# **Toxoplasmosis – Laboratory Diagnosis, Investigation, Treatment and Management (incl. Pregnancy)**

## **1. Infectious Agent and Lifecycle**

* *Toxoplasma gondii* – obligate intracellular protozoan (Apicomplexa).
* Forms:
  + **Oocysts** - shed in cat faeces; infectious after sporulation.
  + **Tachyzoites** – rapidly replicating; cause acute disease.
  + **Bradyzoites** in tissue cysts – latent infection (brain, muscle, eye).
  + **Gametocytes** – sexual reproduction in definitive host (cat).
* Transmission:
  + Ingestion of oocysts from contaminated food/water/soil, cat litter.
  + Ingestion of tissue cysts from undercooked meat.
  + **Vertical**: maternal–fetal during primary maternal infection.
  + Rare: organ transplantation, transfusion.

## **2. Clinical Manifestations**

**Immunocompetent**: Often asymptomatic; may present with fever, lymphadenopathy, myalgia.

**Immunocompromised (e.g. HIV, transplant, chemotherapy)**: Severe encephalitis, chorioretinitis, myocarditis, pneumonia, disseminated infection (often reactivation).

**Pregnancy**:

* Transmission risk increases with gestation (15% 1st trimester → 70% 3rd).
* Severity decreases with gestation (early infection → severe CNS/ocular damage; later infection → often subclinical at birth, but may cause delayed sequelae).
* **Congenital toxoplasmosis**: Hydrocephalus, intracranial calcification, chorioretinitis, developmental delay; may present at birth or later.

## **3. Specimens for Diagnosis**

**Fluids**: Blood, CSF, BAL, vitreous/aqueous humour, urine, pleural, peritoneal, ascitic fluid.

**Tissue**: Placenta, fetal tissue, lymph node, brain, skeletal/cardiac muscle, eye.

## **4. Laboratory Diagnosis**

### **Serology (Mainstay)**

* **IgG**: Appears within 1–2 weeks, peaks ~8 weeks, persists lifelong. Negative = no prior infection (but beware early acute or severe immunodeficiency).
* **IgM**: Appears within 1 week of infection, but may persist months–years. Negative essentially rules out recent infection (<6 months). False positives occur.
* **IgA/IgE**: Useful markers of acute infection, esp. in pregnancy; disappear sooner than IgM.
* **IgG avidity**:

High avidity → infection >12–16 weeks earlier.

Low/equivocal avidity can persist months; not definitive.

**Specialist tests**:

* Sabin–Feldman dye test (IgG; reference only).

**Key principle**: Interpretation requires **combination of tests**; reference laboratory consultation essential in pregnancy/immunocompromised.

### **Direct Detection**

* **PCR**:

Detects *T. gondii* DNA in fluids/tissues.

High specificity (~100%), sensitivity variable (blood 15–85%, CSF 11–77%).

Amniotic fluid PCR (≥18 wks GA, ≥4 wks post maternal infection) confirms congenital infection.

May detect DNA from latent organisms.

* **Microscopy/Histology**:

Tachyzoites in tissue/fluids diagnostic.

Tissue cysts, esp. with inflammation, also significant.

Giemsa/Wright stains; IHC increases yield.

* **Culture**:

Isolation via mouse inoculation or tissue culture; rarely used in routine labs.

* **Radiology**:

CNS: MRI > CT; multiple ring-enhancing lesions with oedema (esp. thalamus, grey–white junction).

Congenital: intracranial calcification, ventriculomegaly, hydrocephalus.

Chest CT: ground-glass opacities, nodules.

* **Other lab findings**:

↑ LDH (esp. pulmonary toxoplasmosis in AIDS).

CSF: high protein (>500 mg/dL) in congenital; PCR useful.

Peripheral eosinophilia absent (differentiates from helminthic infections).

## **5. Investigations in Pregnancy / Neonates**

**Maternal**:

Screen: IgG + IgM.

IgM+/IgG– → repeat to confirm acute infection.

IgM+/IgG+ → perform avidity testing.

**Fetal**:

Amniotic fluid PCR (after 18 wks).

Serial US: ventriculomegaly, hepatosplenomegaly, growth restriction.

**Neonate**:

Serology: IgM/IgA, persistence of IgG >12 months.

Cranial US/MRI, ophthalmology, CSF.

## **6. Treatment Principles**

**Only tachyzoites are killed**; bradyzoites persist.

Drugs block **folate metabolism**, so folinic acid needed.

### **Key Drugs**

* **Pyrimethamine**: Loading 200 mg PO, then 50–75 mg/day.

Side effect: marrow suppression → folinic acid required (10–25 mg/day).

*Do not substitute folic acid*.

* **Sulfadiazine**: 1–1.5 g QID PO (max 4 g/day in pregnancy).
* **Folinic acid (leucovorin)**: Prevents marrow toxicity.
* **Clindamycin**: 600 mg QID PO/IV if sulfa-allergic.
* **Atovaquone**: Alternative agent.
* **TMP-SMX**: Effective, especially for prophylaxis in HIV.

## **7. Treatment by Clinical Context**

### **Immunocompetent**

Often self-limiting; no Rx unless:

Ocular disease, myocarditis, hepatitis, encephalitis.

Severe/persistent disease.

Rx: pyrimethamine + sulfadiazine (or clindamycin) × 2–4 wks.

### **Immunocompromised**

**Acute CNS/pulmonary disease**: pyrimethamine + sulfadiazine + folinic acid.

Alternatives: pyrimethamine + clindamycin; atovaquone.

Empiric therapy often started in HIV with low CD4 and suggestive MRI.

If no response in 10–21 days → brain biopsy.

Rx duration: ≥6 wks then maintenance until immune recovery.

**Prophylaxis**: TMP-SMX (also covers *Pneumocystis*).

HIV: if CD4 <100 and IgG positive.

Transplant: protocol dependent.

### **Pregnancy**

**Maternal infection**:

Spiramycin (1 g PO q8h) until delivery if no confirmed fetal infection.

Reduces transmission (esp. <14 weeks).

**Confirmed fetal infection (PCR+, abnormal US, >14 wks GA)**:

Pyrimethamine + sulfadiazine + folinic acid.

Pyrimethamine avoided <12–14 wks (teratogenic).

Alternate: monthly alternating spiramycin and triple therapy.

**HIV-positive pregnant women**: specialist consultation, as reactivation risk higher.

### **Congenital infection (neonate)**

**Pyrimethamine + sulfadiazine + folinic acid** for 12 months.

Monitor: CBC, ophthalmology, neuroimaging, development.

## **8. Prevention**

* **Food safety**:

Avoid raw/undercooked meat (cook >67 °C, freeze –20 °C × 48h).

Wash fruit/veg.

Avoid unpasteurised goat milk, raw shellfish.

* **Cat/litter precautions**:

Avoid handling litter/soil; use gloves.

Clean litter daily; oocysts need 1–5 days to sporulate.

* **Counselling**:

Pregnant & immunocompromised should be warned if seronegative.

* **Screening**:

**Not routine in UK** (per UK NSC).

Some European countries (e.g. France, Austria) have antenatal screening.

## **9. Summary Table**

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| **Situation** | **Investigation** | **Treatment** |
| Maternal suspected acute infection | IgM/IgG,  IgG avidity;  repeat serology | Spiramycin until delivery (if fetus not infected) |
| Confirmed fetal infection (PCR+) | Amniotic fluid PCR, serial US | Pyrimethamine + sulfadiazine + folinic acid (>14 wks GA) |
| Neonatal congenital toxoplasmosis | Serology,  imaging, ophthal. exam | Triple therapy × 12 months |
| Immunocompromised (CNS, disseminated) | PCR (blood/CSF), MRI, serology | Pyrimethamine + sulfadiazine + folinic acid; alternatives as above |
| Prophylaxis | Serostatus, CD4 count (HIV) | TMP-SMX |