therapy of toxoplasmosis in pregnancy

- We use:
  spiramycin
  or
  pyrimethamin + sulfadiazin
- Therapeutic schema:
  rotation of usage 3 weeks spiramycin and next 3 weeks pyrimethamin + sulfadiazin
- KI of pyrimethamin: the 1st trimestr of gravidity
- KI of sulfadiazin: the 1st trimestr of gravidity and the last 4-6 weeks before the birth

Cerebral form of toxoplasmosis

- Great oportunic infection in HIV+
- It is reactivation of latent infection
- Therapy: pyrimetamin + sulfadiazin or pyrimethamin + clindamycine
- Duration of the therapy 6 (4-8) weeks
- Antiedematic therapy:
  5 days dexamethazon i.v.

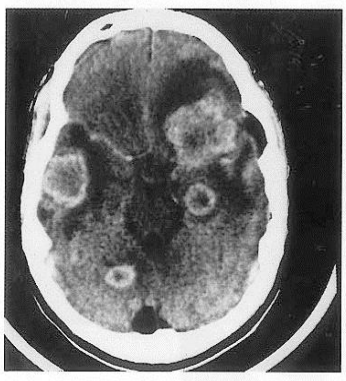


Fig. 42 Cerebral toxoplasmosis. CT scan showing multiple ring-enhancing hypodense lesions, in the left frontotemporal, right temporal, right occipital and left uncal regions, with surrounding cerebral oedema. Toxoplasma encephalitis is the most common opportunistic infection of the central nervous system in patients with AIDS.

Prevention of cerebral form of toxoplasmosis

- *Primary prophylaxis* when is decrease of CD4+ below 100-150/µl – cotrimoxazol 3x960 mg/week or 1x480 mg/day
- *Secundary prophylaxis* after the cerebral form of toxoplasmosis:
  pyrimethamin
  or
  pyrimethamin + sulphadiazin
  or
  pyrimethamin + clindamycin

Cerebral form of toxoplasmosis

- No or bad treated – always is fatal
- Serological tests are not very useful (helpful) in HIV+ patients:
  - we do not detect strong changes in the level of antibodies,
  - IgG is +, but not pronounced,
  - IgM is mostly negative