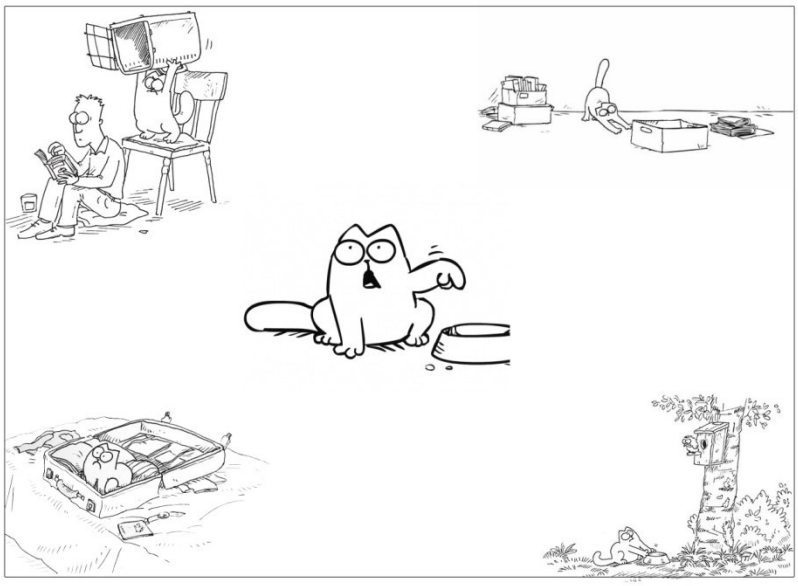
TOXOPLAMOSI I L'EMBARÀS

(o "Quan les dones tenen gats")



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1. INTRODUCCIÓ

Primer dia del nostre nou curs. Per fi cinquè, una fita que "no fa gaire" semblava inabastable, i malgrat tot aquí estem, asseguts de nou amb els nostres companys de sempre, alguns de nous i altres que s'han anat quedant pel camí...

Ens trobem davant de noves assignatures, nous petits reptes que una vegada més haurem de superar i que encara que sembli impossible ho farem, com fins ara, com sempre.

Dia de presentacions, entre elles es troba la assignatura que ara ens porta a escriure aquestes lletres; Deontologia Veterinària. El primer que se'ns planteja es que hem de fer un treball de tema obert sobre alguna cosa que tingui a veure amb la matèria. I el primer que a nosaltres ens ve al cap es que hem de fer un altre treball (un de tants...) que ens traurà hores i hores del nostre escàs temps lliure, i a de més, com podem fer un treball d' una assignatura la qual fa poc que hem descobert que no és el mateix que Odontologia Veterinària!!!

En resum, comença l'estrès de nou; benvinguts a Veterinària!!

La bona noticia era que el treball no s'havia d'entregar fins a finals de gener; així que passat l'estrès momentani, tornem a respirar. Fins avui que ja estem a meitat de desembre i tot just em triat el tema.

Així que sense més divagacions ens posarem de dret al treball e intentarem aclarir tot el que ens sigui possible a veure si aconseguim que la gent canvi la seva percepció sobre el tema. Què quin tema? (es veritat quin despiste), el nostre treball va sobre la TOXOPLASMOSI.

La veritat és que no ens va resultar difícil triar la Toxoplasmosi ja que és un tema que ens inquieta i ens preocupa bastant a tots els integrants del nostre grup. Ens preocupa sobretot en la mesura en que és un motiu (nosaltres ho considerem una excusa com qualsevol altre) molt important d'abandonament d'animals de companyia, situant-se el gat a la capçalera i amb diferència.

Tot i que som conscients de què ens serà dificultós trobar informació valida per realitzar un bon treball, ens hem arriscat a intentar-ho, perquè el sol fet de pensar que el nostre treball pot canviar el pensament d'alguna persona, i poder

salvar en conseqüència alguns dels nostres amics felins, ens recompensarà tot l'esforç invertit.

Intentarem, doncs, fer arribar a tothom la veritat d'aquesta malaltia i que la gent es conscienciï de que la solució no passa per desfer-se de la nostra mascota, tal i com molta gent fa, ja sigui per ignorància o per mala informació.

2.TOXOPLASMOSI

La toxoplasmosi és una malaltia parasitària que pot ser de transmissió directa o indirecta. Afecta a gran part de mamífers i també s'ha descrit en aus. Té una gran importància sanitària ja que és zoonosi. També té importància econòmica ja que pot produir avortaments en animals de renda, sobretot en petits remugants.

La prevalença varia en funció de les espècies.

Espècie	Prevalença
Oví adult	46%
Vacum	44.8%
Porcí	52%
Caprí	64%
Conill	70-72% (USA) 68% (França) 90% (Txecoslovaquia)
Èquids	20%
Gos	48%
Aus	42.9%
Humans	45-48%
Gat	45%
Gat (oocists)	<1% (USA)

2.1 ETIOLOGIA

L'agent etiològic de la toxoplasmosi és Toxoplasma gondii. Com a hostes definitius trobem el gat i alguns felins salvatges, i com a intermediaris tots els mamífers (inclosos els definitius, els quals també poden actuar com a intermediaris) i algunes aus. Tot seguit es descriuran breument les diferents formes del paràsit segons l'hoste on es trobin.

Hoste definitiu: Quan el gat funciona com a hoste definitiu elimina per les femtes gran quantitat d'oocists sense esporular molt petits (10-12 µm). Aquests oocists esporulen al medi segons un patró d'esporulació de 2 esporocists amb

4 esporozoïts cadascun. Els oocists esporulats són molt complicats de trobar en femta.

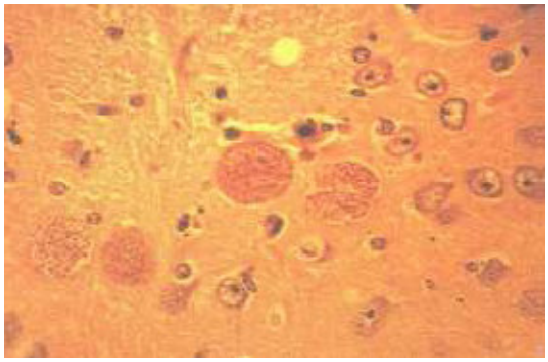
Hoste intermediari: Quan un hoste intermediari s'infecta de seguida apareix el paràsit

en forma de taquizoits (5-6 x 2-3 µm) en molts tipus cel·lulars diferents (fetge, cor, macròfags,…teòricament poden estar a qualsevol teixit) . Aquests taquizoits s'agrupen en unes estructures anomenades pseudoquists (15-30 µm) , tot i que de vegades poden aparèixer lliures.

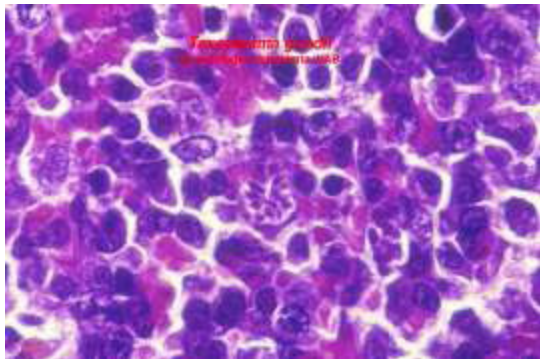
Al cap de 7-10 dies la immunitat de l'hoste intermediari comença a actuar (de seguida hi ha anticossos), per la qual cosa els paràsits comencen a reproduir-se més lentament. A partir d'aquí s'anomenen bradizoïts i són molt semblants morfològicament als taquizoïts. Aquests bradizoïts també poden trobar-se en qualsevol cèl·lula de l'organisme (inclòs teixit nerviós i múscul), tot i que solen aparèixer més freqüentment en cèl·lules amb una elevada activitat metabòlica i mitòtica.

Els bradizoïts estan inclosos dins dels quists (60-100 µm). A cada quist hi ha entre 50.000 i 60.000 bradizoïts. Aquesta és la fase latent o crònica de la malaltia i tant el paràsit com l'hoste intermediari poden romandre en aquest estat durant tota la vida de l'hoste, tot i que depenent de l'espècie aquest últim pot arribar a eliminar completament el paràsit. Per exemple, en el cas dels petits remugants la infecció

persisteix durant tota la vida de l'hoste, mentre que en el cas del bestiar vacú la infecció acostuma a desaparèixer al cap de 2 o 3 anys.



Quists plens de bradizoïts a teixit nerviós.



Pseudoquists plens de taquizoïts

Així doncs tenim les següents formes de Toxoplasma gondii:

Hoste definitiu

- Oocists

Hoste intermediari

- Pseudoquists – Taquizoïts
- Quists – Bradizoïts

Oocist

2.2 **CICLE BIOLÒGIC**

El cicle biològic de Toxoplasma gondii és força complex, ja que presenta diversos tipus de transmissions:

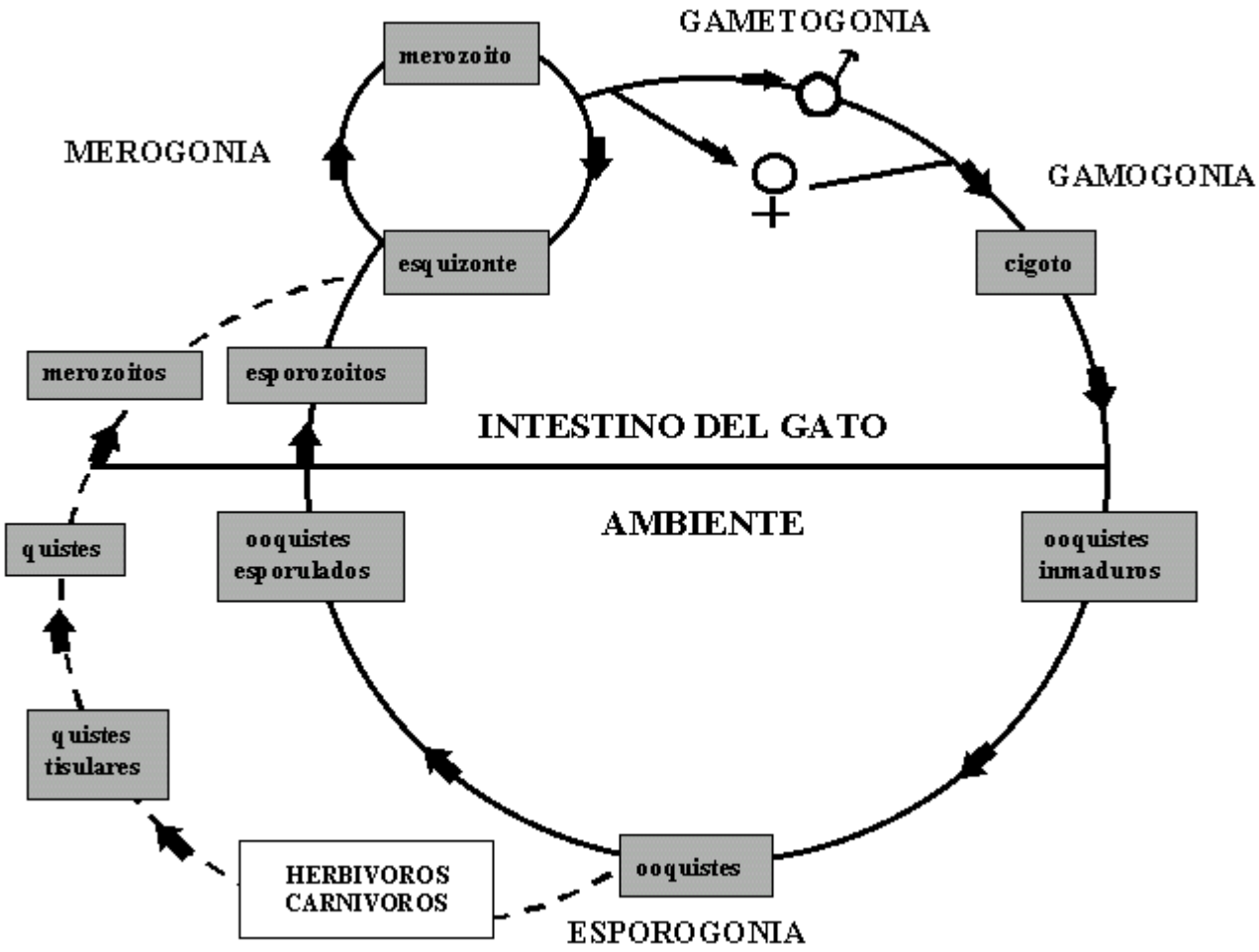
- D'hoste definitiu a hoste definitiu (HD ↔ HD) – Cicle directe
- D'hoste definitiu a hoste intermediari (HD → HI) – Cicle indirecte
- D'hoste intermediari a hoste definitiu (HI → HD) – Cicle indirecte
- D'hoste intermediari a hoste intermediari (HI ↔ HI)
- Transmissió vertical

Una de les raons per la qual Toxoplasma gondii està tan estès és el fet de que es transmeti entre hostes intermediaris (hoste intermediari ingereix quists de teixits d'un altre hoste intermediari). És un dels pocs paràsits capaç de fer-ho.

Abans de començar a explicar el cicle, cal recordar que el gat i alguns felins són els únics hostes definitius coneguts però poden comportar-se també com a intermediaris. Quan parlem d'hostes definitius ens referirem al gat o als felins en exclusiva. Quan parlem d'hostes intermediaris farem referència a qualsevol mamífer inclòs el gat. És a dir, el que es digui sobre hostes intermediaris servirà també per al gat.

Cicle

Comença quan un hoste definitiu elimina oocists sense esporular a través de les seves femtes. Un cop al medi, si les condicions de temperatura i humitat són les idònies, els oocists esporulen en 4-5 dies aproximadament (2 esporocists amb 4 esporozoïts cadascun).



Ara poden passar dues coses:

1) Els oocists esporulats són ingerits per un hoste intermediari (HD → HI)

En aquest cas es dóna un cicle intraorgànic en qualsevol tipus cel·lular. Es produeix una multiplicació ràpida per endodiogènia que donarà lloc a multitud de taquizoïts lliures i/o inclosos en pseudoquists (fase "aguda" de la infecció). Quan comenci a actuar la immunitat de l'hoste, es multiplicaran lentament i apareixeran els quists plens de bradizoïts (infecció latent o crònica).

Ara el primer hoste intermediari té els teixits plens de quists. Un cop més poden passar dues coses:

a) Hoste intermediari: Sí és un segon hoste intermediari el que ingereix teixits amb quists, es tornarà a produir el cicle d'hoste intermediari ja explicat (HI↔ HI). L'única diferència és que en comptes d'infectar-se per ingestió d'oocists esporulats, s'infecta per ingestió de bradizoïts o taquizoïts. Aquesta és la principal via d'infecció a l'home.

b) Gat: Si un gat ingereix els teixits infectats es comportarà com a hoste definitiu o hoste intermediari en funció del seu estat immunitari:

- El gat està immunodeprimit (HD): El gat té una malaltia immunosupressora (FIV), és

vell, és molt jove (encara no ha tingut contacte amb la malaltia), etc. Llavors actuarà com un hoste definitiu, patirà un cicle coccidià típic a l'intestí i eliminarà oocists per femta. Quan el gat actua com a hoste definitiu elimina molts més oocists quan s'ha infectat per bradizoïts que quan ho ha fet per oocists esporulats (punt 2). El més freqüent és que siguin gatets petits els que es comportin com a hostes definitius perquè encara no han tingut contacte amb la malaltia. Mentre la seva immunitat no actuï, eliminaran oocists i es comportaran com a hostes definitius. Ara bé, Toxoplasma gondii és un paràsit molt immunogen, i en quan comenci a actuar el sistema immune, el gat passarà a ser un hoste intermediari amb els teixits infestats de quists amb bradizoïts. També podria donar-se el cas de que un gatet s'infectés durant la gestació i actués com a hoste definitiu al néixer. Això, però, no és gaire freqüent (hauria d'infectar-se durant l'últim terç de la gestació).

- El gat té un estat immunitari correcte (HI): Actuarà com un hoste intermediari. El que passa és el que hi ha explicat al punt 1, apartat a.

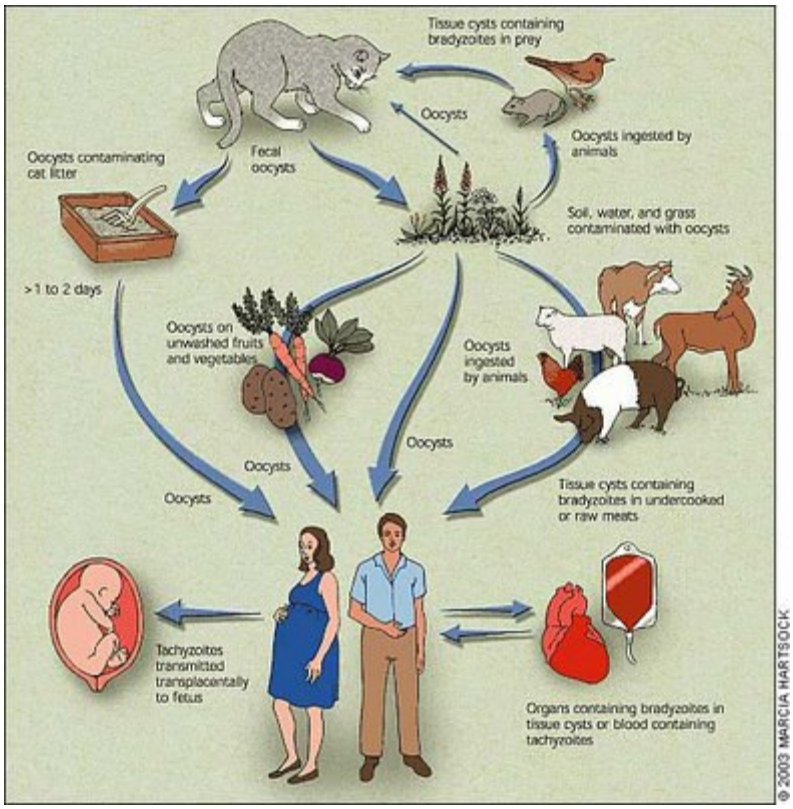
2) Que els oocists esporulats siguin ingerits per un gat

Quan un gat ingereix els oocists esporulats es comportarà com a hoste definitiu o intermediari en funció del seu estat immune.

Transmissió vertical o transplacentària:

A les femelles gestants de qualsevol espècie (hostes intermediaris i definitius) els taquizoïts poden travessar la barrera placentària i arribar al fetus. Pot provocar avortaments i malformacions.

Així doncs, una femella pot infectar-se durant la gestació, o bé que durant la gestació es reactivi la infecció latent. En ambdós casos, els taquizoïts estaran presents al seu organisme i podran travessar la placenta.



En resum:

<u>Hostes intermediaris</u>

Qualsevol mamífer i algunes aus poden actuar com a hostes intermediaris. Aquests s'infecten per ingestió d'oocists esporulats eliminats per un hoste definitiu (gat) o per ingestió de bradizoïts presents en els teixits d'altres hostes intermediaris.

Independentment de la forma d'infecció, el cicle del paràsit serà el d'un hoste intermediari que culminarà amb la instal·lació dels quists plens de bradizoïts a qualsevol teixit de l'organisme.

El gat també pot actuar com a hoste intermediari.

<u>Felins</u>

Són els únics hostes definitius coneguts. Poden infectar-se per ingestió de:

· Oocists esporulats – Eliminats per un hoste definitiu

· Pseudoquists plens de taquizoïts – Presents als teixits d'un hoste intermediari

· Quists plens de bradizoïts – Presents als teixits d'un hoste intermediari

Independentment de la forma d'infecció, es comportarà com a hoste intermediari o definitiu en funció del seu estat immunitari (bon estat immune: hoste intermediari, mal estat: hoste definitiu). Cal recordar que un individu pot passar de comportar-se com un hoste definitiu a un intermediari i al inrevés en

funció de l'estat immunitari. És a dir, si un animal s'infecta en un moment immune desfavorable, segurament actuarà com a hoste definitiu. Quan recuperi l'estat immune adequat, es comportarà com hoste intermediari. També pot donar-se el cas contrari en el que un gat que es comporta com a intermediari passi a comportar-se com a definitiu per una immunosupressió de qualsevol tipus. Això és perquè el paràsit varia el seu cicle en funció d'aquest estat immune. O millor dit, més que variar el cicle, el que fa és "triar" una via o una altra. Si es comporta com a intermediari el paràsit pateix un cicle normal a l'hoste intermediari que culmina amb els quists, i si es comporta com a hoste definitiu, pateix un cicle coccidià típic que culmina amb l'eliminació d'oocists esporulats per femta.

2.3 EPIDEMIOLOGIA

- Resistència dels oocists (HD):

És un factor molt important epidemiològicament. A més a més de la resistència dels oocists, cal tenir en compte que altres factors poden influir en la seva disseminació, com ara l'aigua, el vent o animals (cucs de terra, paneroles, mosques).

Medi/Factor extern	Durada dels oocist
Aigua	9-24 mesos
Dessecació	24 hores
Femta de gat	17 mesos
Formol (1%)	7 dies
Temperatura 70ºC	10 minuts

- Resistència dels quists (HI)

Els quists són sensibles a la dessecació, per aquest motiu els productes carnis dessecats són relativament segurs pel que fa a la toxoplasmosi.

Un altre factor important a tenir en compte és el temps que resisteixen les temperatures a les quals es cuinen les peces de carn. És important que tots els punts de la peça assoleixin la temperatura indicada a la taula. Sovint els temps

de cocció hauran de ser superiors per a que a la part més interna de la carn també arribi a la temperatura correcta.

Els hostes intermediaris poden estar parasitats durant molt de temps, sovint durant períodes superiors a un any, però també hi ha individus que poden mantenir la infecció latent durant tota la seva vida.

Els bradizoïts (quists) resisteixen els sucs gàstrics. En canvi els taquizoïts no sobreviuen als àcids de l'estómac.

Medi/Factor extern	Durada dels oocist
Temperatura 60ºC	20 minuts
Temperatura -20ºC	15 dies
Hoste intermediari	>1 anys

2.4 VIES D'INFECCIÓ

Toxoplasmosi adquirida:

1) Oral: És la via d'infecció més freqüent i per tant la més normal i important.

- Ingestió d'oocists esporulats
- Ingestió de quists
- Ingestió de pseudoquists – Es destrueixen amb els sucs gàstrics.

2) Respiratòria:

- Inhalació d'oocists – Els oocists transportats pel vent poden ser inhalats. De totes maneres, per a que es produeixi la infecció, els oocists han d'arribar obligatòriament a l'aparell digestiu.

3) Sanguínia:

- Inoculació a través d'artròpodes, utilització d'agulles contaminades...
- Transfusions de sang

4) Sexual:

S'han descrit casos en humans. També s'ha observat la presència del paràsit al semen de boc, però per a que la femella s'infectés, la mucosa de la vagina hauria de presentar discontinuïtats.

5) Contacte directe:

Entre hostes intermediaris és molt difícil i entre hostes definitius, degut a que el gat és un animal molt net, també és difícil que es produeixi aquest tipus de transmissió (si els oocists es quedessin al pèl del gat, trigarien 4-5 dies a esporular i en aquest període de temps el gat ja s'hauria netejat).

És fàcil contraure la malaltia a través del contacte amb animals avortats.

Toxoplasmosi congènita:

És la que es transmet transplacentàriament.

2.5 PATOGÈNIA

Factors

-Espècie animal: Els hostes intermediaris principals són els petits remugants i els humans. En petits remugants produeix moltes alteracions, sobretot la forma congènita. Pel que fa a èquids i bòvids, gairebé mai tenen la malaltia. En gos i gat és més freqüent i acostuma a afectar al sistema nerviós.

- Via d'infecció: La forma congènita és la que produeix més alteracions.
- Paràsit: Hi ha soques més patògenes que d'altres. Amb les poc patògenes poden elaborar-se vacunes.
- Nombre de paràsits: Com més elevada és la càrrega parasitària, més greu és la malaltia.
- Època de gestació

Mecanismes

- Multiplicació: Al multiplicar-se, el paràsit provoca alteracions que poden anar des d'una inflamació fins a una necrosi.

Per a dividir-se utilitza àcids nucleics de la cèl·lula hoste, provocant alteracions cromosòmiques (poden produir mongolisme, per exemple).

Durant la multiplicació, Toxoplasma gondii produeix una substància tòxica anomenada

toxoplasmina.

2.6 SÍMPTOMES

Forma adquirida:

La simptomatologia de la forma adquirida de toxoplasmosi és molt variable ja que depèn en gran mesura de la localització del paràsit. La majoria de vegades, però, és subclínica i no presenta símptomes. Els quadres simptomàtics es donen sobretot en animals joves.

- Hipertèrmia – 40-41 ºC.
- Alteracions dels limfonodes
- Mort: en garrins i lludrigons

· En el gos:

- Símptomes digestius – vòmits, diarrea, anorèxia, …
- Símptomes respiratoris – dispnea,…
- Símptomes nerviosos – convulsions, parèsia, paràlisi, atàxia (sobretot de les extremitats),…

· En el gat:

- Símptomes oculars (més del 75% dels gats) – com uveïtis, corioretinitis,…

Forma congènita:

És la forma més greu i important. Les espècies més importants són els petits remugants i l'home. En conill també és important (però menys) perquè produeix avortaments. Després trobem el porc i els bòvids, on és menys important. En èquids és on la malaltia té menys importància.

· Fase d'implantació:

- Mort
- Reabsorció; en aquests casos no s'observen signes de malaltia, només problemes de fecunditat en la mare (En realitat no es veu l'avortament perquè és tan petit que el cos el reabsorbeix i només es veu una irregularitat en la fecunditat de la mare).

·50-60 dies de gestació:

- Mort
- Expulsió
- Retenció

- Momificació del fetus

· 60-120 dies de gestació:

- Mort – Pot produir-se, però no sempre.

- Avortaments – Si es produeixen són edematosos, necrosats,…

- Parts prematurs; en el cas de que no hagin mort. Els animals neixen dèbils i gairebé tots moren.

- Retenció de placenta: Provoca infeccions, metritis sèptiques, piometres,…

·Últim mes de gestació:

- Animals clínicament sans però sempre parasitats

- En humans són freqüents les afeccions oculars

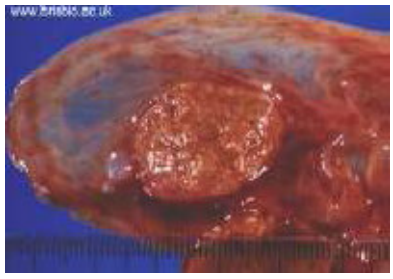
2.7 LESIONS

Forma adquirida:

- Hipertròfia dels limfonodes
- Enteritis: Úlceres necròtiques a l'aparell digestiu en rosegadors i lagomorfs.
- Encefalitis: Apareixen zones necròtiques a la substància grisa, sobretot. També poden aparèixer hemorràgies.
- Pneumònia
- Meningoencefalitis
- Necrosi tissular: Pot aparèixer a qualsevol teixit.
- Congestió generalitzada
- En humans la malaltia té una simptomatologia molt semblant a la d'una grip.

Forma congènita:

- Placenta: Apareixen focus necròtics de color blanquinós i d' aproximadament 1 cm de diàmetre als cotiledons. Aquestes lesions són pràcticament patognòmiques.



- Fetus:

Encèfal: Necrosis i hemorràgies disseminades

Autòlisi: En alguns casos l'animal ni es reconeix.

Edema generalitzat: Sobretot al teixit connectiu subcutani.

2.8 DIAGNÒSTIC

- Clínic + epidemiològic
- Animals vius

Líquids corporals: En teoria pot observar-se el paràsit a qualsevol líquid del cos però costa molt.

Biòpsia dels limfonodes: És més fàcil observar-los.

- Necròpsia:

Lesions a la placenta i al fetus ja comentades

Aïllament del paràsit

Inoculació en animals de laboratori per veure si desenvolupen la malaltia

Histopatologia

Immunohistoquímica

- Serologia

Immunofluorescència indirecta (IFI)

Hemoaglutinació indirecta (HAI)

ELISA

Dye-Test (Sabin i Feldman) o prova de coloració: És una prova molt antiga però molt específica. El seu principal ús és el de referència per a calibrar altres mètodes.

2.9 TRACTAMENT

La toxoplasmosi és una malaltia greu però que si s'agafa a temps pot tractar-se bé.

- Sulfamides
- Pirimetamina
- Espiromicina
- Clindamicina – Molt utilitzada en gos.
- Sulfametacina + pirimetacina
- Sulfaquinoxalina + pirimetacina

2.10 PROFILAXI I CONTROL

La toxoplasmosi és una d'aquelles malalties anomenades "malalties de maneig", ja que és un aspecte fonamental pel que fa a la transmissió i disseminació del paràsit.

Una de les primeres proves que es fa a la dona embarassada es la de la toxoplasmosi a través d'un anàlisi de sang. Si el resultat és positiu, la dona tindrà anticossos en el seu sistema immunològic i per tant no hi haurà cap perill de contraure la malaltia. Però en cas que sigui negatiu, només caldrà adoptar una sèrie de senzilles mesures:

- Fer un test de toxoplasmosis al seu gat per a determinar si és positiu.
- Evitar que el seu gat surti de casa, i donar-li un menjar específic per a ell (evitar la depredació).
- Evitar el contacte amb gats del carrer.
- Canviar la bandeja del gat a diari.
- Evitar la carn crua o semi crua (embotits, per exemple).
- Rentar-se bé les mans després de tocar carn crua o sorra del jardí
- Netejar a consciència fruites i verdures abans de consumir-les.

En altres situacions

-Manipulació de carn: Les persones que acostumen a manipular carn (carnisseries, escorxadors, supermercats, etc) estan exposades a tallar-se i tocar carn contaminada. Per aquest motiu cal extremar la higiene de les mans i els estris de treball.

-Avortaments en ovelles: Manipulació amb compte i extremant les mesures higièniques.

-Vacunació en ovella: Estan elaborades a partir d'una soca anomenada "soca 48" que no produeix quists i és molt immunògena (atorga una molt bona protecció).

3.ASSOCIACIONS FELINES

Hem considerat interessant consultar a expert en la matèria felina per poder abastar totes les opinions i possibles crítiques sobre el tema que ens preocupa. Així doncs, hem contactar amb Albert Lloret, Veterinari de l'Hospital Clínic Veterinari de la UAB i membre de l'associació GEMFE, perquè ens assessorés sobre el tema, i ens hem posat en contacte amb la Fundación Silvestre que ens han proporcionat informació sobre les xerrades de la Toxoplasmosis i uns díptics informatius sobre la malaltia i el seu contagi (annexe).

3.1 Associació GEMFE

GEMFE va ser creat a l'any 2000 dins l'estructura d'AVEPA com a grup de treball en medicina felina i com a resposta al creixent interès que aquesta espècie està cobrant en l'actualitat i en front a la gran necessitat que existeix d'especialitzar-se en ella.

En el 2009 GEMFE ja estava format per 88 membres distribuïts per tota Espanya.

El grup disposa d'un Comitè Científic i un comitè Gestor per aconseguir que el grup compleixi amb tots els seus objectius.

La funció del Comitè Científic és revisar totes les publicacions i xerrades del grup. La del Comitè Gestor és coordinar, actualitzar i dur a terme totes les activitats del grup.

Les principals activitats de GEMFE són:

•Organització de congressos i activitats científiques:

-Congrés anual de dues jornades dins del congrés de grups de treball anual d'AVEPA.

-Reunions mensuals locals a Madrid i Barcelona.

-Organització esporàdica de conferències, seminaris i reunions científiques amb ponents nacionals e internacionals.

•Col·laboració amb empreses del sector veterinari en estudis o assajos clínics en medicina felina.

•Preparació d'articles científics i revisions per la seva publicació en la revista d'AVEPA.

•Creació d'un bolletí propi que serà publicat cada 3-4 mesos.

Posicionament de GEMFE en relació a la TOXOPLASMOSI I l'EMBARÀS

Aquest posicionament ha estat acabat de publicar. En ell es fa referència a tot allò que preocupa a la gent del carrer sobre aquest tema, per tal d'aclarir qualsevol dubte al respecte.

La infecció per *Toxoplama gondii* és molt freqüent; entre el 30-40% de la població mundial és seropositiva.

La toxoplasmosi en persones pot presentar-se de forma diversa:

-En persones inmunocompetents provoca quadres subclínics o malaltia lleu similar a la grip.

-En persones inmunodeprimides (malats de SIDA, pacients en tractaments de quimioteràpia o medicaments inmunosupresors, malalts amb leucèmies o limfomes etc), poden aparèixer formes greus e inclús mortals de la toxoplasmosi amb quadres de pneumònia , miocarditis i meningoencefalitis. En aquestes persones el quadre clínic pot ser degut a una infecció recent, però amb major freqüència és degut a la reactivació d'una antiga infecció com a conseqüència de l'estat d'immunosupressió.

-En les dones embarassades no exposades prèviament a *T. Gondii* (seronegatives) la infecció pot provocar avortaments, morts neonatals, importants malformacions congènites i seqüeles neurològiques greus en el fetus.

La severitat del quadre produït per la infecció amb *Toxoplama gondii* durant la gestació varia amb l'edat del fetus en el moment de la infecció; és major en les infeccions contretes durant el primer trimestre.

En canvi, si la dona embarassada ha estat infectada prèviament a la gestació (i per tant, presenta anticossos en front a *T. Gondii*), **MAI** es produirà el contagi al fetus ja que la seva immunitat la protegeix en front de noves infeccions.

A Espanya, la detecció d'anticossos front *Toxoplama gondii* forma part de les proves rutinàries realitzades en les revisions ginecològiques a les què assisteix la dona durant l'embaràs.

La toxoplasmosi en gats és una malaltia poc freqüent. El gat representa el hoste definitiu per al paràsit i la majoria de gats portadors no mostren mai signes clínics de malaltia en el moment de la infecció. Quan aquests es produeixen, la severitat del quadre depèn de l'òrgan afectat i del grau de necrosi que el paràsit origini.

En gats immunodeprimits i gatets pot provocar quadres severs amb pneumònia, hepatopaties, pancreatitis, miocarditis i encefalitis.

En gats inmunocompetents ocasionalment pot induir la presentació de quadres de febre, miositis i malalties ocular, principalment uveïtis.

Donat que el gat és l'únic animal que pot eliminar en les femtes les formes infectives del paràsit *T. Gondii,*és freqüent que els metges i ginecòlegs adverteixin a les dones prenyades o amb plans de tenir fills de els perills potencials del contacte amb els gats.

Existeixen nombroses evidències científiques que demostren que el contagi del paràsit als essers humans per contacte amb les femtes d'un gat infectat és poc probable i que la gran majoria de les persones que s'infecten ho fan a través de la ingestió de carn poc feta, de vegetals u hortalisses contaminats amb oocists del paràsit o pel contacte directe amb terres contaminades. **Per tant, és erroni, assumir que sempre que una persona s'infecta amb *T. gondii*, l'origen de la infecció ha estat el contacte amb un gat.**

Els gats infestats per *T. gondii* són els responsables de disseminar el paràsit a l'ambient dins de les seves defecacions, però les femtes de gat resen eliminades no suposen un risc real de contagi, ja que contenen oocists encara no esporulats que no són infecciosos. Per ser infecciosos, els oocists han d' esporular, i això succeeix entre les 24 hores i els 5 dies després de la deposició de les femtes.

Durant la primoinfecció per *T. gondii*, el gat allibera oocists no esporulats a través de les femtes durat només d'una a tres setmanes i, després, queda com a portador de quists en els seus músculs i visceres. A partir d'aquest moment no elimina oocists en les femtes, i, per tant, no suposa cap risc per a les persones.

Com s'infecten els gats?

-Ingerint carns i teixits infectats amb quists provinents de carns poc fetes.

-Ingerint carns i teixits infectats amb quists provinents de preses caçades en el seu hàbitat.

-Bevent aigües no controlades (aigua de testos, rius..), contaminades amb oocists esporulats.

-Durant la gestació, per disseminació transplacentaria en mares seronegatives.

-Durant la lactació.

-Mitjançant una transfusió de sang provinent d'un gat amb infecció activa.

Per tant, els gats, s'han d'alimentar preferentment amb menjar comercial. Qualsevol altre aliment ha d'estar cuinat a altes temperatures durant 10 minuts i en el cas d'alimentar-los amb carn crua, aquesta s'ha de congelar a temperatures inferiors a -20º durant 2 dies. S'ha d'intentar que no cacin i per això es pot utilitzar cascavells que avisin a les seves preses o sortides controlades sota vigilància.

Com s'infecten les persones?

-Menjant carn poc cuinada o crua.

-Manipulant carn crua sense guants.

-Ingerint llet crua de cabra.

-Menjant verdures fresques contaminades no rentades adequadament.

-Durant feines de jardineria o en patis de jocs per nens, si la sorra està contaminada (el contagi requereix que es fiquin les mans a la boca sense rentar).

-Beure aigua contaminada amb oocist esporulats.

-Ingerint directament restes de femtes de gats infectats per *Toxoplasma gondii* que es trobin en la fase d'eliminació d'oocists. Al menys han de transcorre 24 hores després de la deposició.

-**La infecció no es produeix tocant o acariciant al gat**. Els veterinaris de petits animals, que estan en contacte físic freqüent amb gats, no presenten una major seroprevalència que persones d'altres professions.

Mesures que s'han de tenir per evitar el contagi per part d'una dona embarassada o qualsevol altra persona:

-S'ha de menjar sempre carn cuinada a altes temperatures durant 10 minuts, o congelar les carns a -20º durant dos dies si s'han de consumir poc fetes.

-S'han de rentar adequadament les verdures sempre abans del seu consum.

-Només s'ha de beure aigua potable o de procedència coneguda. Si no es coneix l'origen s'ha de filtrar o bullir prèviament al seu consum.

-S'han d'utilitzar guants durant la les feines de jardineria i al manipular carns crues, o rentar-se adequadament les mans després de fer-ho.

-Les safates de la sorra dels gats s'han de netejar diàriament amb una paleta. Les dones embarassades han d'evitar manipular la safata de sorra, però si això no es possible es recomanable que ho facin amb guants d'un sol ús i amb mascareta. Per desinfectar la safata el millor mètode és l'aigua bullint o el vapor a pressió, ja que els oocists esporulats són resistents a la majoria de desinfectants.

Les evidències científiques de les que disposem a l'actualitat demostren que el contagi de toxoplasmosi de gats a persones, incloses les dones embarassades i malalts de SIDA, és altament improbable seguint unes normes bàsiques d'higiene. Per tant, considerem totalment injustificat l'abandonament o el rebuig dels gats en cas d'un embaràs en la família, encara que aquest sigui el consell d'alguns metges.

Els gats aporten nombrosos beneficis psicològics i benestar emocional a les persones que gaudeixen de la seva companyia, especialment quan formen part de la família com un més dels seus membres.

És discutible la utilitat de la realització de proves de sang per determinar si un gat és seropositiu o seronegatiu ja que no indiquen si el gat està o no eliminant oocist el aquest moment i a més a més, les mesures preventives e higièniques que ha de prendre una dona embarassada han de ser les mateixes en ambdós casos.

3.2 Fundació silvestre

Qui són?

Son un grup de gent que estima els animals i que creu que mereixen tenir una vida digna.

Els animals comparteixen la terra amb nosaltres i tenen una funció força important en les nostres vides. Per això creuen que s'han de tractar com a éssers vius, ja que també tenen sentiments.

Els animals tant poden ser feliços com estar tristos. També pateixen o saltem d'alegria. Tot depèn del tracte que rebin. És molt important que visquin feliços i estiguin ben tractats.

Malauradament, avui dia, els seus drets no estan prou reconeguts i, moltes vegades són maltractats, tant els animals domèstics, com els de granja i també

els salvatges. Ells treballen per mirar de millorar les seves vides i defensar els seus drets.

És un projecte força ambiciós en què treballen dur cada dia, un treball que, de vegades, els costa algun disgust i d'altres els dóna satisfaccions. Per això no perden les esperances d'arribar a millorar la situació dels animals arreu del món.

Conferència organitzada per FUNDACIÓ SILVESTRE

Títol: **La Toxoplasmosi, primera causa d'abandonament d'animals domèstics?**

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- Sra. Regina Farré (periodista)
- Sr. Albert Lloret (Veterinari)
- Dra. Luisa Burrel (Ginecologia i Obstetrícia)
- Moderador, Sr. Lluís Reales (periodista)

A Catalunya cada any abandonem entre 25.000 i 30.000 animals de companyia, xifra que no té en compte aquells que són atropellats o be són adoptats per particulars sense passar per refugis o protectores d'animals.

Cal fer entendre a la societat que un animal de companyia no és un objecte que hom pot adquirir de manera arbitraria i sense tenir en compte les conseqüències i responsabilitats que comportarà. L'animal, sigui gat o gos, dependrà absolutament per a la seva supervivència d'aquell a qui ell mateix considera el seu amo i la seva família, i així doncs, quan un animal és abandonat, a més de gana, fred o altres perills, pateix un trauma psicològic inesborrable.

Si té sort, acabarà a una protectora on procuraran fer per a ell el que els hi sigui possible, tanmateix, la saturació i la falta de mitjans econòmics són problemes habituals d'aquestes organitzacions. En cas que sigui més desafortunat i el

capturi una gossera municipal, la seva vida tindrà una durada inferior a una setmana si ningú el reclama.

Sovint, els professionals de la salut (metges, infermers, psicòlegs, i fins i tot farmacèutics) per manca de coneixements sobre el cicle de la toxoplasmosi, contribueixen a estendre el fenomen de l'abandonament en aconsellar de manera equivocada els seus pacients. És per aquest motiu que considerem de vital importància l'assistència d'aquests professionals a la conferència.

Abandonament i embaràs

L'embaràs és una de les causes més freqüents d'abandonament i és per això important preveure aquest tipus de situacions i proporcionar la informació necessària a fi de reduir aquestes xifres desoladores.

Quan arriba un fill a la família aquesta s'omple de satisfacció, però en ocasions, si en aquesta hi ha un animal domèstic sorgeixen dubtes respecte d'aquest últim, por per la criatura, que pot desembocar en un abandonament.

Un gos o gat que visqui amb la família mai atacarà al nen ja que predominarà el instint protector cap al membre nouvingut. És important que s'inclogui a l'animal a l'esdeveniment que té lloc, per reduir en la mesura que sigui possible la gelosia que inevitablement patirà.

La vacunació és necessària per allunyar qualsevol tipus de dubte en relació a la transmissió de malalties.

Toxoplasmosi

La convivència satisfactòria amb un animal de companyia sovint pot veure's afectada per la feliç noticia d'un embaràs a la família. És llavors quan arriben els dubtes i preguntes: Afectarà l'animal a la salut del meu fill? Hi haurà problemes de convivència? I per acabar-ho d'enllestir el metge ens parla de la

toxoplasmosi , una malaltia que es transmet mitjançant els excrements dels gats, i que per falta d'informació suposa l'abandonament d'un elevat nombre de gats cada any.

La toxoplasmosi és una infecció causada pel paràsit toxoplasma fondal, que es transmet al fetus en menjar carn semi crua, fruites mal rentades, o bé pel contacte amb excrements del gat que pateixi la malaltia.

Una de les primeres proves que es fa a la dona embarassada es la de la toxoplasmosi a través d'un anàlisi de sang. Si el resultat és positiu, la dona tindrà anticossos en el seu sistema immunològic i per tant no hi haurà cap perill de contraure la malaltia. Però en cas que sigui negatiu, només caldrà adoptar una sèrie de senzilles mesures:

- Fer un test de toxoplasmosis al seu gat per a determinar si és positiu.
- Evitar la carn crua o semi crua (embotits, per exemple).
- Rentar-se bé les mans després de tocar carn crua o sorra del jardí
- Netejar a consciència fruites i verdures abans de consumir-les.
- Evitar que el seu gat surti de casa, i donar-li un menjar específic per a ell.
- Evitar el contacte amb gats del carrer.

Estàs embarassada i convius amb animals? Responem a les preguntes més habituals:

1. Es pot prevenir? Com fer-ho? En cas de conviure amb un gat, cal evitar el contacte amb els excrements de l'animal, prenent mesures com ara utilitzar guants de plàstic a l'hora de netejar-los. De fet, hi ha veterinàries que estan en constant contacte amb animals durant la gestació, i no contrauen la malaltia.
2. Detecció: en cas d'embaràs el toco-ginecòleg farà un seguiment del procés de gestació, que implica els periòdics

anàlisis sanguinis. Els símptomes són semblants als d'una grip, de manera que es possible que la dona hagi passat la malaltia abans quedant, d'aquesta manera, immunitzada.

Conclusió

La toxoplasmosi és una realitat que no podem deixar de banda en cas que ens trobem en les circumstàncies esmentades. Tot i això, el fet de que l'animal sigui capaç de transmetre toxoplasmosi i la carència d'anticossos en el nostre organisme no ha d'implicar necessariament la contracció de la malaltia. En cap cas l'abandonament de l'animal ha de ser una solució a prendre, una solució cruel i exagerada que suposarà una condemna a mort segura per a un ésser viu amb dret a una vida digna, de la qual ens vam responsabilitzar en adoptar-lo.

Per últim, cal dir que nombrosos estudis han afirmat que la convivència amb animals és favorable per a la salut, ja que la seva presència és relaxant i a la vegada incita al joc i a l'imprescindible riure.

4.LEGISLACIÓ

4.1 Llei de Protecció Animal

Degut a la manca de legislació concreta sobre la Toxoplasmosis i les precaucions en dones embarassades, ens hem referit a la Llei de Protecció Animal per veure si calen alguns motius en concret per desfer-se d'un animal de companyia o si aquest fet té alguna penalització econòmica o legal.

Fragments de la Llei de la Comunitat Autònoma de Catalunya 22/2003 del 4 de juliol de protecció dels animals:

TÍTULO I

DISPOSICIONES GENERALES Y NORMAS GENERALES DE PROTECCIÓN DE LOS ANIMALES

Capítulo II

Normas generales de protección de los animales

Artículo 4

Obligaciones de las personas propietarias y poseedoras de animales

1. Las personas propietarias y poseedoras de animales deben mantenerles en buenas condiciones higiénico-sanitarias de bienestar y seguridad, de acuerdo con las características de cada especie.

2. La persona poseedora de un animal debe darle la atención veterinaria básica para garantizar su salud.

Artículo 5

Prohibiciones

Quedan prohibidas las siguientes actuaciones con respecto a los animales:

a) Maltratarlos, agredirles físicamente o someterlos a cualquier otra práctica que les produzca sufrimientos o daños físicos o psicológicos.

b) Suministrarles sustancias que puedan causarles alteraciones de la salud o del comportamiento, excepto en los casos amparados por la normativa vigente o por prescripción veterinaria.

c) Abandonarlos.

d) Mantenerlos en instalaciones indebidas desde el punto de vista higiénico-sanitario de bienestar y seguridad del animal.

e) Practicarles mutilaciones, extirparles las uñas, cuerdas vocales y demás partes u órganos, salvo las intervenciones hechas con asistencia veterinaria en caso de necesidad terapéutica, para garantizar su salud o para limitar o anular su capacidad reproductiva. Por motivos científicos o de manejo, podrán realizarse dichas intervenciones previa obtención de la autorización de la autoridad competente.

f) No facilitarles la suficiente alimentación.

g) Hacer donación de ellos como premio, recompensa, gratificación o regalo de compensación por otras adquisiciones de naturaleza distinta a la transacción onerosa de animales.

h) Venderlos a personas menores de dieciséis años y a personas incapacitadas sin la autorización de quienes tienen su potestad o custodia.

i) Comerciar con ellos fuera de los certámenes u otras concentraciones de animales vivos y establecimientos de venta y de cría autorizados, salvo las transacciones entre las personas particulares cuando se limiten a sus animales de compañía, no tengan afán de lucro y se garantice el bienestar del animal.

j) Exhibirlos de forma ambulante como reclamo.

k) Someterlos a trabajos inadecuados en lo que concierne a las características de los animales y a las condiciones higiénico-sanitarias.

l) Mantenerlos atados durante la mayor parte del día o limitarles de forma duradera el movimiento necesario para ellos.

m) Mantenerlos en locales públicos o privados en condiciones de calidad ambiental, luminosidad, ruido, humos y similares que pueda afectarlos físicamente así como psicológicamente.

n) Matarlos por juego o perversidad o torturarlos.

TÍTULO VII

INFRACCIONES Y SANCIONES

Capítulo I

Infracciones

Artículo 30

Clasificación

1. Las infracciones de las disposiciones de la presente Ley se clasifican en leves, graves o muy graves.

2. Son infracciones leves:

a) Poseer un perro o un gato no inscritos en el registro censal o poseer otros animales que deben registrarse obligatoriamente.

b) No llevar un archivo con las fichas clínicas de los animales que deben vacunarse o tratar obligatoriamente, de acuerdo con lo que establece la presente Ley.

c) Vender animales de compañía a personas menores de dieciséis años y a personas incapacitadas sin la autorización de quienes tienen su potestad o custodia.

d) Hacer donación de un animal como premio o recompensa.

e) Transportar animales que incumplan los requisitos establecidos por el artículo 8.

f) No llevar identificados los gatos, perros y demás animales que deban identificarse de acuerdo con el reglamento, o incumplir los requisitos establecidos por la presente Ley y la normativa que la desarrolla con relación a esta identificación.

g) No poseer, el personal de los núcleos zoológicos que manipule animales, el certificado correspondiente al curso de cuidador o cuidadora de animales, reconocido oficialmente.

h) Filmar escenas ficticias de crueldad, maltrato o sufrimiento de animales, sin previa autorización administrativa.

i) Usar colas o sustancias pegajosas como método de control de poblaciones de animales vertebrados.

j) No tener en lugar visible la acreditación de la inscripción en el Registro de Núcleos Zoológicos.

k) No tener actualizado el libro registro oficial o tramitado por la administración competente establecido para los núcleos zoológicos.

l) Exhibir animales en los escaparates de los establecimientos de venta de animales.

m) Practicar la caza, la captura en vivo, la venta, la tenencia, el tráfico, el comercio, la exhibición pública y la taxidermia de ejemplares de las especies incluidas en el anexo con la categoría D, así como de partes, huevos, crías o productos obtenidos a partir de estos ejemplares.

n) Practicar la caza y captura de pájaros vivos de longitud inferior a 20 cm, fuera de los supuestos del artículo 9.2.

o) Hacer exhibición ambulante de animales como reclamo.

p) Mantener a los animales en instalaciones inadecuadas desde el punto de vista de su bienestar, si no les conlleva un riesgo grave para la salud.

q) No evitar la huida de animales.

r) Maltratar a animales, si no les produce resultados lesivos.

s) Suministrar a un animal sustancias que le causen alteraciones leves de la salud o del comportamiento, salvo en los casos amparados por la normativa vigente.

t) No dar a los animales la atención veterinaria necesaria para garantizar su salud, si no les causa perjuicios graves.

u) Vender o hacer donación de animales mediante revistas de reclamo o publicaciones asimilables sin la inclusión del número de registro de núcleo zoológico.

v) Cualquier otra infracción de las disposiciones de la presente Ley o normativa que la desarrolle que no haya sido tipificada de grave o muy grave.

3. Son infracciones graves:

a) Mantener a los animales sin la alimentación necesaria o en instalaciones inadecuadas desde el punto de vista higiénico-sanitario, de bienestar y de seguridad, si les supone riesgo grave para la salud.

b) No tener el libro registro oficial o tramitado por la administración competente establecido para los núcleos zoológicos.

c) No vacunar a los animales domésticos de compañía o no aplicarles los tratamientos obligatorios.

d) Incumplir, por parte de los núcleos zoológicos, cualquiera de las condiciones y requisitos establecidos en el título IV.

e) Realizar venta ambulante de animales fuera de mercados, ferias y cualquier otro certamen autorizado.

f) Vender o hacer donación de animales, por parte de los centros de cría, si éstos no han sido declarados núcleos zoológicos.

g) Anular el sistema de identificación sin prescripción ni control veterinario.

h) No mantener en cautividad o en las condiciones que por vía reglamentaria se establezca, o exhibir y pasear por las vías y los espacios públicos animales salvajes pertenecientes a especies de comercio permitido que por sus características puedan causar daños a las personas, a los bienes y al medio ambiente.

i) Practicar el tiro de pichón.

j) Incumplir la obligación de vender animales desparasitados y libres de todas las enfermedades a que se refiere el artículo 24.1.c.

k) No entregar la documentación exigida en toda transacción de animales.

l) Maltratar o agredir físicamente a los animales, si les conllevan consecuencias graves para la salud.

m) Realizar matanzas públicas de animales.

n) Instalar atracciones feriales de caballitos donde se utilicen animales.

o) Hacer un uso no autorizado de animales en espectáculos.

p) Suministrar sustancias a un animal que le causen alteraciones graves de la salud o del comportamiento, salvo en los casos amparados por la normativa vigente.

q) La caza, la captura en vivo, la venta, la tenencia, el tráfico, el comercio y la exhibición pública, así como de partes, huevos y crías de ejemplares de

especies de la fauna autóctona y no autóctona declaradas protegidas por tratados y convenios internacionales vigentes en el Estado español.

r) Practicar la caza, la captura en vivo, la venta, la tenencia, el tráfico, el comercio, la exhibición pública y la taxidermia de ejemplares de las especies incluidas en el anexo con la categoría C, así como de partes, huevos, crías o productos obtenidos a partir de estos ejemplares.

s) La falta de inscripción en el Registro de Núcleos Zoológicos.

t) Oponer resistencia a la función inspectora o poner obstáculos a la inspección de instalaciones que alojen animales.

u) No dar a los animales la atención veterinaria necesaria para garantizar su salud.

v) Abandonar animales, si se ha efectuado en unas circunstancias que no suponen riesgo alguno para el animal.

w) Cazar en espacios declarados reservas naturales de fauna salvaje donde la caza está prohibida y en refugios de fauna salvaje, salvo en los casos autorizados por el Departamento de Medio Ambiente.

x) Incumplir las obligaciones establecidas por el artículo 22.5 con el fin de procurar el bienestar de los animales utilizados en carreras una vez finalizada su participación en las mismas.

y) Participar en competiciones y carreras en las cuales se hacen apuestas de los animales que no están identificados y registrados en el Registro de Animales de Competición.

z) Reincidir en la comisión de infracciones leves durante el último año.

4. Son infracciones muy graves:

a) Maltratar o agredir físicamente a los animales, si les comporta consecuencias muy graves para la salud.

b) Sacrificar a gatos y perros fuera de los casos mencionados por el artículo 11.1.

c) Abandonar animales, si se ha realizado en unas circunstancias que puedan comportarles daños graves.

d) Capturar perros y gatos asalvajados con uso de armas de fuego sin la correspondiente autorización del Departamento de Medio Ambiente.

e) No evitar la huida de animales de especies exóticas o especies híbridas, de manera que pueda suponer una alteración ecológica grave.
f) Esterilizar animales, practicar mutilaciones a animales y sacrificar animales sin control veterinario o en contra de las condiciones y los requisitos establecidos por la presente Ley.
g) Organizar peleas de perros, de gallos u otros animales, así como participar en este tipo de actos.
h) Mantener a los animales sin la alimentación necesaria o en instalaciones inadecuadas desde el punto de vista higiénico-sanitario y de bienestar, si los perjuicios a los animales son muy graves.
i) Practicar la caza, la captura en vivo, la venta, la tenencia, el tráfico, el comercio y la exhibición pública de animales o de los huevos y las crías de ejemplares de especies de la fauna autóctona y de la no autóctona declaradas altamente protegidas o en peligro de extinción por tratados y convenios internacionales vigentes en el Estado español.
j) Practicar la caza, la captura en vivo, la venta, la tenencia, el tráfico, el comercio, la exhibición pública y la taxidermia de ejemplares de las especies incluidas en el anexo con las categorías A y B, así como de partes, huevos y crías de estos ejemplares.
k) Reincidir en la comisión de infracciones graves durante el último año.

Capítulo II

Sanciones

Artículo 31

Multas, comiso y cierre de instalaciones

1. Las infracciones cometidas contra la presente Ley están sancionadas con multas de hasta 20.000 euros.
2. La imposición de la multa puede conllevar el comiso de los animales objeto de la infracción, sin perjuicio de la aplicación del comiso preventivo que puede determinarse a criterio de la autoridad actuante en el momento del levantamiento del acta de inspección o la denuncia.

3. La comisión de las infracciones muy graves o la reiteración en las infracciones graves puede comportar el cierre temporal de las instalaciones, los locales o los establecimientos respectivos, con la correspondiente anotación en el Registro de Núcleos Zoológicos, así como la inhabilitación para la tenencia de animales por un período de dos meses a cinco años.
4. El incumplimiento de alguna de las normativas o condiciones de una autorización excepcional para la captura o la posesión de un animal de una especie de fauna autóctona puede suponer la retirada cautelar in situ e inmediata de dicha autorización por parte de los agentes de la autoridad.
5. Las personas que disponen de estas autorizaciones excepcionales, en el caso de ser sancionadas por incumplimiento de alguno de sus términos o normativas en la materia, deben ser inhabilitadas para la actividad a que se refiere el apartado 3 por un período de uno a cinco años.

Artículo 32

Cuantía de las multas

1. Las infracciones leves están sancionadas con una multa de 100 euros hasta 400 euros ; las graves, con una multa de 401 euros hasta 2.000 euros, y las muy graves, con una multa de 2.001 euros hasta 20.000 euros.

2. En la imposición de las sanciones debe tenerse en cuenta, para graduar la cuantía de las multas y la imposición de las sanciones accesorias, los siguientes criterios:
a) La trascendencia social y el perjuicio causado por la infracción cometida.
b) El ánimo de lucro ilícito y la cuantía del beneficio obtenido en la comisión de la infracción.
c) La reiteración o la reincidencia en la comisión de infracciones.
d) La irreparabilidad de los daños causados al medio ambiente o el elevado coste de reparación.
e) El volumen de negocio del establecimiento.
f) La capacidad económica de la persona infractora.
g) El grado de intencionalidad en la comisión de la infracción.
h) El hecho de que exista requerimiento previo.

3. Existe reincidencia si en el momento de cometerse la infracción no ha transcurrido un año desde la imposición por resolución firme de otra sanción con motivo de una infracción de la misma calificación. Si se aprecia la reincidencia, la cuantía de las sanciones puede incrementarse hasta el doble del importe máximo de la sanción correspondiente a la infracción cometida, sin exceder en ningún caso del límite más alto fijado para la infracción muy grave.

4. Ante la comisión de infracciones de carácter leve, pueden llevarse a cabo actuaciones de educación ambiental o de advertencia, sin necesidad de iniciar un procedimiento sancionador.

L'article 4 d'aquesta llei obliga a mantenir els animals de companyia en bones condicions, i l'apartat c) de l'article 5 prohibeix explícitament el seu abandonament. L'abandonament d'animals és considerat una falta greu o molt greu, segons les circumstàncies en les que tingui lloc (Article 30.3 apartat v) i Article 30.4 apartat c), respectivament); el que segons l'article 32.1 suposaria una multa d'entre 401€ i 20.000€. Segons els articles 32.2 i 32.3 la reincidència en l'abandonament, així com en qualsevol altre falta, podria suposar un increment de fins el doble del import màxim de la sanció (fins un màxim de 20.000€); sempre i quant no hagi transcorregut un any entre les dues infraccions.

4.2 Toxoplasmosis a Espanya

Actualment a Espanya existeix una legislació referent a la vigilància i investigació epidemiològica de malalties zoonòtiques com la toxoplasmosi, però es limita a l'àmbit de les infeccions i intoxicacions alimentàries procedents de productes animals i d'origen animal. Es tracta del Reial Decret 1940/2004, del 27 de setembre, sobre la vigilància de les zoonosis i els agents zoonòtics. L'única menció que fa aquest Reial Decret a la toxoplasmosi la trobem en un dels seus annexes:

ANEXO I

A. Zoonosis y agentes zoonóticos que deben ser objeto de vigilancia: brucelosis y sus agentes causales, campilobacteriosis y sus agentes causales, equinococosis y sus agentes causales, listeriosis y sus agentes causales, salmonelosis y sus agentes causales, triquinosis y sus agentes causales, tuberculosis por Mycobacterium bovis y Escherichia coli verotoxigénica.

B. Lista de zoonosis y agentes zoonóticos que deben ser objeto de vigilancia en función de la situación epidemiológica.

1. Zoonosis víricas: calicivirus, virus de la hepatitis A, virus de la gripe, rabia y virus transmitidos por artrópodos.

2. Zoonosis bacterianas: borreliosis y sus agentes causales, botulismo y sus agentes causales, leptospirosis y sus agentes causales, psitacosis y sus agentes causales, tuberculosis distintas de la indicada en la parte A, vibriosis y sus agentes causales, yersiniosis y sus agentes causales.

3. Zoonosis parasitarias: anisakiasis y sus agentes causales, criptosporidiosis y sus agentes causales, cisticercosis y sus agentes causales, toxoplasmosis y sus agentes causales.

4. Otras zoonosis y agentes zoonóticos.

A part d'això no hi ha cap mena de legislació que reguli els mètodes de diagnòstic, tractament i prevenció; ni cap document que decreti a quines proves han de sotmetre's les dones embarassades per a poder prevenir eficaçment aquesta malaltia. El perfil TORCH és una prova laboratorial per a detectar anticossos enfront *Toxoplasma gondii* (juntament amb anticossos enfront rubèola, citomegalovirus i herpes; i a vegades també sífilis i VIH) que es duu a terme freqüentment en centres ginecològics, però no és obligatori ni està

regulat de cap manera. Una dona seropositiva per a la toxoplasmosis no té cap risc de tornar a agafar la malaltia i per tant és innecessari que digui a terme d'una manera tant estricta les pautes de prevenció. És molt probable que si aquesta prova es fes de forma obligatòria, s'abandonarien molts menys gats.

4.3 La toxoplasmosi fora d'Espanya

Per a comparar la situació espanyola en matèria legislativa sobre zoonosis, hem consultat les bases de dades legislatives virtuals de 7 països més (3 europeus i 4 d'Amèrica del nord i llatina): França, Italia, Regne Unit, Estats Units, Canadà, Mèxic i Argentina.

- França: hem trobat 2 documents que fan referència a la prevenció i el serodiagnòstic de la toxoplasmosis: *Circulaire DGS et DH n° 605 du 27 septembre 1983 relative à la prévention de la toxoplasmose (Bulletin officiel du ministère chargé de la santé n° 83/49, texte n° 1989)* i *Circulaire du 29 mai 1979 relative aux sérodiagnostics de la rubéole et de la toxoplasmose (Bulletin officiel du ministère chargé de la santé n° 79/35, texte n° 17206)*. Al ser documents tant antics, no hi hem pogut accedir des de la base de dades virtual.

- Itàlia: l'Annexe I del decret legislatiu del 4 d'abril de 2006 (*Attuazione della direttiva 2003/99/CE sulle misure di sorveglianza delle zoonosi e degli agenti zoonotici*.) fa referència a la toxoplasmosi com una de les zoonosis parasitàries que han d'estar sota control i vigilància; però no fa cap mena d'especificació en quant a mètodes de diagnòstic, tractament o prevenció. Tampoc es fa referència al cas especial de les embarassades.

- Regne Unit: no hem trobat cap document referent a la toxoplasmosi.

- Estats Units: l'única referència que hem trobat a la toxoplasmosis és l'article 4.109 del Decret de les Condicions del Treballador, que declara que una treballadora embarassada no hauria d'estar obligada a dur a terme treballs

amb agents biològics de la toxoplasmosis i el virus de la rubèola a no ser que hi hagi evidència que n'és immune. Tot i que en aquest cas sí que fa menció a les dones embarassades, la seva aplicació es limita a l'àmbit laboral.

- Canadà: de la mateixa manera que amb el Regne Unit, no hem trobat res en relació a la toxoplasmosi.

- Mèxic: l'Article 134 de la Llei General de Salut descriu la toxoplasmosis com una de les malalties transmissibles per a les que és necessari realitzar activitats de vigilància epidemiològica, prevenció i control; però com en el cas de Itàlia no fa cap referència al problema de les embarassades.

- Argentina: la cerca virtual no dóna cap resultat per a la toxoplasmosis, però actualment està en marxa un Projecte de Llei per a prevenir la toxoplasmosi congènita. Aquest Projecte, iniciat pel senador provincial d'Entre Ríos Eduardo Melchiori el mes de juliol de 2010, dictamina que serà obligatori a l'examen prenupcial i d'ingrés al nivell secundari el diagnòstic serològic de la toxoplasmosi; excepte que un anàlisi anterior (com a mínim 3 mesos) indiqui que la dona n qüestió és immune. Es determina també que aquests anàlisis seran gratuïts, i que els seus resultats seran registrats a la llibreta sanitària o escolar. Aquests resultats seran exigits per a la celebració del matrimoni, per al ingrés a escoles de nivell mig, per a l'assignació prenatal i per part. Les llibretes matrimonials, a més, hauran de tenir referències a la toxoplasmosi congènita i adquirida, la seva prevenció, origen, desenvolupament i conseqüències. El 16 de novembre de 2010 la Comisión de Salud Pública, Medio Ambiente Humano y Drogadicción de la Càmera Alta de la província d'Entre Ríos va considerar favorable el projecte. El 9 de desembre del 2010 la Càmera Alta provincial li va donar mitja sanció al projecte de llei, passant així a mans dels diputats en espera de la sanció definitiva.

5.DIFUSIÓ DE LA TOXOPLASMOSIS

Hem trobat interessant buscar diferents fonts d'informació per investigar l'opinió que hi ha sobre aquest tema i les noticies que han succeït en els últims anys. Tot seguit adjuntem articles de diaris que ens han semblat representatius, opinió de blogs de veterinaris i articles científics.
També hem vist que hi ha algunes webs i fòrums sobre embarassades que en general tenen opinions bastant alarmistes.

5.1 Articles de premsa

La Vanguardia

"Muchas embarazadas abandonan a sus gatos por miedo a contraer la toxoplasmosis"

La Fundació Silvestre organiza unas conferencias para aclarar las dudas en torno a esta enfermedad

Vida | 13/10/2008 - 01:23h | Actualizado el 13/07/09 - 09:48h

Marta Cuatrecasas

Barcelona

Cada año muchos gatos son abandonados por mujeres embarazadas por miedo a contraer la toxoplasmosis, una enfermedad que puede tener consecuencias muy graves en el feto. No obstante, esta enfermedad es poco común y tomando ciertas precauciones no hay razón alguna para desprenderse de un gato sano. Así lo afirma Cristina Dalmau, presidenta de la Fundació Silvestre, que cada día recibe llamadas de mujeres embarazadas que amenazan con abandonar a sus gatos si una protectora no se hace cargo. Por este motivo, la fundación organiza este miércoles en el Ateneu Barcelonès a las siete y media de la tarde una conferencia con ginecólogos y veterinarios

para resolver las cuestiones sobre la toxoplasmosis y la tenencia de felinos durante el embarazo.

¿De qué se trata esta enfermedad?

La toxoplasmosis la ocasiona un parásito. Se puede contraer a través de la manipulación de las heces de gato o por la ingesta de carne cruda, sobretodo de cerdo, cordero y vaca. Aunque el parásito también puede estar en las verduras, los huevos mal lavados, leche mal tratada, etc.

Otra vía de transmisión es de la madre al feto.

Sí, la madre puede transmitir la enfermedad al feto del primer mes al tercero. Aunque si una persona ha estado en contacto con carne cruda o vegetales quizá ya es inmune a la enfermedad porque ya la ha pasado sin darse cuenta. En el caso de que el gato fuera positivo y la embarazada negativa, es decir, la madre nunca haya estado en contacto con este parásito, entonces sí se debe tomar alguna precaución. ¡Pero jamás deshacerse del animal!

¿Qué precauciones?

El contagio se efectúa cuando tocamos heces de gato contaminadas y luego nos chupemos los dedos, con lo que hay que evitar cambiar la arena del gato, por ejemplo. En caso de tener mucho miedo podemos buscarle una casa temporal.

Y el gato, ¿cómo se contagia?

A través de la ingesta de comida cruda, como pájaros o ratas. Por eso es muy difícil que un gato doméstico sea protador.

¿Cómo podemos saber si nuestro gato es positivo?

Con una simple prueba. Hoy en día a todas las embarazadas se les hace esta prueba porque hay mucha alarma con este tema. El problema es que los médicos aconsejan a las embarazadas a que se deshagan del animal.

¿Por qué son tan alarmistas?

Porque ante la duda prefieren prevenir al máximo. Los médicos actúan igual en caso de alergias: aconsejan que te deshagas del animal, en vez de tratar esa alergia que, afortundamente, hoy en día es posible. Como no te pasa nada si abandonas a tu gato, la gente lo hace sin pensárselo demasiado.

¿Tan frecuente es el abandono de gatos por la toxoplasmosis?

Mucho. Y nos encontramos muchas veces con una mujer que nos llama y nos dice: "Estoy embarazada y el ginecólogo me ha dicho que tengo que deshacerme del gato." Lo más sorprendente es que muchos ginecólogos admiten que ha habido muy pocos casos de transmisión de la toxoplasmosis.

Imagino que deben abandonar a los gatos positivos.

¡Que va! Casi nunca les hacen la prueba. Las mujeres se suelen alarmar mucho y rápidamente se deshacen del felino. Luego las calles se abarrotan de gatos, la gente se queja y, en el peor de los casos, alguien los envenena para intentar disminuir la población. Uno de nuestros proyectos más grandes es el control de colonias de gatos callejeros.

Cuéntame.

Controlamos las colonias de gatos en los barrios de Sarriá y San Gervasio. Se calcula que hay alrededor de 100.000 gatos malviviendo en las calles de la ciudad. No existe una gatera municipal con lo que estos animales han de vivir en la calle. Antigüamente, el Ayuntamiento envenenaba a los gatos para reducir las poblaciones pero ahora hay una ley que prohíbe esta práctica que, además de ser inútil, es muy peligrosa.

¿Qué hacéis vosotros para controlar las colonias?

Detectamos una colonia y, lo primero, contactamos con la persona que alimenta a estos gatos para explicarle lo que vamos a hacer. A veces es muy difícil que te entiendan porque para estas personas los gatos son su vida y se

creen que se los vamos a quitar. Si colaboran entonces el trabajo es rápidisimo y muy bien coordinado.

¿Y luego?

Esterilizamos a machos y hembras, desparasitamos, alimentamos y retiramos a los cachorros para donarlos en adopción. Situamos un comedero de pienso limpio y visitamos la colonia tres veces por semana para vigilar que ningún gato enferme o aparezcan nuevos miembros. Trabajamos con 40 colonias que significan un total de 500 gatos.

¿Cómo reaccionan los vecinos cuando os ven haciendo esta labor? Cuando les explicas lo que haces la gente responde muy bien, por eso siempre llevo un par de trípticos en la mano. Cuando ven que somos una fundación que esterilizamos, saneamos y alimentamos bien a los gatos, entonces están contentos. No hay que olvidar que los gatos callejeros provienen de los abandonos.

¿Cómo responde el Ayuntamiento?

Estamos empezando a sensibilizar a las administraciones de que han de hacerse cargo de este problema. Hemos firmado algunos convenios con el Ayuntamiento de Barcelona y de otros municipios para que se ocupen de pagar las esterilizaciones. Una colonia controlada es mucho mejor ya que desaparece el olor de los orines de los machos durante la época de celo, como también las peleas. Los gatos están tranquilos, sanos e incluso impiden que entren nuevos miembros. ¡Encima evitan que las ratas y ratones vengan!

El Supremo eleva en 210.000 euros la indemnización a los padres de un niño que nació con toxoplasmosis

Esta enfermedad infecciosa se desarrolló por la falta de premura con la que fue tratada la madre durante el embarazo

Vida | 28/08/2007 - 10:04h | Actualizado el 28/08/07 - 10:08h

MÁS INFORMACIÓN

Madrid. (EFE).- El Tribunal Supremo ha elevado en casi 210.000 euros la indemnización concedida por la Audiencia Nacional a los padres de un niño que nació con una enfermedad infecciosa, toxoplasmosis congénita, debido a la falta de premura con la que fue tratada la madre durante el embarazo.

En una sentencia de la Sala de lo Contencioso-Administrativo, el Alto Tribunal acuerda incrementar de 270.456 euros a 480.000 euros la indemnización que la Administración del Estado debe pagar al estimar que la primera cantidad "no es suficiente" para compensar a los recurrentes por los gastos "derivados de la atención por un tercero" de su hijo.

La mujer, embarazada de nueve semanas, ingresó el 30 de julio de 1995 en el hospital Ciudad de Coria de esta localidad cacereña aquejada de sangrado vaginal y se le prescribió reposo domiciliario ante el riesgo de aborto, al tiempo que se ordenaba la práctica de varias pruebas, entre ellas un análisis de sangre que se llevó a cabo el 17 de agosto y que determinó que tenía toxoplasmosis.

A pesar de este resultado, no se realizó una nueva prueba de serología hasta el 23 de noviembre de ese año, en la semana 24 de gestación, que de nuevo dio positivo para la toxoplasmosis.

El 23 de febrero de 1996 la mujer dio a luz a un niño "diagnosticado de toxoplasmosis congénita e hidrocefalia", aunque en mayo siguiente su cuadro clínico incluía también meningitis, diabetes insípida e hipercalcemia (alta concentración de calcio en la sangre).

La Consejería de Bienestar Social de la Junta de Extremadura estableció el 28 de agosto de 1996 que el niño, entonces de seis meses, padecía un grado de minusvalía del 76 por ciento.

La Audiencia Nacional concluyó que la paciente "no fue tratada con premura, dada la grave afección, una vez constatada la positividad de toxoplasmosis".

Además recordaba que, según un informe de la inspección médica, "una vez detectada esta patología debía de hacerse una segunda determinación entre una y tres semanas posteriores, pues si la infección para el feto se confirma la evolución de éste es muy problemática".

Ante estos hechos, el tribunal decidió conceder a los padres una indemnización de 270.456 euros "correspondiente a los daños al hijo por las lesiones producidas por el nacimiento y sus secuelas, derivadas del hecho de haber sido infectado por la toxoplasmosis que padecía la madre y que no fue adecuadamente tratada y se contagió al hijo", cuyo grado actual de minusvalía es del 94 por ciento.

La Audiencia Nacional también valoró el sufrimiento de los padres a consecuencia de la enfermedad de su hijo "y las consecuencias que de ello se derivan en el ámbito familiar y personal", pero rechazó indemnizarles por otros conceptos al estimar que la sanidad pública y los servicios de asistencia social atenderían las necesidades del niño en el futuro.

El Supremo dice ahora, sin embargo, que la indemnización concedida a los padres "no es suficiente para compensar a los mismos por los (gastos) derivados de la atención por un tercero del hijo de los recurrentes, que ha sufrido una grave enfermedad y cuyos daños (...) estima esta sala que resultan insuficientemente valorados" por la primera sentencia.

El Alto Tribunal cifra la indemnización en 480.000 euros y dice que esa cantidad "ha de entenderse que comprende ya el total de la compensación actualizada del conjunto de daños sufridos por los recurrentes y su hijo menor".

El bajo peso al nacer aumenta el riesgo de diabetes y cardiopatías

Vida | 16/04/2004 - 02:55h | Actualizado el 31/05/06 - 09:34h

Barcelona. (EFE).- El bajo peso al nacer está directamente asociado a las enfermedades cardiovasculares y la diabetes en la edad adulta, según se ha destacado en una jornada sobre el retraso de crecimiento intrauterino en la que se ha tratado de los beneficios de la hormona de crecimiento al tratar a estos niños.

Según se ha explicado en esta jornada, celebrada en el hospital de Sant Joan de Déu de Barcelona, en los últimos años ha aumentado el número de niños con bajo peso, que son los que nacen al término del periodo de gestación pero con menos de 2,5 kilogramos.

También se ha constatado que con el tratamiento con la hormona del crecimiento, además de mejorar la talla, se reduce la incidencia de enfermedades asociadas a esta patología, aunque la secreción de dicha hormona sea aparentemente normal.

Lourdes Ibáñez, endocrina del hospital, ha remarcado que la desnutrición del feto puede ser por problemas en la placenta, que es el órgano que aporta los nutrientes y el oxígeno, o por infecciones como rubéola, sífilis o toxoplasmosis, y en estos casos el bebé usa sus reservas para que los órganos vitales como el cerebro o el corazón se puedan desarrollar, lo que hace que disminuyan su peso y talla.

5.2 Articles de veterinaris

Toxoplasmosis

por Dr. Félix Vallejo López

Publicado: 20/05/2001

Dr. Félix Vallejo López es el Director Veterinario y Cirujano Jefe del Hospital Veterinario Happy Animal (Zona Arturo Soria, calle General Aranaz).

Doctor estoy embarazada y tengo gatos, puedo contagiarme con la Toxoplasmosis ¿sí o no?

Con esta pregunta tan radical comienzan muchas de nuestras consultas, cuando abordamos este tema o mejor dicho al escucharla nos damos cuenta cuál es la preocupación de nuestra interlocutora, en algunos casos la pregunta es otra "Mire, el medico me ha dicho que soy negativa a toxoplasma, y que puedo contagiarme de mi propio gato".

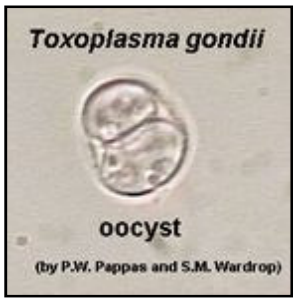
El drama familiar está servido "micifu", "tobias" o "jonas" nuestro gatito, nuestro fiel compañero parece ser que puede llevar un ALIEN dentro que nos arruine la vida. **Pues bien esto no es así**, lo primero es saber quien es este criminal cual es la auténtica verdad sobre sus fechorías.

Nombre: *Toxoplasma Gondii*

Residencia Habitual : Carne cruda, verdura sin lavar, heces de gato.

Lugar de reproducción : Intestino del gato.

Historial delictivo: Diarreas leves, síntomas neurologicos y malformaciones fetales, desde leves a muy graves o incluso mortales.



Con estos cargos en la mano nos damos cuenta que lo que realmente es importante es saber en qué momento este delincuente puede afectarnos.

El toxoplasma es un protozoo es decir es un animal unicelular microscópico y parásito, ¿se puede tener una vida más triste?, pues sí, ya que además es dañino para la salud. **Su única posibilidad de reproducirse es en el intestino de los gatos**, al gato no le causa en la inmensa mayoría de los casos ningún problema, sólo una leve apatía y en algunos casos diarrea, que pasa incluso inadvertida. A los pocos días de la infección el gato eliminará oocistos (huevos), pero sólo durante dos o tres semanas durante toda su vida, de modo que nuestro pobre gato tiene poca incidencia de contagio de este problema, además debemos saber que estos oocistos necesitan al menos 24 horas para poder infectar. De modo que el manejo de las deposiciones en estas primeras 24 horas no acarrea ningún riesgo.

El contagio aparece por ingestión de estos oocistos que en nuestro digestivo como en el resto de los mamíferos y aves no se reproduce sino que lo atraviesa y se enquista en nuestro sistema muscular, nervioso o bien atraviesa la placenta fetal en caso de embarazo siendo responsable de alteraciones en le feto. Todas estas cosas terribles aparecen en personas inmunodeprimidas o sometidas a estrés fisiológico como puede ser un embarazo, **un hombre sano vencerá al protozoo sin problemas**.

La otra vía de infección es la de ingestión de quistes, que se encuentren en la carne poco hecha, por eso es importante cocinar la carne mucho, el microondas no asegura por tiempo ni por temperatura la consecución de la NO infectividad del alimento, al mismo tiempo la congelación doméstica tampoco lo consigue.

Poco a poco tenemos claro como podemos contagiarnos, así que ahora será más fácil prevenirlo. Esta claro que en nuestros animales domésticos la vía de la ingestión de quistes es posible, si nuestro gato sale al exterior y caza ratones o pajarillos, por lo tanto no debemos permitirlo. Y al mismo tiempo que bandejas de arena o jardines muy concurridos por colectivos felinos pueden ser un lugar de entrada para estos molestos parásitos, con respecto a nuestro gato.

Manejemos cifras, sólo entre 4 y 7 gatos de cada 10 en España ha sido expuesto a *Toxoplasma gondii*, y sólo 3 ó 4 personas de cada 10 presenta anticuerpos de toxoplasma.

Expliquemos estos datos y desentrañemos más la maraña. **¿Qué significa tener anticuerpos de toxoplasma?** Simplemente significa que en algún momento hemos sido expuestos a este germen y nuestro cuerpo evidentemente ha reaccionado correctamente venciendo la enfermedad, y estos anticuerpos nos defenderán correctamente si volvemos a ponernos en contacto con el toxoplasma, por este motivo a todas las mujeres embarazadas se les realiza esta prueba por que si ya tenían anticuerpos todo está solucionado esta protegida. Pero si no los tiene es cuando debemos proteger a la madre del posible contagio con el germen, el mayor riesgo aparece en la primera mitad de la gestación pudiéndose ocasionar desde ceguera a retraso mental, en la última mitad de la gestación el contagio es menos grave sólo produciéndose daños leves.

¿Por qué no realizamos las pruebas de anticuerpos a nuestros gatos y así sabemos si lo tienen o no?, pues en este caso nos orienta si hace mucho o poco tiempo que se ha expuesto a la enfermedad pero realmente nos importa poco saber si el gato ha padecido o no la infección ya que lo que nos interesa es saber si realmente esta eliminando oocistos o no. Y con esta prueba no lo tenemos muy claro. Además sabemos que solamente eliminan oocistos durante 2 ó 3 semanas después de la infección intestinal luego no, de modo que **el gato como tal no es una fuente de contagio efectiva real**, la mayoría de los contagios son a nivel alimentario por comer carne poco hecha o bien por manejar carne cruda y no lavarse las manos.

Como conclusión debemos tener claro una serie de normas de actuación para evitar tener problemas como son:

A nivel alimentario

- No comer ni manejar carne poco hecha y si la tocamos lavarnos bien las manos con agua y jabón.
- Lavar muy bien los vegetales y tener una pauta similar a la de la carne.
- Nunca probar las comidas hasta que no estén perfectamente cocinadas.
- No tomar agua en cauces naturales si sospechamos que puedan estar contaminados con heces de gato.

A nivel de nuestra mascota

- No permitir el acceso de nuestra mascota al exterior para evitar que pueda cazar animales, (los pajaritos y los ratones harán fiesta seguro).
- Limpiezas de la bandeja del gato todos los días así evitaremos que los oocistos se hagan infectivos, aunque lo más útil sería que le endosáramos tal cometido a otro miembro de la familia, pero si no se dejan entonces deberíamos usar guantes de jardinería y después lavarnos bien las manos . Usar mascarilla también es interesante evitaremos el polvillo que puede ser también infectivo.
- No jugar con gatos desconocidos y sino lo podemos evitar lavarnos bien las manos.
- Lavarnos las manos con agua y jabón tras jugar con nuestros gatos.

Pues esto es todo por hoy, no debemos hacer las maletas de nuestro gato, todo tiene solución.

5.3 Artícles científics (annexes)

Toxoplasmosis in pregnancy. *The American Journal of Medecine* (2005, nº 118, pág. 212-216)

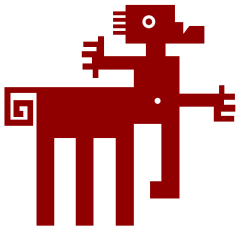
Toxoplasmosis. *The Lancet* (2004, 363, pág 1965-1976)

Management of *Toxoplasma gondii* Infection during Pregnancy. *Clinical Infectious Diseases* (2008, 47, pág. 554-566)

6. ENQUESTES D'OPINIÓ

Per comprovar la opinió dels grups afectats en aquest tema, vam voler entrevistar a dones que han estat embarassades (algunes amb gat, d'altres sense), veterinaris de petits animals i ginecòlegs.

A continuació posem les enquestes i les conclusions que hem tret després del buidatge.



1. **Tens gat/Tenies gat quan estaves embarassada?**
    a. **Si**
    b. **No**

2. **El teu ginecòleg et va informar sobre els riscos de la toxoplasmosis?**
    a. **Si**
    b. **No**

3. **Quins consells et va donar?**
    a. **Fer-te el panell TORCH**
    b. **No menjar carn crua**
    c. **Netejar bé fruites i verdures**
    d. **Rentar-se bé les mans després de manipular carn crua/fruites i verdures/un gat**

    (només en el cas de tenir gat)
    e. **Que una altra persona s'ocupi de la neteja de la sorra del gat**
    f. **Netejar i desinfectar periòdicament la zona on el gat està habitualment**
    g. **Vigilar que el gat no sortís de casa/mengés carn crua**
    h. **Desfer-se del gat.**

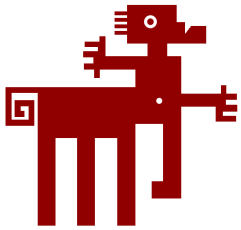
    i. **Altres:**

4. **Et vas fer el panell de TORCH?**
    a. **Si: quin va ser el resultat?**
    b. **No: per què?**

5. **Portes habitualment el teu gat al veterinari? (vacunes, desparasitacions, etc.)**
    a. **Si**
    b. **No**

6. **Vas consultar al veterinari quan et vas quedar embarassada?**
    a. **Si: què et va dir?**
    b. **No: perquè?**

7. **Què vas fer/què hauries fet?**
    a. **Fer-li la prova al gat per comprovar si era positiu/si eliminava oocists**
    b. **No manipular el gat durant l'embaràs**
    c. **Desfer-te del gat**



1. **T'has trobat amb casos de dones embarassades mal aconsellades pel seu ginecòleg?**
   a. **Si**
   b. **No**

2. **T'has trobat amb casos d'abandonament de gats degut a la toxoplasmosis?**
   a. **Si**
   b. **No**

3. **Informes a les propietàries de gats sobre aquesta malaltia i les aconselles?**
   a. **Si**
   b. **No**

4. **En cas que la pregunta 3 sigui SI: què els hi aconselles?**
   a. **Netejar bé fruites i verdures**
   b. **No menjar carn crua**
   c. **Prendre precaucions a l'hora de netejar la sorra del gat (guants, etc.)**
   d. **Rentar-se bé les mans després de netejar la sorra i/o manipular el gat**
   e. **No netejar ni manipular el gat durant l'embaràs**
   f. **Evitar que el gat surti de casa**
   g. **Desfer-se del gat**

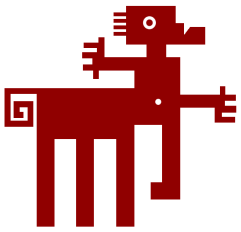
5. **Tens disponible algun mètode diagnòstic per a detectar toxoplasmosis? S/N**
   a. **Detecció d'ooquists en femtes**
   b. **Aïllament per inoculació**
   c. **Detecció d'anticossos per IFI**
   d. **Altres:**

6. **Realitzes de forma rutinària aquesta prova?**
   a. **Si**
   b. **No**

7. **Preu aproximat de la prova:**

8. **Consideres que aquesta és una malaltia important en la nostra geografia i que suposa un risc per a les dones embarassades?**

   a. **Si: per què?**
   b. **No: per què?**



Enquesta a ginecòlegs

1. **Li agraden els animals?**
    a. **Si**
    b. **No**

2. **Informa les seves pacients sobre la toxoplasmosis?**
    a. **Si**
    b. **No**

3. **En cas que tinguin un gat a casa, pren alguna mena de mesura especial?**
    a. **Si: quines?**
    b. **No: per què?**

4. **Què els hi aconsella?**
    a. **No menjar carn crua**
    b. **Rentar bé i/o pelar fruites i verdures**
    c. **Relitzar-se el panell de TORCH**

    (si la pacient té gats)
    d. **Prendre mesures preventives a l'hora de netejar la sorra/manipular el gat (guants, etc.)**
    e. **Netejar-se bé les mans després de netejar la sorra/manipular el gat**
    f. **No netejar la sorra ni manipular el gat durant tot l'embaràs**
    g. **Evitar que el gat surti de casa**
    h. **Que el gat estigui fora de casa durant l'embaràs**
    i. **Portar el gat al veterinari**
    j. **Desfer-se del gat**

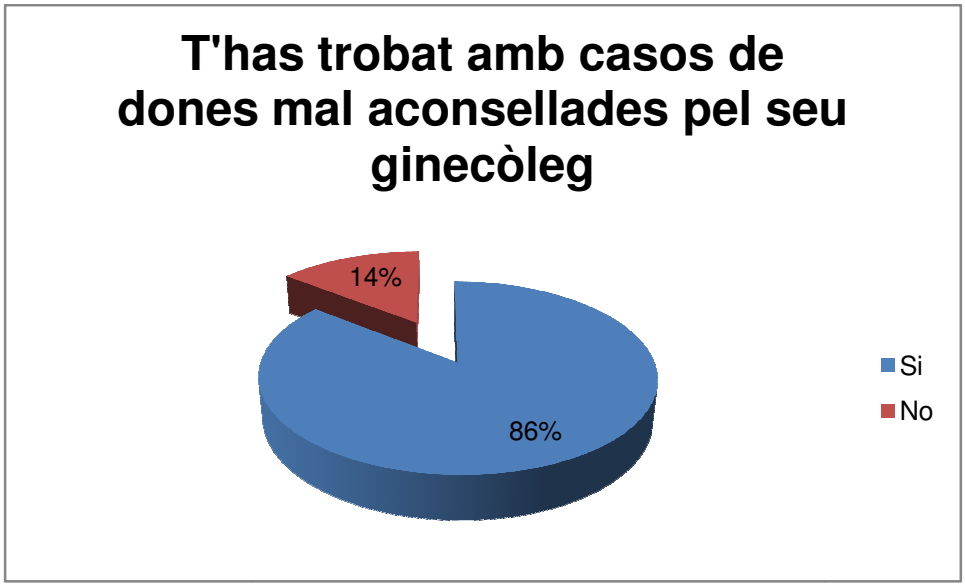
5. **Realitza/aconsella de forma rutinària que les seves pacients es facin el panell de TORCH?**
    a. **Si: per què?**
    b. **No: per què?**

6. **Està d'acord amb que s'abandoni un gat en cas d'embaràs, tot i que existeixin mesures per a prevenir el contagi?**
    a. **Si**
    b. **No**

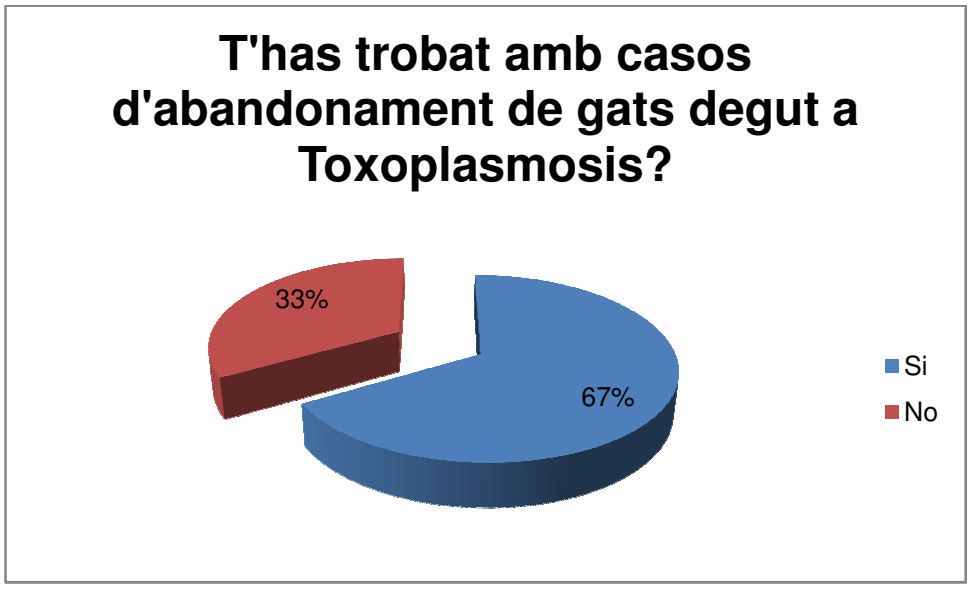
7. **Coneix la probabilitat de contraure la malaltia durant els diferents trimestres de l'embaràs?**
    a. **Si: quina és?**
    b. **No: per què?**

Conclusions enquestes

6.1 Veterinaris:

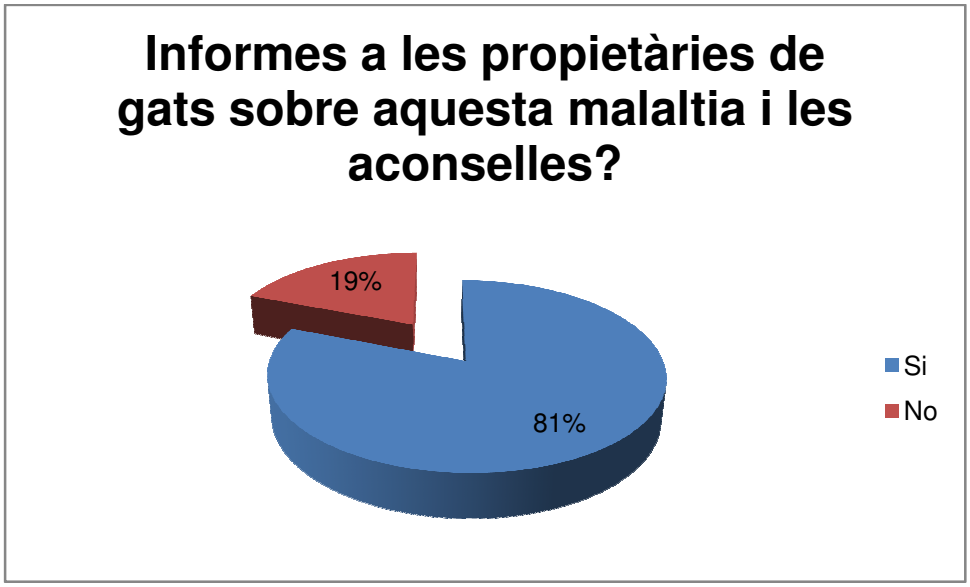


1. La majoria de veterinaris s'han trobat alguna vegada al llarg de la seva vida amb algun cas de dones embarassades preocupades pel perill que suposa aquesta malaltia i buscant altres consells a part dels del ginecòleg. En el cas dels que no s'hi ha trobat mai són veterinaris que porten menys de 3 anys en la professió. Per tant veiem que efectivament és un problema que preocupa a la població femenina i que si demanen el consell del veterinari és perquè, a més a més del seu fill, també els preocupa la seva mascota.

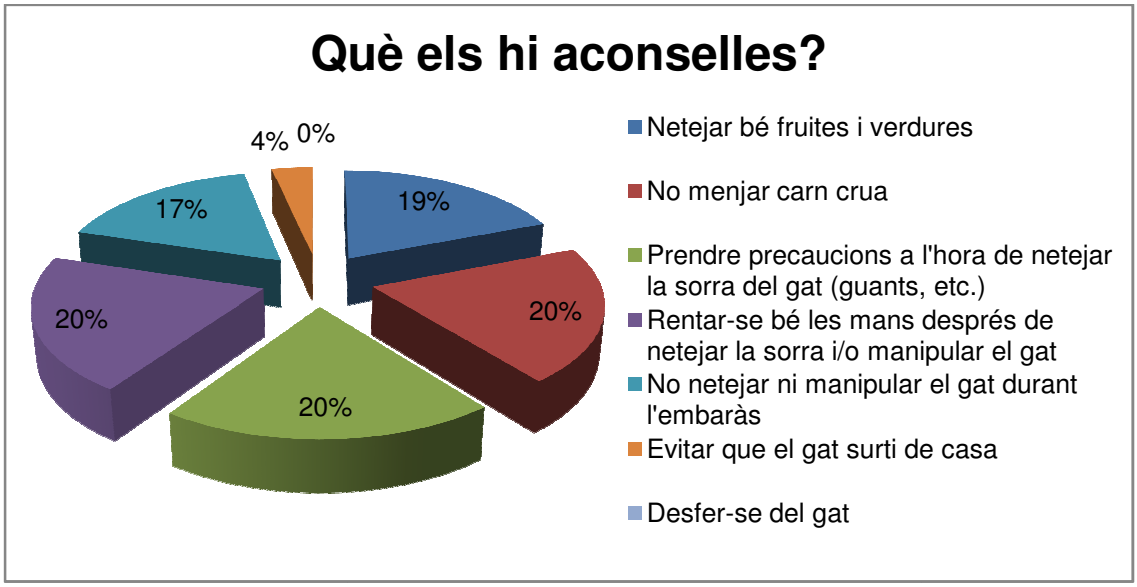


2. Els casos que ens descriuen els veterinaris entrevistats la majoria són gats que al final s'han donat en adopció per por que transmetés la malaltia, tot i que s'hagi intentat convèncer els propietaris del petit risc que suposa en realitat el seu gat. Alguns dels veterinaris que han contestat que ells personalment no coneixien casos d'abandonament per aquest motiu, creuen que el realitat si que s'ha donat l'abandonament però que ells no n'han tingut constància

explícita. De fet és lògic, quan abandones el teu gat per un motiu així no ho expliques al veterinari si saps que no hi estarà gens d'acord.

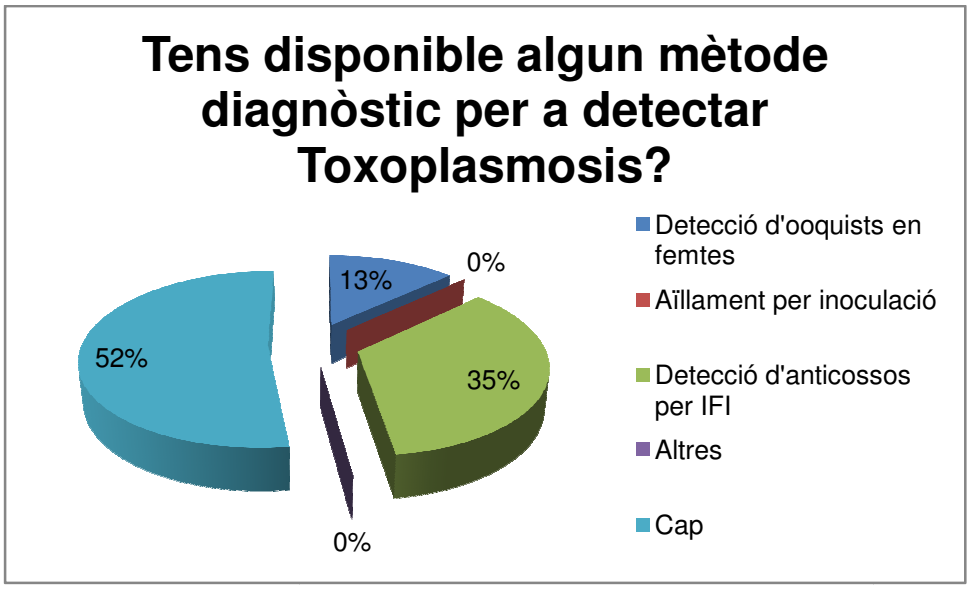


3. El 81% dels veterinaris informen a les dones embarassades de les vies de contagi de la malaltia i de les mesures preventives referents al gat. El 19% restant diuen que només informen si les propietàries pregunten sobre el tema, però si elles no treuen el tema no.

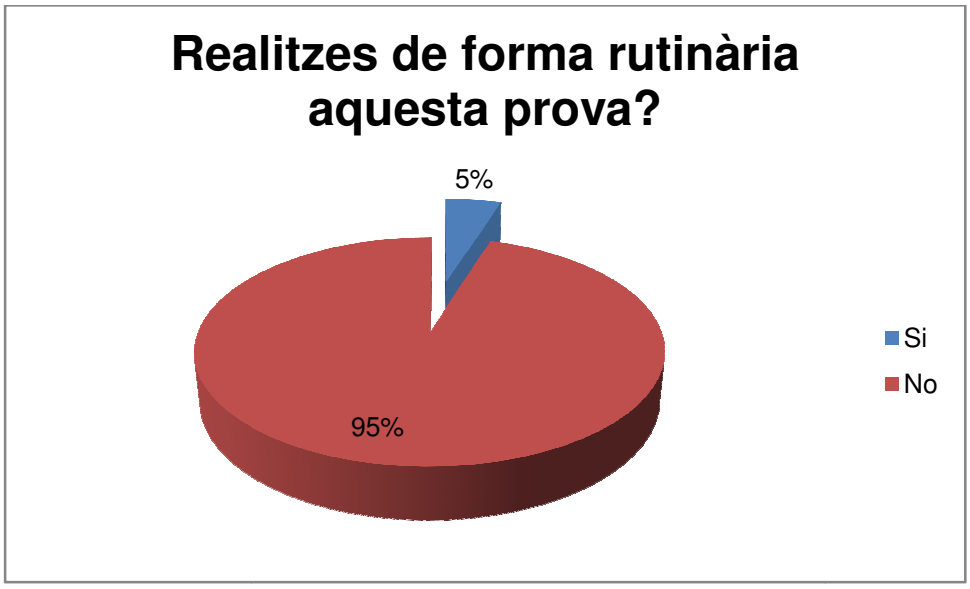


4. Les mesures preventives que més aconsellen els veterinaris són, evidentment, les referents al gat. A més a més aconsellen mesures higièniques correctes pel què fa a la manipulació dels aliments crus. Durant les entrevistes ens hem adonat que destaquen sobretot que els motius de contagi més importants són precisament una manca d'higiene alimentària mentre que és poc habitual que

el gat hi tingui res a veure ja que la majoria de gats de casa estan ben controlats sanitàriament. Tot i això creuen que "no està de més" prendre precaucions a l'hora de manipular les femtes dels gats i el propi gat, però pocs veterinaris recomanen no manipular el gat en tot l'embaràs i els que ho fan només es refereixen a no netejar-lo, però si tocar-lo. Només el 4% dels veterinaris creuen que impedir que el gat surti de casa és una mesura eficaç per evitar que agafi la malaltia.

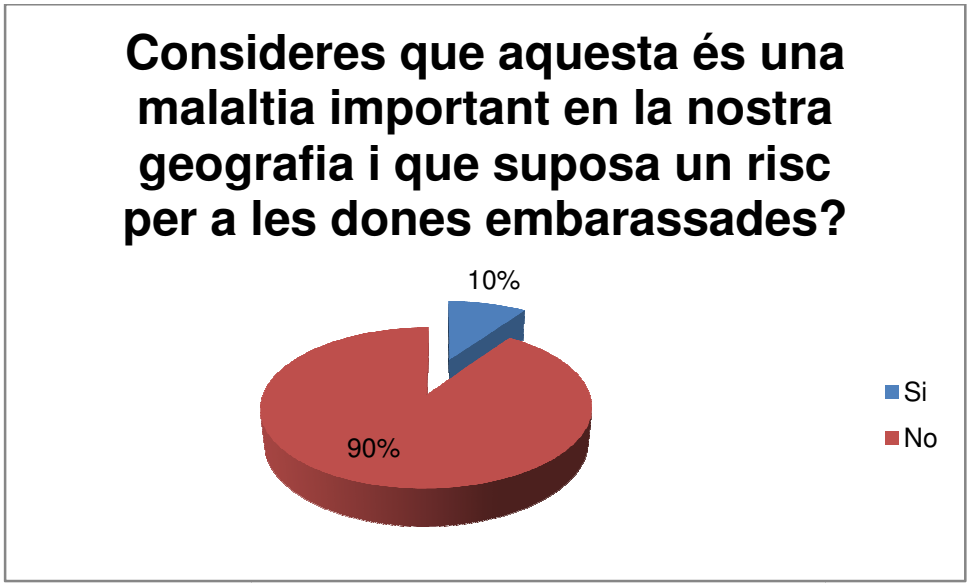


5. La majoria de clíniques veterinàries no tenen disponible cap mètode diagnòstic per detectar la Toxoplasmosis. Els que si que poden diagnosticar-la ho fan a través d'un simple anàlisi coprològic o, més freqüentment, envien la sang al seu laboratori de confiança per detectar els anticossos.



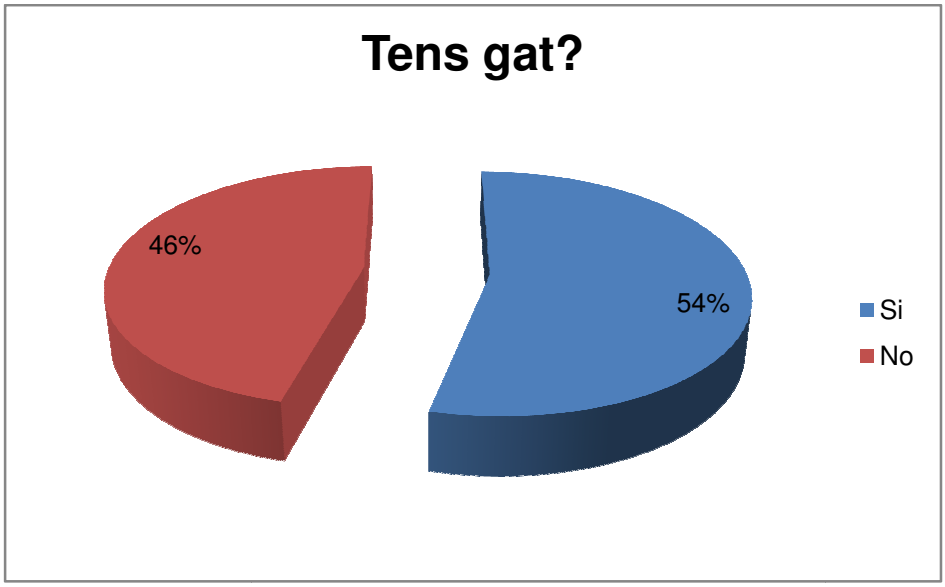
6. Per les enquestes podem concloure que no és una prova que es realitzi rutinàriament a tots els pacients felins de les clíniques, sinó que més aviat es realitza quan ho demanen els propietaris o quan hi ha algun altre signe que faci sospitar la possible afectació del gat.

7. El preu aproximat d'aquesta prova és entre 30-50€ (com un test serològic de Leishmania). Per tant és un preu en la majoria de casos assequible pels propietaris i que permet evitar l'abandonament i els maldecaps causats per la incertesa.

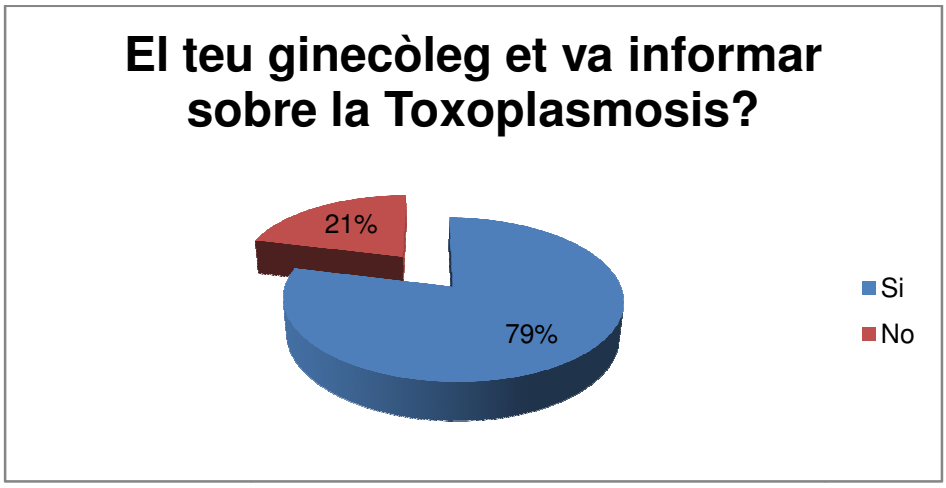


8. Només 1 de cada 10 veterinaris consultats creuen que sigui una malaltia important en la nostra geografia i quan els hi preguntem el motiu, tots contesten que el què realment els preocupa és que és una malaltia molt greu pels efectes en el fetus i que mereix ser tinguda en compte pels ginecòlegs. Els veterinaris que no la consideren important ho justifiquen dient que estadísticament hi ha pocs casos i que la majoria de dones són positives. Segons els nostres estudis (veure els resultats de les enquestes en dones embarassades) això no és del tot correcte ja que gairebé el 80% de les dones que es realitzes el panell de TORCH són negatives, per tant si que és un risc per elles.

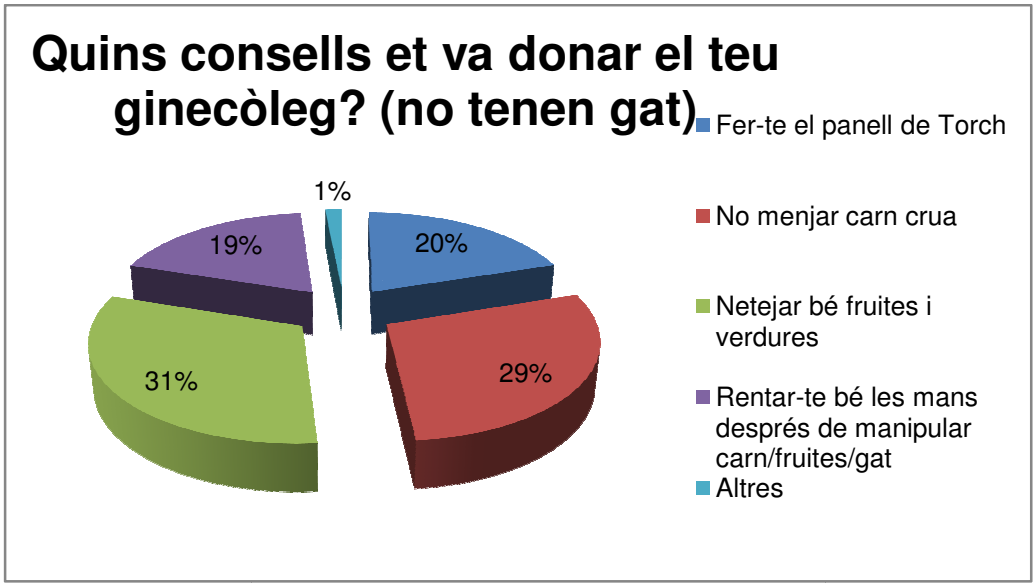
6.2 Dones:

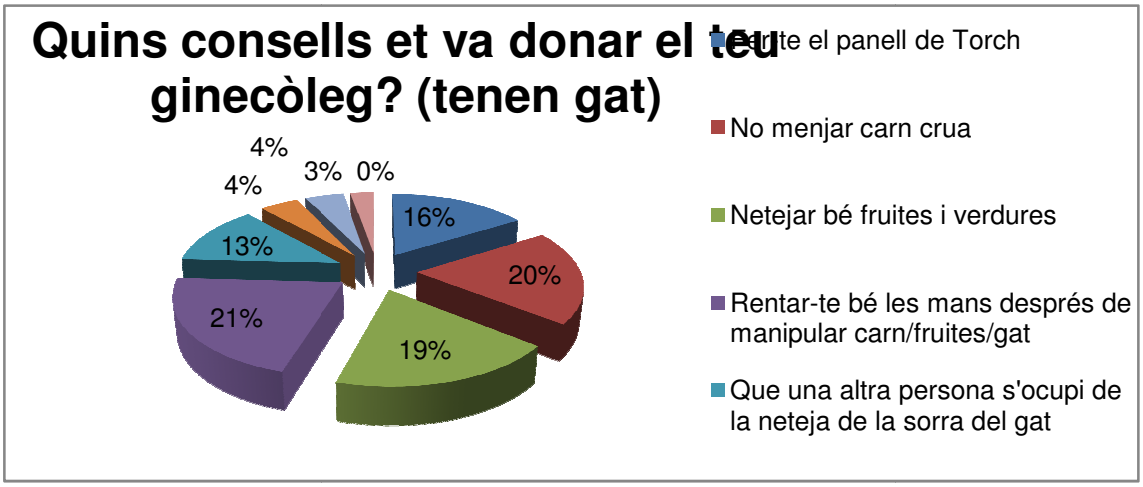


1. Hem entrevistat tant dones que durant l'embaràs han tingut gat com dones que no perquè creiem que és interessant conèixer també l'opinió des d'un punt de vista extern i contrastar-ho amb les decisions reals de les dones que si que es van trobar amb el problema del gat durant aquells nou mesos tant importants per elles.

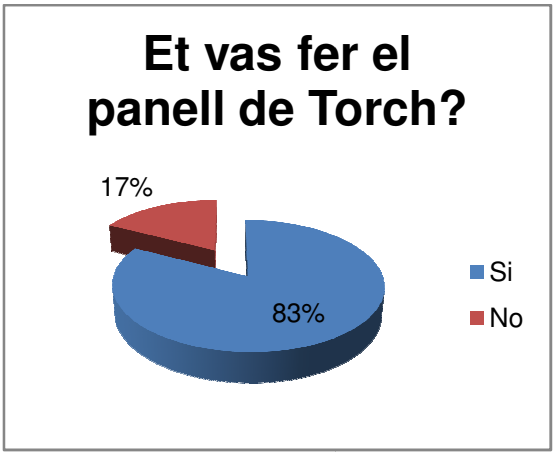


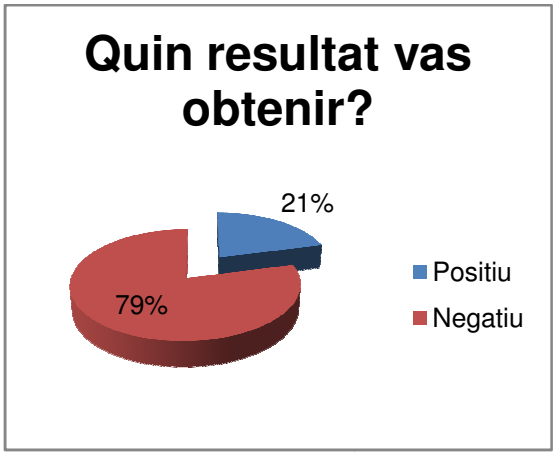
2. Tant en el cas de les dones que havien tingut gat com les que no, el seu ginecòleg o ginecòloga els va advertir del possible perill que suposa aquesta malaltia pel fetus.



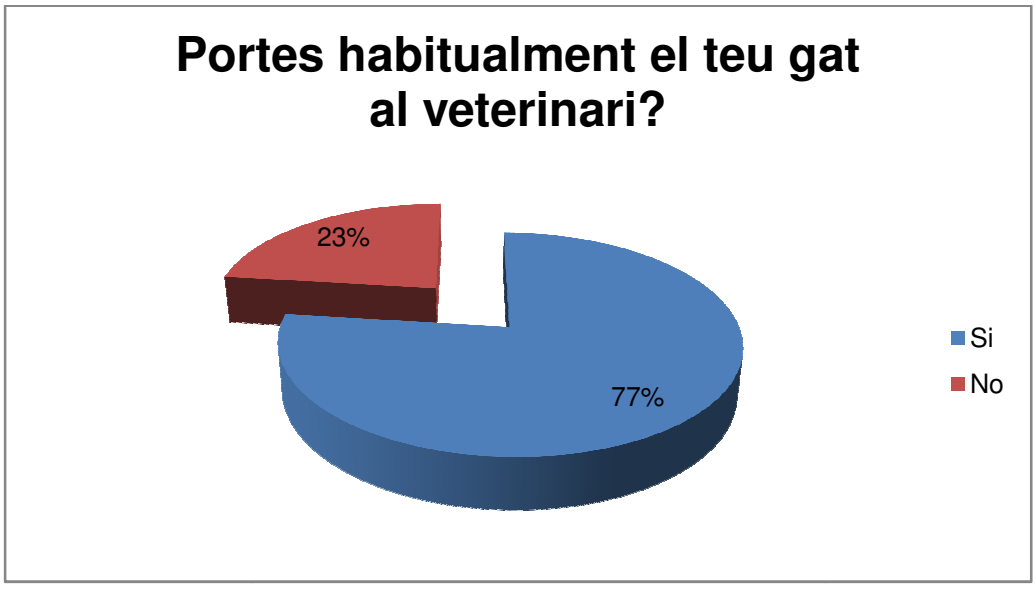


3. Pel què fa a les recomanacions si que són diferents si tenien gat o no. En el cas de que no tinguessin gat, les precaucions es centraven en la bona higiene personal i dels aliments. En un cas el ginecòleg va recomanar que no es tingués contacte amb gats de carrer per evitar el contagi. Pel què fa a les dones que tenien gat, a més a més d'una bona higiene personal i dels aliments, tots recomanaven anar amb més precaució amb el gat: la majoria simplement netejar més freqüentment la zona del on el gat està normalment per evitar que els oocists esporulessin, alguns recomanaven directament cedir les cures i atencions del gat a una altra persona mentre durés l'embaràs. Un 3% recomanaven desfer-se del gat ja que el consideraven la principal (en un cas, la única) font de contagi de la Toxoplasmosis. Es recomanava la realització del panell de TORCH trimestralment sobretot en les dones que tenien gats.



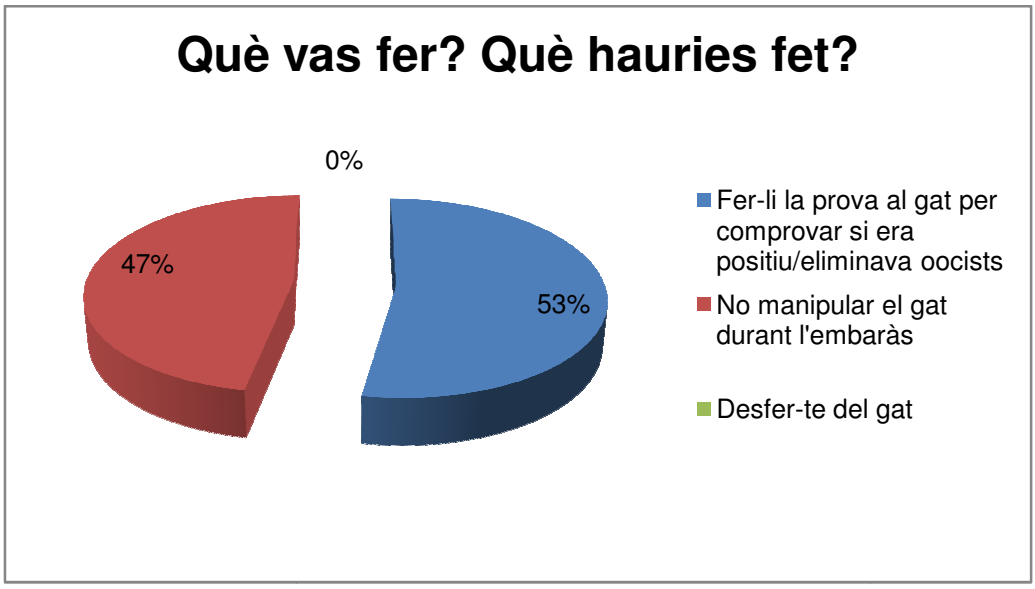


4. Més d'un 80% de les dones embarassades es van realitzar aquesta prova independentment de si tenien gat o no perquè el ginecòleg els hi ho recomanava degut a les altres vies de contagi possibles. El resultat és que en gairebé un 80% de la població que el realitzava el resultat era negatiu, per tant no havien estat mai infectades per Toxoplasma. Això ens fa pensar en positiu ja que, malgrat el risc, el contagi és difícil.



5. Les dones que tenien gat contestaven que mantenien una bona condició sanitària del seu gat realitzant-li habitualment controls veterinaris i oferint-lis una bona alimentació i qualitat de vida.

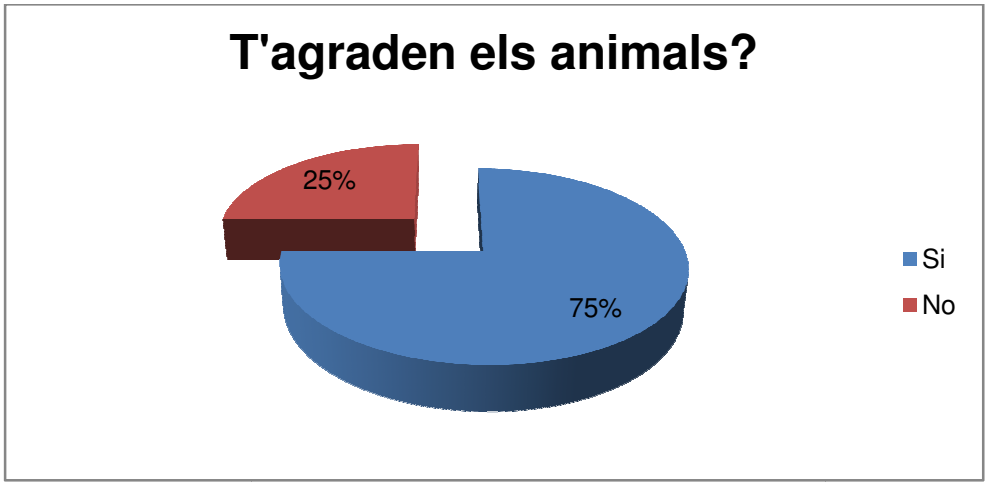
6. Referent a si van buscar una segona opinió en el seu veterinari de habitual, gairebé un 70% diuen que no. Hem observat que les dones que no van recórrer al seu veterinari són les que el seu ginecòleg ja les havien aconsellat sobre les cures del gat, mentre que les dones les quals el seu ginecòleg no els explicava bé les vies de transmissió, o que directament els hi deia que deixessin el seu gat, si que acudien al veterinari per contrastar la informació. Algunes de les dones entrevistades són veterinàries i per tant s'inclouen dins el grup de "No" perquè elles ja tenien aquesta informació.



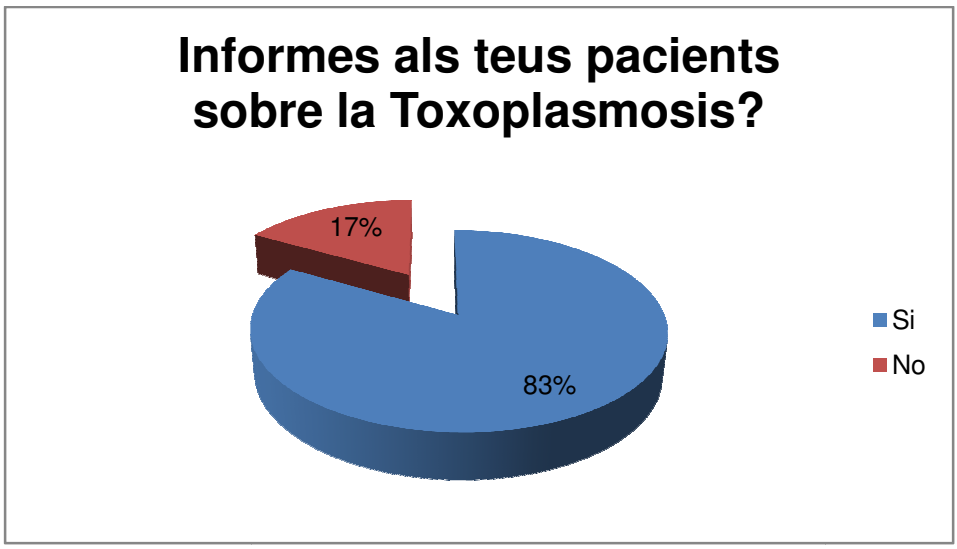
7. Gairebé la mateixa proporció de dones van fer o haurien fet una prova al seu gat per comprovar si resultava un focus d'infecció o si estava sa que les que directament haurien decidit no manipular el gat durant tot l'embaràs per "si de cas". Comprovant les enquestes veiem que la gran majoria de dones que van

decidir no manipular el gat durant l'embaràs són les que no van consultar al seu veterinari.

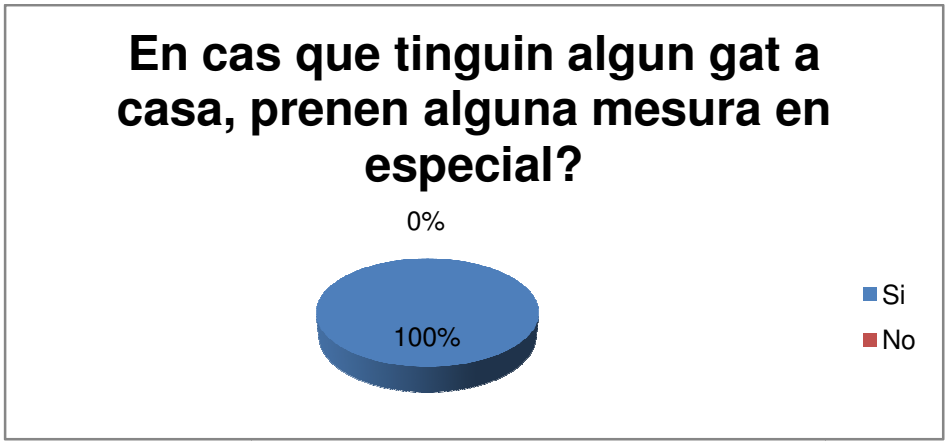
6.3 Ginecòlegs:



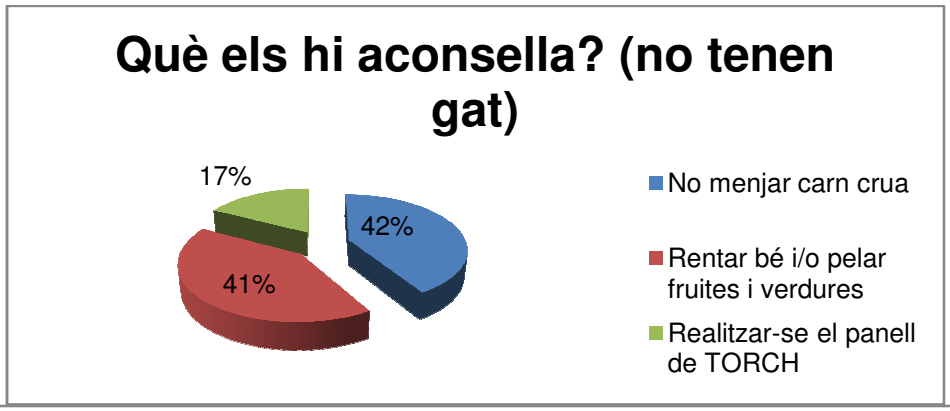
1. La majoria de ginecòlegs entrevistats tenen o els agraden els animals, de manera que esperem que els resultats siguin favorables a aquest animals.

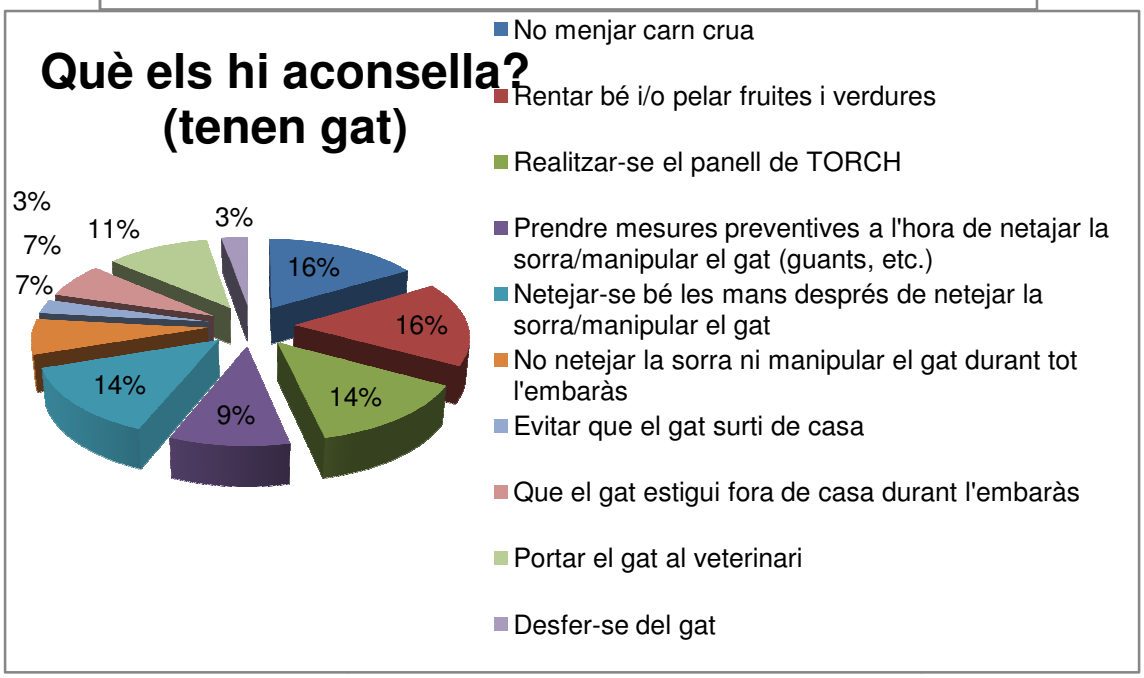


2. Més del 80% dels ginecòlegs informen a les pacients que tenen gats del risc de la malaltia, però si no tenen gats normalment ja no els hi expliquen res dels riscos sobre la transmissió pels gats, només la prevenció amb mesures higièniques.



3. En tots els casos es recomanen precaucions especials a tenir en compte a casa si tenen un gat.

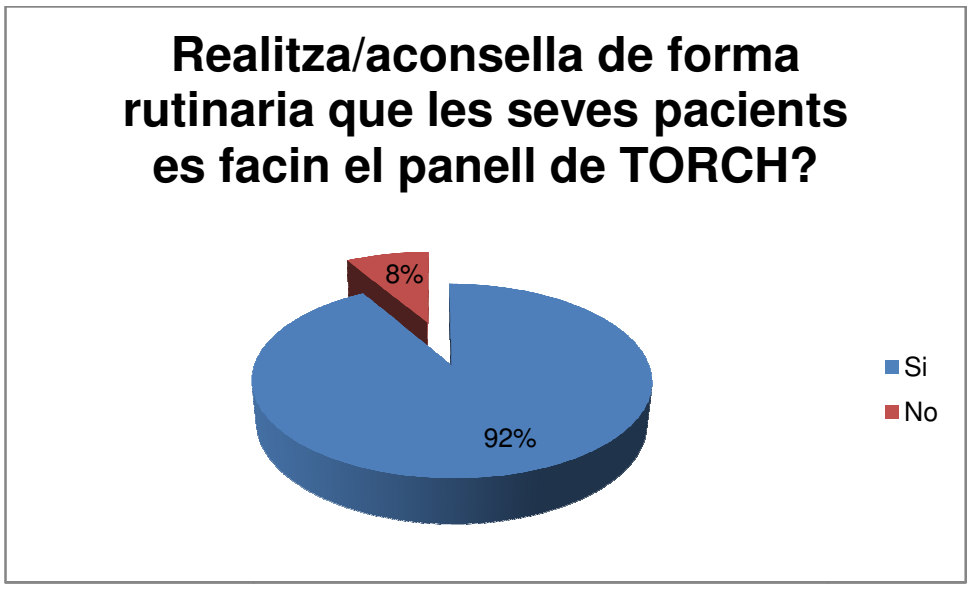




4. Com ja hem comentat, les mesures que s'aconsellen tenen a veure amb la neteja de les fruites i verdures i de la carn crua. En pocs casos es recomana

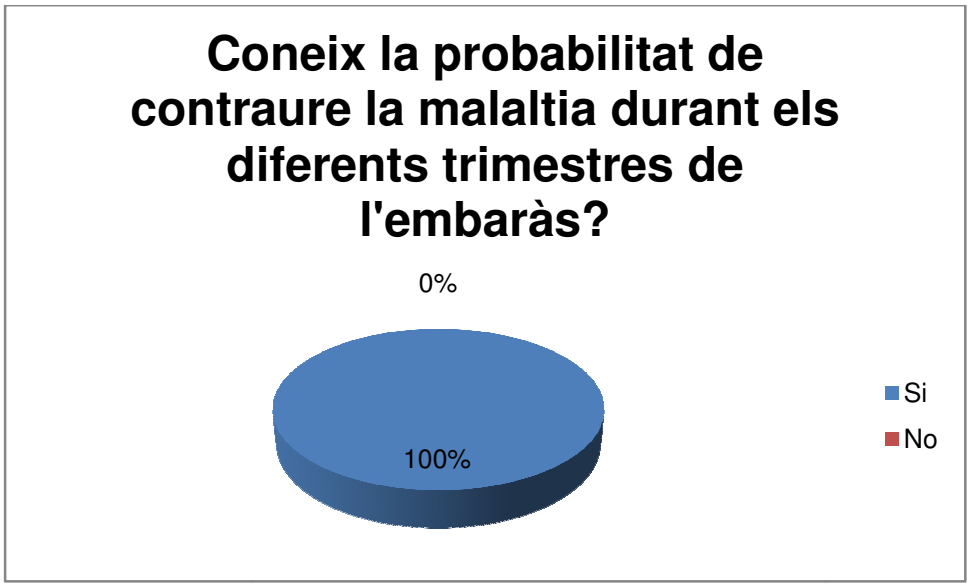
realitzar el panell de TORCH ja que ho relacionen només amb el risc de contraure-ho per tenir gat.

Si tenen gat, la cosa canvia: la majoria de ginecòlegs recomanen anar en compte amb les femtes dels animals. Malauradament en pocs casos es recomana dur el gat al veterinari. Alguns ginecòlegs aconsellen que el gat no surti de casa per tal d'evitar que agafi la malaltia menjant carn crua o contacte amb altres gats. A part de les mesures relacionades amb el gat també tenen en compte que es pot transmetre per una mala higiene de les fruites i verdures i consum de carn crua i per tant reconeixen que també són una font de contagi important.



5. Pel què sembla el panell de TORCH és una prova rutinaria que recomanen la majoria de ginecòlegs, sobretot quan es tracta d'una dona que tingui gats a casa o que hi pugui estar en contacte. Si no hi estan en contacte, no ho recomanen tant.

6. Aquests resultats s'assemblen a la gràfica inicial de si els hi agraden o no els animals. Això ens fa pensar que les preferències del ginecòleg influeixen directament en els seus consells i, per tant, en la decisió de la dona embarassada.



7. Tots els ginecòlegs reconeixen que segons el terç de l'embaràs és més o menys probable contraure la malaltia i que per tant cal prendre precaucions diferents segons l'estat de gestació.

7.CONCLUSIONS

Arribat aquest punt del treball, intentarem sintetitzar el que hem intentat transmetre en ell.

La nostre idea és aconseguir que tota la mala informació que fins ara hi ha hagut sobre el tema de la toxoplasmosi quedi enrere. Que a partir d'ara cap més gat es trobi menyspreat i abandonat per por a que pugui contagiar aquesta malaltia.

Durant el procés d'elaboració del treball hem sortit al carrer a parlar i preguntar a la gent què saben sobre la transmissió de la toxoplasmosis deguda als gats. Hi ha hagut respostes de tot tipus, des de gent que no té ni idea, altres que tenen una pinzellada més o menys certa fins els que creuen que ho saben tot però realment no saben res.

Els veterinaris enquestats, òbviament (al menys la majoria), tenen clar el tema i com informar als seus clients, però el problema és que no es una cosa que es faci de manera rutinària.

En quant als ginecòlegs lamentablement la decisió que prenen en front la malaltia depèn en gran part de si els hi agraden o no els animals. Això és una actitud totalment incorrecta que porta al abandonament innecessari i cruel dels nostres animals. Personalment creiem que aquesta actitud és intolerable i hauria de ser denunciable i condemnable. No pot ser que encara a dia d'avui el futur de la teva mascota depengui d'algú que és capaç de distorsionar la realitat d'una malaltia pel fet de que a ell no li agraden els animals. És cert també que moltes dones embarassades (la majoria de les enquestades) han estat ben informades pels seus metges i/o matrones.

Les dones (tant embarassades com no), tenen respostes varies. N'hi ha que mai es desfarien del seu animal i d'altres que no necessiten gaires influències per fer-ho. Qualsevol d'aquestes no representa cap problema (encara que per desgracia alguna se'n desfaria ràpidament), en el sentit de que ja tenen les coses clares; el problema més important segons el nostre parer es dóna en les persones que per desconeixement es deixen influenciar pels consells de gent que tampoc sap res sobre el tema i arriben al fatal desenllaç.

En quant a legislació, pensem que aquest és un tema sobre el que és difícil legislar. Com s'ha vist no existeix cap model a seguir, i trobem el projecte de llei presentat a Argentina una mica abusiu (veure l'apartat de 4 d'aquest treball). El que pensem que seria una bona idea és regular d'alguna manera que els ginecòlegs estiguessin obligats a informar les seves pacients sobre els riscs reals de la toxoplasmosis i les eines que hi ha per prevenir-la. Degut a la manca de legislació, creiem que si un ginecòleg no té els coneixements necessaris o no es veu capacitat per transmetre'ls de manera correcte; el més adient és que referís a la futura mare a un veterinari.
Pel que fa a la informació disponible, els ginecòlegs i els veterinaris no en són l'única font: articles de premsa, articles científics, blogs i pàgines d'internet, etc. Tot i així, recomanem fer un ús responsable d'aquestes fonts i consultar sempre en última instància un a veterinari o a una associació com la Fundació Silvestre o GEMFE, especialitzades en medicina felina.

Esperem doncs que hagin quedat clares certes coses com:
-La toxoplasmosi és una malaltia difícilment transmissible pel contacte amb gats.
-Les fonts de transmissió més habituals són la carn poc cuinada i les verdures mal rentades.
-Els gats només poden transmetre la malaltia la primera vegada que s'infecten i durant un període de fins a tres setmanes.
-Si les femtes de gats infectats es retiren abans de 24h o després d'una setmana no hi ha contagi possible.
-Si la dona embarassada s'ha fet la prova de la toxoplasmosi i és positiva ja no es pot tornar a infectar i no ho pot transmetre al fetus.
-Amb un mínim d'higiene no hi ha d'haver-hi cap problema per seguir tenint la mateixa relació amb el teu gat que abans d'estar embarassada.

Aquest treball ens ha servit per a conèixer més sobre el tema, però sobretot per a saber quina és la situació actual i l'opinió de la gent (tant especialistes en medicina com gent del carrer). Aquest coneixement ens ajudarà a ser més conscients d'aquest problema un cop estiguem de cara al públic, el que

esperem que pugui ajudar a reduïr el nombre d'animals que s'abandonen degut a la ignorància dels seus propietaris. També esperem que la nostra feina serveixi per a obrir els ulls a tota aquella gent que hi tingui accès, o si més no, a aquells que hem entrevistat i enquestat durant la realització d'aquest treball.

8.BIBLIOGRAFIA

Llibres

- Acha PN, Szyfres B. (1992). Toxoplasmosis. En: Acha PN, Szyfres B (ed). Zoonosis y enfermedades transmisibles comunes al hombre y a los animales. Washington. Panamericana, 646-658.
- Bowman DD. (2007). Parasites of cats. En: Baker DG (ed). Flynn's Parasites of laboratory animals. Iowa. Blackwell Publishing, 579-615

Articles

- Kravetz JD, Federman DG. (2005). Toxoplasmosis in pregnancy. The American Journal of Medecine 118(3). 212-216
- Montoya JG, Liesenfeld O. (2004). Toxoplasmosis. The Lancet 363(9425). 1965-1976
- Montoya JG, Remington JS. (2008). Management of *Toxoplasma gondii* Infection during Pregnancy. Clinical Infectious Diseases 47(4). 554-566

Pàgines web

- http://www.lexureditorial.com/boe/0308/15900.htm#ind1590014
- http://www.aesan.msc.es/ca/AESAN/web/cadena_alimentaria/detalle/introduccion_zoonosis.shtml
- http://www.umm.edu/esp_ency/article/003350.htm
- http://www.saludymedicinas.com.mx/articulos/1996/perfil-de-torch-por-un-embarazo-seguro/4
- http://www.legifrance.gouv.fr/
- http://www.legislation.gov.uk/browse/uk
- http://www.normattiva.it/
- http://www.diputados.gob.mx/LeyesBiblio/
- http://laws.justice.gc.ca/eng/
- http://www.lexadin.nl/wlg/legis/nofr/usstates/lxweusa.htm
- http://www.elsitiodelderecho.dtj.com.ar/leg_arg.htm
- http://senadoreduardomelchiori.blogspot.com

IMPORTANTE

- El gato es la única especie animal que puede transmitir la forma contagiosa del parásito de la Toxoplasmosis y sólo lo puede hacer una vez en su vida.
- En la mayoría de los casos, el contagio no se debe al gato de casa.
- Siguiendo unas pautas básicas de higiene, se puede evitar el riesgo de contraer la enfermedad.
- La Toxoplasmosis no debería ser un motivo para abandonar a nuestro gato.

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LOS GATOS Y LA TOXOPLASMOSIS

Riesgos reales de contraer la enfermedad

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LOS GATOS Y LA TOXOPLASMOSIS

Riesgos reales de contraer la enfermedad

La Toxoplasmosis es una enfermedad infecciosa ocasionada por un parásito, el Toxoplasma gondii. En la mayoría de los casos, la infección suele ser asintomática y como mucho se asemejará a una gripe. Pero en el caso de mujeres embarazadas y personas con problemas de inmunodeficiencia es preciso tener en cuenta una serie de precauciones.

Vías de infección de la Toxoplasmosis

La infección por Toxoplasmosis puede ocurrir por cuatro vías:

- Teniendo contacto oral con tierra, agua y hortalizas infectadas.
- Comiendo carne cruda o poco hecha infectada.
- Teniendo contacto oral con heces de gato infectadas.
- Por transmisión congénita.

En la mayoría de los casos, el gato de casa no es el transmisor y, siguiendo unas pautas básicas de higiene, se puede evitar el riesgo de contraer la Toxoplasmosis.

El gato como portador del parásito

El gato es la única especie animal que puede transmitir la forma contagiosa del parásito aunque muchos animales, entre ellos el ser humano, pueden ser portadores del mismo mediante la presencia de quistes tisulares microscópicos en los músculos.

Pero para que se produzca esta transmisión, deben darse las siguientes coincidencias:

1) El gato debe infectarse comiendo un ratón, un pájaro, otro animal o carne cruda previamente infectada.

   ➜ *El gato casero que no sale de casa y que come alimentación preparada, no se puede infectar.*

2) Si el gato se infecta, sólo libera el parásito en las heces una vez en su vida y durante unas pocas semanas. Aunque se infecte de nuevo, ya no liberará más veces el parásito.

3) Para que el parásito de las heces sea contagioso, éstas tienen que estar en contacto con el aire más de 24 horas.

   ➜ *Limpiando la bandeja a diario, este riesgo no existe.*

4) Para infectarse con este parásito, se tienen que manipular las heces con las manos y tiene que haber contacto oral con las mismas.

   ➜ *Limpiando la bandeja con pala y con guantes a diario, este riesgo no existe.*

El embarazo

En el caso de mujeres embarazadas, en el primer trimestre la probabilidad de que la enfermedad se transmita al feto es más baja, pero por el contrario el riesgo para el feto es más grave.

En el tercer trimestre ocurre lo contrario, la probabilidad de contraer la enfermedad es más elevada pero la sintomatología es más leve.

Pautas básicas de higiene a seguir para evitar el contagió de toxoplasmosis

- Lavarse las manos varias veces al día.
- Quitar las heces de la bandeja a diario con una pala.
- Limpiar la bandeja con agua caliente.
- No dar carne cruda al gato de casa.
- Que el gato no salga de casa.
- Realizar los trabajos en el jardín o huerto con guantes.
- No comer carne cruda o poco hecha, y quitar la piel o lavar las hortalizas antes de consumirlas.

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REVIEW

Toxoplasmosis in pregnancy

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KEYWORDS:
Toxoplasmosis;
Congenital infection;
Primary prevention;
Risk factors

ABSTRACT: Pregnant women who acquire infection from *Toxoplasma gondii* usually remain asymptomatic, although they can still transmit the infection to their fetuses with severe consequences. Given the asymptomatic nature of most *Toxoplasma* infections, primary prevention in pregnant women may lower the risk of congenital toxoplasmosis. Both consumption of undercooked meat and unprotected contact with soil are independent risk factors for *T. gondii* seroconversion during pregnancy, while contact with cat litter may pose a risk in certain situations. However, many pregnant women lack knowledge of these risk factors. This article reviews toxoplasmosis infection in pregnancy, with an emphasis on risk factors and appropriate counseling of pregnant women.

Toxoplasma gondii is an obligate intracellular protozoan that can infect all mammals, who serve as intermediate hosts. In immunocompetent subjects, 90% of *T. gondii* infections are asymptomatic. Symptomatic infections usually cause a mononucleosis-like illness with low-grade fever, malaise, headache, and cervical lymphadenopathy. Other manifestations, such as encephalitis, myocarditis, hepatitis, and pneumonia, are rare but can complicate acute toxoplasmosis.[1] Primary infection in pregnant women, which is transmitted transplacentally, can cause congenital toxoplasmosis. Congenital toxoplasmosis can then lead to a wide array of manifestations, ranging from mild chorioretinitis, which can present many years after birth, to miscarriage, mental retardation, microcephaly, hydrocephalus, and seizures. Pregnant women and their primary care physicians and obstetricians need to be informed about the risk factors for toxoplasmosis to lower the risk of congenital infection.

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Epidemiology

Evidence of prior infection with *T. gondii* is common throughout the world. In the United States, the overall age-adjusted seroprevalence is 22.5%,[2] and 15% among women of childbearing age (15 to 44 years). There are approximately 225,000 cases of *T. gondii* infection per year, which result in 5000 hospitalizations and 750 deaths, making *T. gondii* the third most common cause of fatal foodborne illness in the country.[3] Although evidence of prior infection is common, congenital toxoplasmosis is relatively uncommon in the United States, with an estimated 400 to 4000 cases per year.[4]

Pathophysiology

There are three forms of *T. gondii* during its life cycle. Oocysts are the product of sexual reproduction, which occurs in the small intestine of a cat that has recently ingested tissue cysts, usually in uncooked meat. Oocysts, which contain infective sporozoites, are then produced in a cat for approximately 2 weeks after the initial infection. Once the oocysts are deposited by a cat, they become infective 1 to 5 days later.[5] Tachyzoites are the rapidly dividing products of

asexual reproduction, which occurs in macrophages following invasion of the host intestinal wall by either sporozoites (from oocysts) or bradyzoites (from tissue cysts). Macrophages then serve as the vehicle for hematogenous dissemination of the tachyzoites in an intermediate host until an adequate immune response occurs after 7 to 10 days. Once an immune response develops, the protozoan becomes contained within tissue cysts as bradyzoites, or slowly dividing *T. gondii*. These tissue cysts can remain dormant for the lifetime of the intermediate host in various tissues, including the lymph nodes, muscle, brain, retina, myocardium, lungs, and liver.[6] If immunity wanes, such as with the use of immunosuppressive therapy or the acquired immunodeficiency syndrome, bradyzoites can resume rapid division and hematogenously disseminate as tachyzoites again.

There are three means of *T. gondii* infection in humans. First, humans can ingest tissue cysts in infected, undercooked meat. Bradyzoites can be found in up to 8% of beef, 20% of pork, and 20% of lamb.[7] Cooking meat to an internal temperature of 67°C or freezing meat to below –12°C kills bradyzoites and eliminates the risk of this mode of infection.[8] Second, infective oocysts can be ingested through fecal-oral contact, releasing sporozoites that cause infection following intestinal wall invasion. Third, although very uncommon, blood transfusions can cause infection if blood is transfused from an infected patient with circulating tachyzoites to a nonimmune recipient.

Congenital toxoplasmosis develops from the transplacental passage of tachyzoites to a fetus. Assuming a normal immune system, this form of infection only occurs when a pregnant woman develops a primary infection. Previously infected subjects only rarely are reinfected once they have had an adequate immune response. The risk of congenital toxoplasmosis infection from a mother with primary toxoplasmosis increases during pregnancy, from 0% to 9% in the first trimester to 35% to 59% in the third trimester.[9,10] Fortunately, the later in pregnancy that congenital infection occurs, the less severe the consequences are to the fetus.

Risk factors

Since more than 90% of acute toxoplasmosis infections are asymptomatic, primary prevention is the best way to lower the risk of congenital infection. This section reviews studies of various risk factors for toxoplasmosis seroconversion (i.e., primary infection) during pregnancy to allow practitioners to counsel pregnant women appropriately on risk factor reduction.

A prospective case-control study involving 63 women in Norway revealed the following predictors for *T. gondii* seroconversion during pregnancy:[11] eating raw or undercooked mutton; washing kitchen knives infrequently after preparation of raw meat prior to handling another food item; cleaning the cat litter box; eating raw or undercooked minced meat products; eating raw or undercooked pork; and eating unwashed raw vegetables or fruits. Four of these six risk factors involve contact with undercooked meat, which allows direct ingestion of tissue cysts. Cleaning the litter box allows contact with oocysts if the cat was infected in the past 2 weeks. Following exposure to contaminated cat litter, subjects must then touch their mouths for fecal-oral transmission to occur. Eating unwashed vegetables also allows fecal-oral transmission of oocysts, as outdoor cats are known to deposit their feces in gardens, a risk factor that is likely to be independent of cat ownership since many outdoor cats roam to neighboring sites to deposit their feces.

In a high-risk group of women aged 15 to 45 years in Belgrade, Yugoslavia, where the overall mean rate of *T. gondii* infection was 77%, only consumption of undercooked meat was found to be associated with *T. gondii* infection.[12] In a subgroup analysis of women below age 20 years, exposure to soil was also found to be associated with *T. gondii* infection, but cat ownership itself was not linked to *Toxoplasma* infection.

A case-control study in France involving 80 cases of *T. gondii* seroconversion during pregnancy also revealed consumption of undercooked beef and raw vegetables to be predictors of seroconversion.[13] Cat ownership was of borderline importance, although handling cat litter was not found to be associated with *T. gondii* seroconversion.

A large multicenter European case-control study involving 252 cases and 858 controls also revealed contact with raw or undercooked beef, lamb, or other meat, as well as with soil, to be independent risk factors for *T. gondii* seroconversion during pregnancy.[14] Further analysis of the data showed that up to 63% of seroconversions were due to consumption of undercooked or cured meat products and up to 17% were a result of soil contact. In addition, travel outside of Europe, the United States, and Canada was a risk factor for seroconversion, while tasting meat during cooking was of borderline importance. Multiple different cat exposures were assessed, but none were found to be risk factors for toxoplasmosis infection. Specifically, having a cat or kitten at home, cleaning the litter box, and owning a cat that hunts were not risk factors for *T. gondii* seroconversion.

In the United States, there are no published studies assessing the risk factors for seroconversion during pregnancy. A seroprevalence study found that 15% of women aged 15 to 44 years had *T. gondii* immunoglobulin G (IgG) antibodies.[2] Further analysis found the following risk factors to be associated with seroprevalence: increasing age, being foreign born, lower educational level, living in crowded conditions, and working in soil-related occupations. Since this study was not designed to assess new seroconversions during pregnancy, it is not known if these risk factors apply to pregnant women and the risk of congenital toxoplasmosis. Thus, although this study shows that 85% of women of childbearing age are at risk of primary *Toxoplasma* infection, it does not reveal risk factors for seroconversion and congenital disease.

Each study of *T. gondii* seroconversion during pregnancy independently links the consumption of undercooked meat and soil contact through gardening or consumption of unwashed vegetables with primary infection. Although uncooked meat products carry a risk of containing tissue cysts that are potentially infective, soil contact is a lesser-known risk factor. Soil contact through gardening allows contact with infective oocysts deposited by any recently infected cat. While oocysts take 1 to 5 days to become infective, they can remain infective in soil for up to 1 year.[5] Thus, there need not be evidence of recent cat feces for a garden to remain a risk factor for pregnant women. Since this method of transmission also requires fecal-oral transmission, wearing gloves and washing hands after gardening or soil contact should eliminate this risk factor.

The risk of changing cat litter is less well established. Only one of the four studies of seroconversion found cleaning the litter box to be associated with *T. gondii* seroconversion.[11] One other study showed cat ownership to be of borderline importance, although handling cat litter was not found to be a risk factor.[13] Cat ownership and changing the cat litter are less likely to be risk factors for seroconversion for several reasons. First, only outdoor cats that hunt or indoor cats that are fed raw meat are at risk of primary infection. Indoor cats that are fed canned and prepackaged food do not consume tissue cysts and thus will never produce oocysts. Second, transmission of *T. gondii* through oocysts requires fecal-oral transmission. Most persons who clean a cat's litter box are likely to practice good hygiene and wash their hands following handling cat litter regardless of their knowledge of toxoplasmosis.[15] Finally, there is a narrow window when oocysts are produced and when they become infective. Oocysts are shed in a cat's feces for approximately 2 weeks after primary infection. Once a cat has been exposed to *T. gondii*, it develops immunity and is less likely to become reinfected. In addition, oocysts require at least 1 day to become infective after being deposited, allowing for safe removal of oocysts from a cat's litter through daily changing of the litter.[5]

Based on these established risk factors for primary toxoplasmosis, pregnant women (or women trying to become pregnant) should be appropriately advised by their obstetricians and primary care providers on how to lower the risk of congenital toxoplasmosis. Table 1 summarizes general recommendations for primary prevention of toxoplasmosis infection. In addition, since approximately 15% of women aged 15 to 44 years already possess *T. gondii* IgG antibodies, an anxious pregnant cat owner can also be offered an antibody test via indirect immunofluorescence assay to determine if she is at risk of primary infection. Evidence of prior exposure almost completely eliminates the risk of primary infection during pregnancy.[2]

Table 1 Recommendations for lowering the risk of primary toxoplasmosis infection among pregnant women

1. Avoid consumption of undercooked meat. Cook all meat until it is no longer pink and the juices run clear.
2. Always use gloves while, and wash hands thoroughly after, handling raw meat.
3. Thoroughly wash all utensils that are in contact with undercooked meat.
4. Wash all uncooked vegetables thoroughly.
5. Wear gloves when gardening or working in soil. Wash hands immediately after contact with soil.
6. If possible, keep cats indoors throughout pregnancy and do not feed cats uncooked meat.
7. Use gloves while, and wash hands immediately after, changing cat litter.

Knowledge of risk factors

While the risk factors for toxoplasmosis infection are well established, it is less clear if pregnant women are being advised appropriately. In a 1999 survey of 364 U.S. obstetricians, 100% of responders counseled pregnant women on the appropriate handling of cat litter, while only 83% and 77% counseled on the consumption of undercooked foods and handling of raw foods. Even less (68%) gave advice on the risk of gardening.[16] Gardening and the consumption of undercooked meat, the most direct risk factors for primary toxoplasmosis infection, need to be addressed.

Another survey designed to assess knowledge of toxoplasmosis among 403 pregnant women in the United States revealed that 60% of respondents cited cat litter as a risk factor, but only 30% were aware of the risk of undercooked or raw meat and 29% believed that toxoplasmosis could be transmitted by gardening without gloves.[15] Pregnant women need further reinforcement of the risk of undercooked meat and soil contact to lower the risk of congenital toxoplasmosis. Education of women has been shown to be effective in increasing general knowledge of toxoplasmosis and potentially decreasing the incidence of congenital toxoplasmosis.[17,18]

Prenatal and neonatal diagnosis of toxoplasmosis

Since more than 90% of primary toxoplasmosis infections in immunocompetent persons are asymptomatic, the diagnosis of maternal infection is difficult. In asymptomatic women, the only sign of primary infection during pregnancy is seroconversion via detection of IgG or IgM by the immunofluorescence antibody test, the enzyme-linked immune filtration assay, the immunosorbent agglutination assay (ISAGA), or other similar assays.[10] IgG antibody levels become detectable 1 to 2 weeks after infection and remain elevated indefinitely, while IgM antibody levels increase

within days and usually remain elevated for 2 to 3 months.[6] However, IgM antibody levels can remain positive for more than 2 years in up to 27% of women when using ISAGA, making it difficult to pinpoint the timing of infection.[19] Thus, the detection of IgG in a woman at the beginning of pregnancy indicates prior infection and thus eliminates the risk of congenital transfer of tachyzoites. Only new seroconversions (IgM or IgG) place a developing fetus at risk of congenital toxoplasmosis.

Whether or not pregnant women should be screened for primary *T. gondii* infection through serological testing remains controversial for several reasons. First, the false-positive rate of IgM antibody detection during pregnancy has been estimated to be as high as 1.3%.[20] Up to 20% of pregnant women who are informed about a positive IgM antibody test result and the risk of congenital toxoplasmosis infection will request early termination of pregnancy.[21] If these decisions are made based on false-positive results, many uninfected fetuses would be aborted.

Second, the incidence of maternal primary infection is relatively low, with seroconversion rates ranging from 0.15% in Norway to 0.5% in Hungary.[20,22] If the rate of false-positive IgM test results exceeds the rate of true-positive IgM results, the screening test would be ineffective. However, in certain high-risk populations, maternal infection rates of up to 3.5% have been detected, making screening a more viable option.[23] Screening of pregnant women is practiced in France and Austria, but not routinely in the United States and the United Kingdom, due to differences in prevalence. However, certain groups of women should be screened for acute infection in the United States if deemed to be at high risk by their obstetricians on the basis of exposure to risk factors (e.g., raw meat, soil contact).

Finally, if maternal infection is diagnosed, it is not known if antenatal treatment is effective. Unfortunately, there are no randomized controlled trials to assess the effect of prenatal antimicrobial therapy with either spiramycin or pyrimethamine-sulfadiazine. A large prospective cohort trial of 1208 pregnant women in Europe with primary *T. gondii* infection failed to reveal any difference in the risk of congenital infection with treatment (with spiramycin or pyrimethamine-sulfadiazine) or no treatment.[24] However, other uncontrolled studies have demonstrated the benefits of prenatal treatment with spiramycin or pyrimethamine-sulfadiazine. One study of 5288 susceptible pregnancies showed the risk of congenital toxoplasmosis to be four times greater in neonates born to untreated mothers when compared with treated mothers.[23] Another study of 88 pregnant women with primary toxoplasmosis infection who were treated with spiramycin alone showed a 0% rate of congenital toxoplasmosis at 2 years.[22] A systematic review of nonrandomized studies found therapy to be effective in five trials but ineffective in four studies.[25] Of the four trials without statistical benefit, two demonstrated a nonstatistically significant reduction in congenital toxoplasmosis with antiparasitic therapy. Thus, while there are no randomized studies yet, it is still recommended that all pregnant women who have been diagnosed with primary toxoplasmosis infection be treated with spiramycin with or without pyrimethamine-sulfadiazine. Pyrimethamine is teratogenic and contraindicated in the first trimester.[7]

Once an infant is born to a mother with primary toxoplasmosis, the diagnosis of congenital toxoplasmosis can be made by either indirect or direct methods. The detection of IgM or IgA antibodies to *T. gondii* in an infant is highly sensitive for the diagnosis of congenital toxoplasmosis. Amplification of *T. gondii* DNA by polymerase chain reaction (PCR) is almost 100% sensitive and specific and can be detected in most body fluids of a congenitally infected neonate.[10] PCR amplification of amnionic fluid or fetal blood samples obtained via cordocentesis can identify congenitally infected fetuses while still in utero, but is associated with certain inherent procedure-related risks.[3] If an infant is diagnosed with congenital toxoplasmosis, recommendations include treatment with pyrimethamine, sulfadiazine, and leucovorin for up to 1 year.[10]

Conclusion

Although uncommon in the United States, congenital toxoplasmosis can have serious effects on the developing fetus. Since most primary infections during pregnancy are asymptomatic and screening for primary infection is problematic, primary prevention is the most logical method to lower the risk of congenital infection. Both women of childbearing age and physicians need to be informed of the risks associated with undercooked meat and soil contact. There is also a need to educate women on the safe handling of cat litter during pregnancy.

References

1. Kravetz JD, Federman DG. Cat-associated zoonoses. *Arch Intern Med*. 2002;162:1945–1952.
2. Jones JL, Kruszon-Moran D, Wilson M, et al. *Toxoplasma gondii* infection in the United States: seroprevalence and risk factors. *Am J Epidemiol*. 2001;154:357–365.
3. Mead PS, Slutsker L, Dietz V, et al. Food-related illness and death in the United States. *Emerg Infect Dis*. 1999;5:607–625.
4. Centers for Disease Control and Prevention. CDC Recommendations regarding selected conditions affecting women's health. *MMWR Morb Mortal Wkly Rep*. 2000;49:59–68.
5. Markell EK, John DT, Krotoski WA. *Toxoplasma gondii*. In: *Markell and Voges's Medical Parasitology*. 8th ed. Philadelphia, Pennsylvania: W.B. Saunders Co: 161–171, 1999.
6. Despommier DD, Gwadz RW, Hotez PJ. *Toxoplasma gondii*. In: *Parasitic Diseases*. 3rd ed. New York, New York: Springer-Verlag: 162–169; 1995.
7. Beazley DM, Egerman RS. Toxoplasmosis. *Semin Perinatol*. 1998;22:332–338.
8. Dubey JP. Strategies to reduce transmission of *Toxoplasma gondii* to animals and humans. *Vet Parasitol*. 1996;64:65–70.

9. Mombro M, Perathoner C, Leone A, et al. Congenital toxoplasmosis: assessment of risk to newborns in confirmed and uncertain maternal infection. *Eur J Pediatr*. 2003; 162:703–706.
10. Montoya JG, Liesenfeld O. Toxoplasmosis. *Lancet*. 2004 363:1965–1976.
11. Kapperud G, Jenum PA, Stray-Pedersen B. Risk factors for *Toxoplasma gondii* infection in pregnancy. Results of a prospective case-control study in Norway. *Am J Epidemiol*. 1996;144:405–412.
12. Bobic B, Jevremovic I, Marinkovic J. Risk factors for *Toxoplasma* infection in a reproductive age female population in the area of Belgrade, Yugoslavia. *Eur J Epidemiol*. 1998;14:605–610.
13. Baril L, Ancelle T, Goulet V, et al. Risk factors for *Toxoplasma* infection in pregnancy: a case-control study in France. *Scand J Infect Dis*. 1999;31:305–309.
14. Cook AJ, Gilbert RE, Buffolano W, et al. Sources of *toxoplasma* infection in pregnant women: European multicentre case-control study. *BMJ*. 2000;321:142–147.
15. Jones JL, Ogunmodede F, Scheftel J, et al. Toxoplasmosis-related knowledge and practices among pregnant women in the United States. *Infect Dis Obstet Gynecol*. 2003;11:139–145.
16. Jones JL, Dietz VJ, Power M, et al. Survey of obstetricians-gynecologists in the United States about toxoplasmosis. *Infect Dis Obstet Gynecol*. 2001;9:23–31.
17. Pawlowski ZS, Gromadecka-Sutkiewicz M, Skommer J, et al. Impact of health education on knowledge and prevention behavior for congenital toxoplasmosis: the experience of Poznan, Poland. *Health Educ Res*. 2001;16:493–502.
18. Foulon W, Naessens A, Ho-Yen D. Prevention of congenital toxoplasmosis. *J Perinat Med*. 2000;28:337–345.
19. Gras L, Gilbert RE, Wallon M, et al. Duration of the IgM response in women acquiring *Toxoplasma gondii* during pregnancy: implications for clinical practice and cross-sectional incidence studies. *Epidemiol Infect*. 2004;132:541–548.
20. Jenum PA, Stray-Pedersen B, Melby KK, et al. Incidence of *Toxoplasma gondii* infection in 35,940 pregnant women in Norway and pregnancy outcome for infected women. *J Clin Microbiol*. 1998;36: 2900–2906.
21. Liesenfeld O, Press C, Montoya JG, et al. False-positive results in immunoglobulin M (IgM) *Toxoplasma* antibody tests and the importance of confirmatory testing: the platelia toxo IgM test. *J Clin Microbiol*. 1997;35:174–178.
22. Szenasi Z, Ozsvar Z, Nagy E, et al. Prevention of congenital toxoplasmosis in Szeged, Hungary. *Int J Epidemiol*. 1997;26:428–435.
23. Ricci M, Pentimalli H, Thaller R, et al. Screening and prevention of congenital toxoplasmosis: an effectiveness study in a population with a high infection rate. *J Matern Fetal Med*. 2003;14:398–403.
24. Gilbert R, Gras L. European multicentre study on congenital toxoplasmosis. Effect of timing and type of treatment on the risk of mother to child transmission of Toxoplasma gondii. *BJOG*. 2003; 110:112–120.
25. Wallon M, Liou C, Garner P, Peyron F. Congenital toxoplasmosis: systematic review of evidence of efficacy of treatment in pregnancy. *BMJ*. 1999;318:1511–1514.

Seminar

Toxoplasmosis

J G Montoya, O Liesenfeld

***Toxoplasma gondii* is a protozoan parasite that infects up to a third of the world's population. Infection is mainly acquired by ingestion of food or water that is contaminated with oocysts shed by cats or by eating undercooked or raw meat containing tissue cysts. Primary infection is usually subclinical but in some patients cervical lymphadenopathy or ocular disease can be present. Infection acquired during pregnancy may cause severe damage to the fetus. In immunocompromised patients, reactivation of latent disease can cause life-threatening encephalitis. Diagnosis of toxoplasmosis can be established by direct detection of the parasite or by serological techniques. The most commonly used therapeutic regimen, and probably the most effective, is the combination of pyrimethamine with sulfadiazine and folinic acid. This Seminar provides an overview and update on management of patients with acute infection, pregnant women who acquire infection during gestation, fetuses or infants who are congenitally infected, those with ocular disease, and immunocompromised individuals. Controversy about the effectiveness of primary and secondary prevention in pregnant women is discussed. Important topics of current and future research are presented.**

Introduction

The organism

Toxoplasma gondii is an obligate intracellular protozoan that belongs to the phylum Apicomplexa, subclass coccidia. It can take several different forms: the oocyst; the tachyzoite; and the cyst. The *T gondii* genome is haploid, except during sexual division in cats, and contains about 8×10^7 base pairs.[1]

Oocysts

Members of the cat family are definitive hosts of *T gondii*; replication of the parasite happens in the intestine of the cat, resulting in production of oocysts (figure 1).[2] During acute infection, several million oocysts (10×12 μm) are shed in the faeces of cats for 7–21 days. After sporulation, which takes place between 1 and 21 days,[3] oocysts containing sporozoites are infective when ingested by mammals (including man) and give rise to the tachyzoite stage.

Tachyzoites

Tachyzoites (2–4 μm wide and 4–8 μm long) are crescentic or oval and are the rapidly multiplying stages of the parasite (figure 1). They enter all nucleated cells by active penetration and form a cytoplasmic vacuole.[4] After repeated replication, host cells are disrupted and tachyzoites are disseminated via the bloodstream and infect many tissues, including the CNS, eye, skeletal and heart muscle, and placenta. Replication leads to cell death and rapid invasion of neighbouring cells. The tachyzoite form causes a strong inflammatory response and tissue destruction and, therefore, causes clinical manifestations of disease. Tachyzoites are transformed into bradyzoites under the pressure of the immune response to form cysts.

Cysts

Bradyzoites persist inside cysts for the life of the host (figure 1). They are morphologically identical to tachyzoites but multiply slowly, express stage-specific molecules, and are functionally different. Tissue cysts contain hundreds and thousands of bradyzoites and form within host cells in brain and skeletal and heart muscles. Bradyzoites can be released from cysts, transform back into tachyzoites, and cause recrudescence of infection in immunocompromised patients. Cysts are infective stages for intermediate and definitive hosts.

Different strains of T gondii

T gondii consists of three clonal lineages designated type I, II, and III, which differ in virulence and epidemiological pattern of occurrence.[5,6] Most strains isolated from patients with AIDS are type II. Type I and II strains have been recorded in patients with congenital disease, whereas strains isolated from animals are mostly genotype III.[6,7] Strain-specific peptides[8] could allow typing of *T gondii* strains with serum from a patient.

Sexual recombination between two distinct and competing clonal lines of the parasite has driven natural evolution of virulence in *T gondii*.[9] Acquisition of direct oral transmission by the parasite seems to be a recent evolutionary change that has led to widespread expansion of Toxoplasma.[10] Generation of specific gene-deficient strains of *T gondii*[11,12] and sequencing of the Toxoplasma genome (http://ToxoDB.org/) will provide further insight into virulence factors of the parasite and specific host immune responses.

Search strategy and selection criteria

MEDLINE searches for recent new literature using a large number of keywords for both clinical and basic research topics were used as a primary source of references. Reference lists in recent book chapters and review articles written by the authors were also used; inclusion or exclusion of individual manuscripts was based on scientific value and clinical importance.

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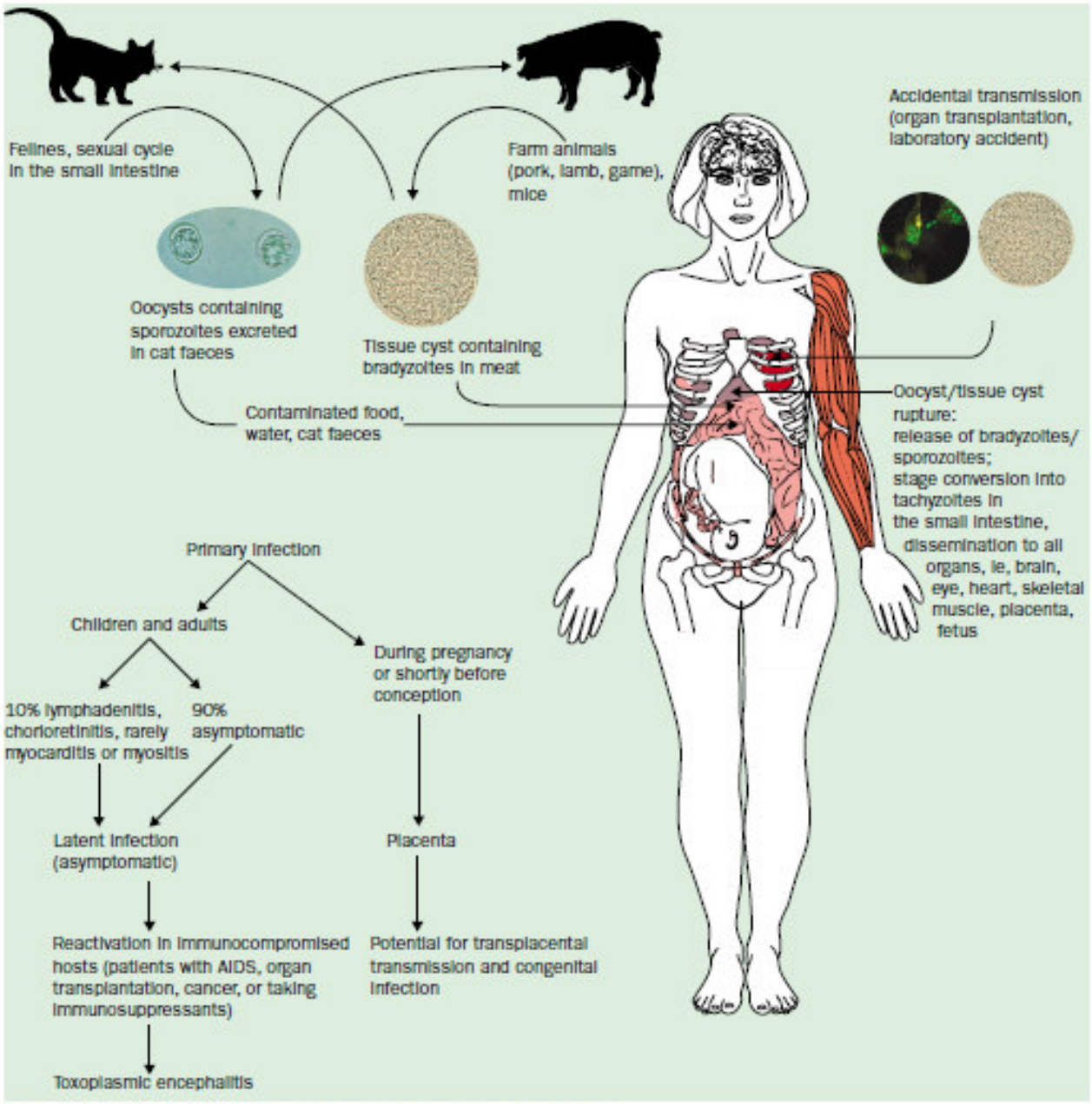

Figure 1: **Life cycle of *T gondii* and clinical manifestations of toxoplasmosis**

Epidemiology

Transmission

Human beings can be infected with *T gondii* by ingestion or handling of undercooked or raw meat (mainly pork and lamb) containing tissue cysts or water or food containing oocysts excreted in the faeces of infected cats (figure 1). Most individuals are infected inadvertently, thus the specific route of transmission cannot usually be established. Variations in seroprevalence of *T gondii* seem to correlate with eating and hygiene habits of a population. This finding lends support to the contention that the oral route is the major source of infection.[13–15] The seroprevalence of *T gondii* in market-weight pigs in the USA has been declining for the past 20 years, and it has been reported as low as 0·58%.[16] However, pigs from isolated small swine farms are still sold for human consumption and prevalence of the parasite in these animals can be as a high as 93%.[16] Epidemics of toxoplasmosis in human beings and sheep attributed to exposure to infected cats indicate an important role of oocyst excretion by cats in the propagation of infection in nature and man.[17] Several outbreaks of toxoplasmosis in human beings have been linked epidemiologically to drinking of unfiltered water.[18,19] Transmission during breastfeeding or direct human-to-human transmission other than from mother to fetus (see below) has not been recorded.

Organ transplantation

Transmission of *T gondii* by organ transplantation from a seropositive donor to a seronegative recipient (donor [D]+/recipient [R]–) is an important potential cause of disease in heart, heart-lung, kidney, liver, and liver-pancreas transplant patients.[20,21] Reactivation of latent infection in the recipient (D–/R+ or D+/R+) is the most usual mechanism for toxoplasmosis to arise in bone marrow, haematopoietic stem cell, and liver transplant patients, and in people with AIDS. Although rare,

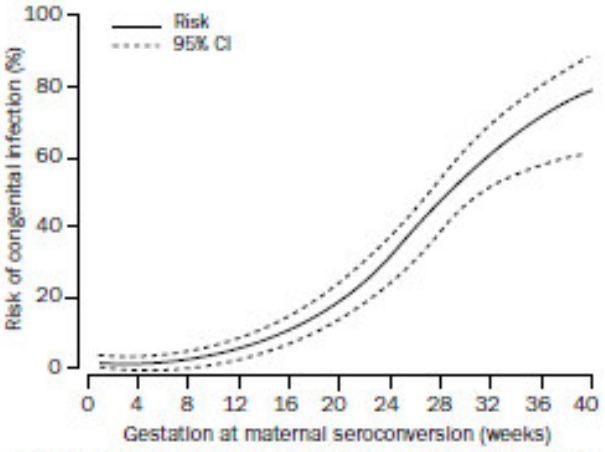

Figure 2: **Risk of congenital infection by duration of gestation at maternal seroconversion**
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T gondii can also be transmitted via blood or leucocytes from immunocompetent and immunocompromised donors.[22,23] Infections in laboratory personnel have arisen by contact with contaminated needles and glassware or infected animals.[24,25]

Congenital transmission

After maternal acquisition of *T gondii* for the first time during gestation, the parasite enters the fetal circulation by infection of the placenta. The birth prevalence of congenital toxoplasmosis ranges from one to ten per 10 000 livebirths.[26–28] Maternal infection acquired before gestation poses little or no risk to the fetus except in women who become infected a few months (at the most, 3) before conception.[29,30] Frequency of congenital transmission varies considerably according to the time during gestation that the mother became infected (figure 2). Infection acquired around the time of conception and within the first 2 weeks of gestation in women taking spiramycin does not result in vertical transmission, whereas rates of transmission are more than 60% in the last trimester.[31–33] Frequency of transmission and severity of disease are inversely related. Early maternal infection (first and second trimester) may result in severe congenital toxoplasmosis and can result in death of the fetus in utero and spontaneous abortion (table 1, figure 3). By contrast, late maternal infection (third trimester) usually results in normal appearing newborns. The overall frequency of subclinical infection in newborns with congenital toxoplasmosis is as high as 85%.[31,33,34] Infection initially goes unnoticed, but if it is not treated babies can later develop chorioretinitis or growth can be delayed in the second or third decade of life.[15,35]

Treatment of the mother during pregnancy is an attempt to reduce the frequency and severity of fetal infection. Spiramycin has been estimated to reduce the incidence of vertical transmission by about 60% (see Management and treatment).[15,36] Vertical transmission of *T gondii* in the setting of chronic infection is only recorded in immunocompromised women—ie, those with AIDS or receiving immunosuppressive drugs including corticosteroids. However, the rate of vertical transmission in this setting seems to be fairly low.[37,38]

Seroprevalence

In man, seroprevalence of *T gondii* infection rises with age, does not vary greatly between sexes, and is lower in cold regions, hot and arid areas, or at high elevations. In general, incidence of the infection varies with the population group and geographic location—eg, seropositivity can be up to 75% by the fourth decade of life in El Salvador versus an overall seroprevalence of 22·5% in the USA.[39] The prevalence of *T gondii* antibodies has been steadily falling in various countries over the past few decades.[40–42]

Pathogenesis

Inoculum size,[43] virulence of the organism,[44] genetic background,[45] sex,[46] and immunological status seem to affect the course of infection in human beings and animal models of toxoplasmosis. Once the parasite has been orally ingested, it actively invades intestinal epithelial cells or it gets phagocytosed by them.[4,47] Intracellularly, *T gondii* induces formation of a parasitophorous vacuole that contains secreted parasite proteins and excludes host proteins that would normally promote phagosome maturation, thereby preventing lysosome fusion. The molecular characterisation and function of several proteins from different parasite organelles, including rhoptries, micronemes, and dense granules, have been reported;[48–50] these molecules, and the immunodominant tachyzoite surface antigen SAG1, are among the most promising vaccine candidates (see Prevention).[51,52]

Infection with *T gondii* results in a strong and persistent T-helper-1 (Th1) response characterised by production of proinflammatory cytokines including interleukin 12, interferon γ, and tumour necrosis factor α. The combined action of these cytokines and other immunological mechanisms protects the host against rapid replication of tachyzoites and subsequent pathological changes. After invasion of enterocytes, *T gondii* infects antigen-presenting cells in the intestinal lamina propria and induces a transient local Th1 response.[43,53]

Dendritic cells—with their ability to produce interleukin 12—are the main activators of the Th1 immune response after infection of mice with *T gondii*.[54] Granulocytes can also contribute to early production of interleukin 12.[55] The activated macrophage inhibits or kills intracellular *T gondii*.[56] However, the parasite can partly counteract these actions even at early stages of infection. *T gondii* can exploit antigen-presenting cells as so-called Trojan horses by downregulation of cell-surface molecules and interference with apoptosis pathways.[57–59] Sensitised CD4+ and CD8+ T lymphocytes are both cytotoxic for *T gondii*-infected cells.[60] Proinflammatory (eg, interferon γ and tumour necrosis factor α)[56,61] and downregulatory (eg, interleukin 10, transforming growth factor β)[56] cytokines are both involved in balancing of this response. The proportion of γδ T cells is enhanced during acute infection.[62,63] Within 2 weeks after infection, IgG, IgM, IgA, and IgE antibodies against many *T gondii* proteins can be detected. Production of IgA antibodies on

	Infection acquired		
	First trimester	Second trimester	Third trimester
Outcome in offspring			
Congenital toxoplasmosis	9·0%	27·0%	59·0%
Subclinical	22·2%	74·4%	89·8%
Clinically apparent	77·8%	15·6%	10·2%
Perinatal death or stillbirth	5·0%	2·0%	0%

Table adapted and modified from Desmonts G, Couvreur J. Congenital toxoplasmosis: a prospective study of the offspring of 542 women who acquired toxoplasmosis during pregnancy. In: Thalhammer O, Baumgarten K, Pollak A, eds. Pathophysiology of congenital disease: perinatal medicine, 6th European congress. Stuttgart: Georg Thieme Verlag, 1979: 51–60. With permission of Georg Thieme Verlag.

Table 1: **Outcome in babies born to women who acquired *T gondii* infection during pregnancy**

	Antibody class/ test	Screening	Pregnancy	Newborns	Eye disease	Immunocompromised patients
Indirect detection/ serology	IgG	+	+ (identification of women at risk and those protected)	+ (maternal antibodies may persist until 12 months of age; differentiation of maternal and fetal IgG by western blot or ELIFA)	+ (low titres are usually seen in patients with reactivation of congenital disease; intraocular antibody production [ratio of ocular and blood antibody titres])	+ (identification of patients at risk of reactivation, ie, AIDS, bone marrow transplant patients)
	IgG avidity	–	+ (high avidity results rule out infection in recent 3–4 months; low avidity antibodies may persist)	–	+ (high avidity results rule out infection in recent 3–4 months; low avidity antibodies may persist)	–
	IgM*	–†	+ (IgM antibodies may persist for prolonged times, negative IgM rules out infection in pregnant women during the first two trimesters)	+ (ISAGA more sensitive than EIA; differentiation of maternal and fetal IgG by western blot)	+ (high titres usually in patients with acute acquired disease, negative results in patients with reactivation of congenital disease)	+ (IgM of little value; may or not be present with active or latent disease)
	IgA	–	+ (IgA antibodies may persist for prolonged times)	+ (increased value compared to IgM tests)	–	–
	IgE	–	+ (high specificity, low sensitivity)	–	–	–
Direct detection	PCR	–	+ (amniotic fluid)	+ (blood, urine)	+ (particulary useful in patients with atypical retinal lesions or suboptimum response to therapy [vitreous or aqueous fluid, vitreous fluid preferred])	+ (cerebrospinal fluid, bronchoalveolar lavage, ocular fluids, ascitic fluid, pleural fluid, peritoneal fluid, bone marrow aspirate, peripheral blood, and/ or tissue)
	Histology (immunohisto-chemistry‡)/ cell culture or mouse inoculation	–	+ (placenta and fetal tissues in cases of fetal loss)	–	–	+ (any affected tissue)
Comments/aims		Determination of sero-prevalence/ epidemiological studies	Combined detection of IgG and IgM antibodies for screening in early pregnancy	Increased sensitivity of combined IgA and IgM antibody detection	Serological distinction between congenital and recently acquired infection	Direct detection more sensitive than indirect detection

ELIFA=enzyme-linked immune filtration assay. *Value of commercially available tests varies considerably. †Detection of IgM may be used for neonatal screening. ‡With *T gondii*-specific antibodies.

Table 2: **Value of serological tests for the diagnosis of infection with *T gondii***

mucosal surfaces seems to protect the host against reinfection.[64,65] Reinfection can happen but does not seem to result in disease or in congenital transmission of the parasite.

Pathology

Histopathological changes in toxoplasmic lymphadenitis in immunocompetent individuals are frequently distinctive and sometimes diagnostic[66] and consist of reactive follicular hyperplasia, irregular clusters of epithelioid histiocytes encroaching on and blurring the margins of the germinal centres, and focal distension of sinuses with monocytoid cells. Langhans giant cells, granulomas, microabscesses, foci of necrosis, and parasites (or their DNA)[67] are not typically seen or detected. Eye infection in immunocompetent patients produces acute chorioretinitis characterised by severe inflammation and necrosis.[68] Granulomatous inflammation of the choroid is secondary to necrotising retinitis. Exudation into the vitreous or invasion of the vitreous by a budding mass of capillaries might happen. Although rare, tachyzoites and cysts can be seen in the retina. The pathogenesis of recurrent chorioretinitis is controversial. Rupture of cysts can release viable organisms that induce necrosis and inflammation; alternatively, chorioretinitis can result from a hypersensitivity reaction triggered by unknown causes.[68] Biopsy-proven toxoplasmic myocarditis and polymyositis in the setting of acute toxoplasmosis have been reported in otherwise immunocompetent individuals and in patients on corticosteroids.[69]

Damage to the CNS by *T gondii* is characterised by many foci of enlarging necrosis and microglia nodules.[70] In infants, periaqueductal and periventricular vasculitis and necrosis are distinctive of toxoplasmosis.[71] Necrotic areas can calcify and lead to striking radiographic findings suggestive—but not pathognomonic—of the disease. Hydrocephalus can result from obstruction of the aqueduct of Sylvius or foramen of Monro. Tachyzoites and cysts are seen in and adjacent to necrotic foci near or in glial nodules, perivascular regions, and cerebral tissue uninvolved by inflammatory change. Presence of many brain abscesses is the most characteristic feature of toxoplasmic encephalitis in severely immunodeficient patients and is especially characteristic in people with AIDS.[70] Identification of tachyzoites is pathognomonic of active infection (see Management). At autopsy in AIDS patients with toxoplasmic encephalitis, almost universal involvement of the cerebral hemispheres is noted, as is a remarkable predilection for the basal ganglia.[72] In cases of

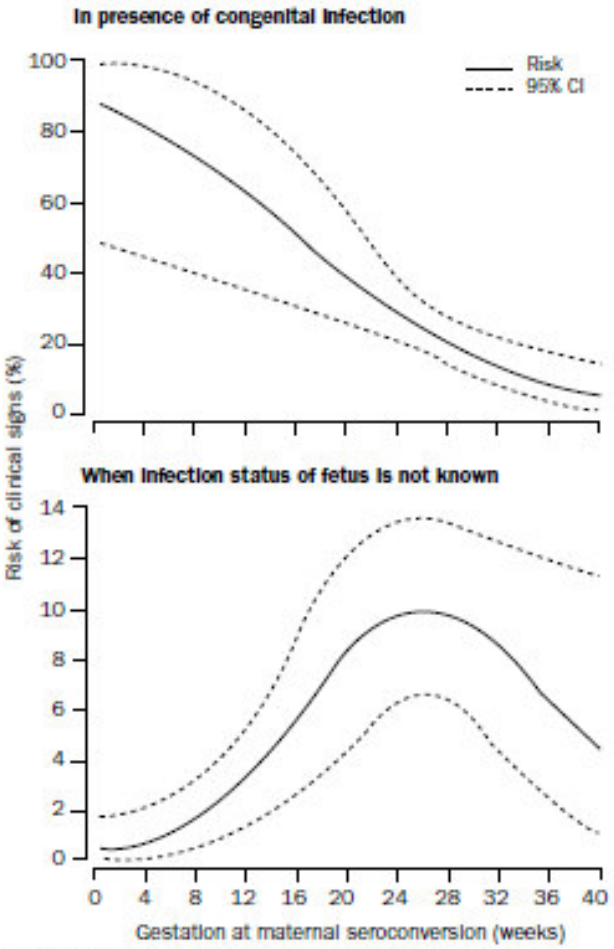

Figure 3: **Risk of developing clinical signs (not necessarily symptomatic) before age 3 years according to gestational age**
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congenital toxoplasmosis, necrosis of the brain is most intense in the cortex and basal ganglia and at times in the periventricular areas.[71] Pulmonary toxoplasmosis in the immunodeficient patient can arise as interstitial pneumonitis, necrotising pneumonia, consolidation, and pleural effusion.[73]

By PCR, *T gondii* DNA can be shown in amniotic, cerebrospinal, bronchoalveolar lavage, ocular, pleural, or ascitic fluids and in peripheral blood or urine.[74]

Clinical presentation

Clinically, infection with *T gondii* can go unnoticed or could cause signs and symptoms that vary depending on the immune status of the patient and the clinical setting—eg, immunocompetent, ocular disease, immunocompromised, or congenital toxoplasmosis.

Immunocompetent adults and children

T gondii primary infection in children and adults (including pregnant women) is asymptomatic in most patients. In about 10%, it causes a self-limited and non-specific illness that rarely needs treatment. The most typical clinical manifestation is isolated cervical or occipital lymphadenopathy. Lymph nodes are not tender, do not suppurate, are usually discrete, and stay enlarged for less than 4–6 weeks. A form of the disease characterised by chronic lymphadenopathy has been described, and lymph-node enlargement can fluctuate for months. Very infrequently, myocarditis, polymyositis, pneumonitis, hepatitis, or encephalitis can arise in otherwise healthy individuals. Acute toxoplasma infection during pregnancy is asymptomatic in most women.

Ocular toxoplasmosis

Toxoplasmic chorioretinitis can be seen in the setting of congenital or postnatally acquired disease as a result of acute infection or reactivation.[75,76] Chorioretinitis in individuals with acute acquired toxoplasmosis can arise sporadically or in the context of an outbreak of acute disease.[77] Typical findings of toxoplasmic chorioretinitis include noticeably white focal lesions with an overlying and intense vitreal inflammatory reaction. The classic "headlight in the fog" appearance is attributable to the presence of active retinal lesions with severe inflammatory reaction. Recurrent lesions are usually recorded at the borders of chorioretinal scars, which are typically found in clusters. Chorioretinitis in adults has been traditionally deemed a late manifestation and reactivation of congenital disease; however, it has been reported with increasing frequency in association with acute infection.[75] To establish whether the original infection was congenital or acquired in patients who have recurrences of chorioretinitis is difficult.

Immunocompromised patients with or without AIDS

By contrast with the favourable course of toxoplasmosis in almost all immunocompetent individuals, the disease can be life-threatening in those who are immuno-compromised.[78] In these individuals, toxoplasmosis almost always happens as a result of reactivation of chronic infection.[79]

The CNS is the site most typically affected by infection. Clinical presentation of toxoplasmic encephalitis varies from a subacute gradual process evolving over weeks to an acute confusional state, with or without focal neurological deficits, evolving over days. Clinical manifestations include mental status changes, seizures, focal motor deficits, cranial nerve disturbances, sensory abnormalities, cerebellar signs, movement disorders, and neuropsychiatric findings. Meningeal signs are rare. Constitutional symptoms and signs such as fever and malaise can vary. The most typical focal neurological findings are hemiparesis and speech abnormalities.[80] The differential diagnosis of toxoplasmic encephalitis lesions includes CNS lymphoma, progressive multifocal leukoencephalopathy, cytomegalovirus ventriculitis and encephalitis, focal lesions caused by other organisms including *Cryptococcus neoformans*, *Aspergillus* spp, *Mycobacterium tuberculosis*, and *Nocardia* spp, or bacterial brain abscess. Toxoplasmosis in immuno-compromised patients can also present as chorioretinitis, pneumonitis, or multiorgan involvement presenting with acute respiratory failure and haemodynamic abnormalities similar to septic shock.[78] Toxoplasma pneumonia seems to be more frequent in recipients of bone-marrow transplants and in patients with AIDS.

Congenital toxoplasmosis

Fetuses with congenital toxoplasmosis usually look normal on prenatal ultrasound. If present, ultrasonographic findings suggestive of congenital disease include intracranial calcifications, ventricular dilatation, hepatic enlargement, ascites, and increased placental thickness.[81] Neonatal clinical manifestations of congenital toxoplasmosis vary widely and include hydrocephalus, microcephaly, intracranial calcifications, chorioretinitis, strabismus, blindness, epilepsy, psychomotor or mental retardation, petechia due to thrombocytopenia, and anaemia.[82,83] The classic triad of chorioretinitis, hydrocephalus, and cerebral calcifications is rather rare. None of the signs described in newborns with congenital disease is pathognomonic for toxoplasmosis and

	Drug	Dosage	Duration
Acute asymptomatic acquired infection	Treatment not recommended*	..	..
Acute toxoplasmosis in pregnant women†	Spiramycin	3 g qd in three divided doses without food	Until term‡ or until fetal infection is documented
Documented fetal infection (after 12 or 18 weeks of gestation)§	Pyrimethamine	Loading dose: 100 mg qd in two divided doses for 2 days, then 50 mg qd	Until term
	plus		
	Sulfadiazine	Loading dose: 75 mg/kg qd in two divided doses (max 4 g qd) for 2 days, then 100 mg/kg qd in two divided doses (max 4 g qd)	Until term
	plus		
	Leucovorin (folinic acid)	5–20 mg qd	During and for 1 week after pyrimethamine treatment
Congenital toxoplasma infection in the infant¶	Pyrimethamine	Loading dose 2 mg/kg qd for 2 days, then 1 mg/kg qd for 2–6 months, then this dose every Monday, Wednesday, and Friday	1 year
	plus		
	Sulfadiazine	100 mg/kg qd in two divided doses	1 year
	plus		
	Leucovorin	10 mg three times a week	During and for 1 week after pyrimethamine treatment
	Corticosteroids‖ (prednisone)	1 mg/kg qd in two divided doses and symptoms	Until resolution of signs
Toxoplasmic chorioretinitis in adults	Pyrimethamine	Loading dose: 200 mg qd, then 50–75 mg qd	Usually 1–2 weeks after resolution of symptoms
	plus		
	Sulfadizine	Oral 1–1·5 g qd	Usually 1–2 weeks after resolution of symptoms
	plus		
	Leucovorine	5–20 mg three times a week	During and for 1 week after pyrimethamine treatment
	Corticosteroids‖	1 mg/kg qd in two divided doses	Until resolution of signs and symptoms
Acute/primary treatment of toxoplasma encephalitis in patients with AIDS			
Standard regimens	Pyrimethamine	Oral 200 mg loading dose, then 50–75 mg qd	At least 4–6 weeks after resolution of signs and symptoms
	Leucovorin	Oral, intravenous, or intramuscular 10–20 mg qd (up to 50 mg qd)	During and for 1 week after pyrimethamine treatment
	plus		
	Sulfadiazine	Oral 1–1·5 g q6h	**
	or		
	Clindamycin	Oral or intravenous 600 mg q6h (up to intravenous 1200 mg q6h)	**
Possible alternative regimens	Trimethoprim	Oral or intravenous 5 mg (trimethoprim sulfamethoxazole component)/kg q12h (daily doses as high as 15–20 mg/kg of the trimethoprim component have been used)	**
	Pyrimethamine plus leucovorin *plus one of the following*	As in standard regimens	**
	Clarithromycin	Oral 1g q12h	**
	Atovaquone	Oral 750 mg q6h	**
	Azithromycin	Oral 1200–1500 mg qd	**
	Dapsone	Oral 100 mg qd	**

Adapted from reference 143, with permission. qd=once a day. *Acute acquired infection in immunocompetent patients does not need specific treatment unless severe or persistant symptoms or evidence of damage to vital organs are present. If such signs or symptoms arise, treatment with pyrimethamine/sulfadiazine, and leucovorin should be initiated (for doses, see Toxoplasmic chorioretinitis in adults). †Practices vary widely between centres. ‡German and Austrian guidelines recommend spiramycin prophylaxis until 17 weeks of pregnancy followed by a 4-week course of pyrimethamine plus sulfadiazine plus leucovorin. §Practices vary widely between centres. Pyrimethamine plus sulfadoxine is used in some centres, monthly alternating cycles of pyrimethamine plus sulfadiazine and spiramycin. ¶Practices vary widely between centres. Monthly alternating cycles of pyrimethamine plus sulfadiazine and spiramycin. ‖When cerebrospinal protein is >1 g/dL and when active chorioretinitis threatens vision. **Duration of treatment as for pyrimethamine in patient with toxoplasma encephalitis.

Table 3: **Guidelines for treatment of *T gondii* infection**

can be mimicked by congenital infection with other pathogens, including cytomegalovirus, herpes simplex virus, rubella, and syphilis.

Diagnosis

T gondii infection can be diagnosed indirectly with serological methods and directly by PCR, hybridisation, isolation, and histology. Whereas indirect serological methods are widely used in immunocompetent patients, definitive diagnosis in immunocompromised people is mostly undertaken by direct detection of the parasite (table 2). Direct demonstration of the organism (mouse inoculation, cell culture, or PCR for *T gondii* DNA) from cerebrospinal fluid, blood, and urine,[84,85] and ophthalmologic testing, radiological studies, and examination of cerebrospinal fluid could assist diagnosis of congenital disease.

Indirect detection

Detection of IgG antibodies to *T gondii* should be done in pregnant women and immunocompromised patients. First, absence of IgG antibodies before or early in pregnancy allows identification of women at risk of acquiring the infection. Second, presence of IgG antibodies allows

identification of immunocompromised patients—ie, bone marrow transplant recipients or people with AIDS—at risk for reactivation of latent infection. The Sabin-Feldman dye test,[85] immunofluorescent antibody test,[87] ELISA,[88] IgG avidity test,[89–91] and agglutination and differential agglutination test[92] can be used for detection of IgG antibodies. These arise within 1–2 weeks after infection and persist for the individual's lifetime.

Tests for the avidity (functional affinity) of IgG antibodies have become standard to discriminate between recently acquired infection and those obtained in the more distant past.[89] Presence of high avidity antibodies essentially rules out infection acquired in the recent 3–4 months; by contrast, low avidity antibodies can persist beyond 3 months of infection.[89–91,93,94] The differential agglutination (AC/HS) test has also proven helpful in differentiation between a probable acute or chronic infection in pregnant women[92] in combination with a panel of other assays.[74,95] The double-sandwich IgM ELISA and IgM immunosorbent agglutination assay (ISAGA) can be used for detection of IgM antibodies that arise within the first week of infection, rapidly increase, and thereafter decline and disappear at highly variable rates.[96,97] False-positive results and persistence of positive titres even years after initial infection hamper correct interpretation of results obtained in IgM antibody tests.[95,98] The greatest value of testing for IgM lies in the fact that a negative test essentially rules out recently acquired infection. However, results of commercial kits used to detect IgM antibodies in non-reference laboratories are sometimes unreliable with false positive rates as high as 60%.[95] The strength of combinations of serological tests in assessment of the stage of infection has been shown by different researchers.[95,99,100]

The IgM ISAGA[101] is highly sensitive and specific and frequently used for diagnosis of congenital infection in newborns. Tests for the detection of IgA antibodies were more sensitive than those for detection of IgM antibodies in the fetus and newborn.[102,103] Presence of IgG antibodies in the newborn's serum could be their own or their mother's antibodies. Testing for IgM and IgA antibodies will identify up to 75% of infected babies.[15,82,103] In babies with suspected congenital toxoplasmosis with positive IgG but negative IgM and IgA tests results, use of IgG/IgM western blots of mother-infant pairs can prove useful.[104] Maternally transferred IgG antibodies usually decline and disappear within 6–12 months.

In adults, IgA antibodies can remain positive for a year or longer, and therefore are of minor value for diagnosis of recent infection. Tests for the detection of IgE antibodies should only be used in combination with other serological methods.[105,106] Local antibody production in the eye has been used successfully for diagnosis of ocular toxoplasmosis.[107]

Direct detection

PCR amplification of the 35-fold repetitive B1 gene for detection of *T gondii* DNA in body fluids and tissues has successfully been used to diagnose congenital,[32,108] ocular,[109] cerebral, and disseminated[110–112] toxoplasmosis. Real-time PCR and use of other genes—ie, 300-fold repetitive AF146527—will probably be more generally used in the future.[113,114]

Sensitivity of PCR results can be affected by the appropriateness of sample handling, shipping and storage conditions, the particular technique used for amplification and detection of PCR products, and by previous use of anti-*T gondii* specific drugs. If contamination is not an issue, specificity and positive predictive value of PCR results approach 100%. In an initial study,[31] sensitivity of amniotic fluid PCR was close to 100%; however, Romand and colleagues[32] estimated sensitivity to be 64%, negative predictive value 87·8%, and specificity and positive predictive value 100%. Sensitivity varied greatly according to gestational age and was significantly higher for maternal infections that arose between 17 and 21 weeks of gestation.[32] Lack of homogeneity in methods used for evaluation and in patients' selection are the most probable explanations for the noted differences. Amniotic fluid PCR undertaken before week 18 is probably less reliable than tests done after this time and has not been systematically studied.

PCR has revolutionised prenatal diagnosis of congenital toxoplasmosis by enabling early diagnosis, thereby avoiding use of more invasive procedures on the fetus.[31,34] Peripheral blood, cerebrospinal fluid, and urine should be considered for PCR examination in any newborn suspected to have congenital disease. PCR of vitreous or aqueous fluid is helpful to establish diagnosis in patients who present with atypical retinal lesions, who show a suboptimum response to appropriate antitoxoplasma treatment, or who are immunocompromised.[108,115] In immunocompromised patients suspected to have localised or disseminated toxoplasmosis, PCR of blood (buffy coat), affected body fluids (including bronchoalveolar lavage or cerebrospinal, pleural, ascitic, peritoneal, or ocular fluids), bone-marrow aspirate, or tissues should be regarded as an important diagnostic aid.[74] A positive result of brain tissue PCR may not differentiate between a patient with toxoplasmic encephalitis and an individual with different brain pathology but who is chronically infected (dormant infection) with *T gondii*.

Isolation of *T gondii* from blood or body fluids shows that infection is acute. Isolation techniques need live parasites and thus are not sensitive; however, they are highly accurate for typing of strains. Attempts to isolate the parasite can be undertaken by inoculation of mice or of cell cultures of virtually any human tissue or body fluid.[74,116]

Demonstration of tachyzoites in tissue sections or smears of body fluid—eg, bronchoalveolar lavage or cerebrospinal fluid—shows that *T gondii* causes the pathological changes seen in that system or patient. Tachyzoites can be recorded in primary acute infection or in reactivation of previously acquired latent infection.

The immunoperoxidase technique, which uses antisera to *T gondii*, has proven both sensitive and specific and is superior to conventionally stained tissue sections. It has been used successfully to show the presence of the parasite in the CNS of AIDS patients.[117]

Management and treatment

Infection in the immunocompetent host

Immunocompetent adults and children with toxoplasmic lymphadenitis are usually not treated unless symptoms are severe or persistent. Characteristic histological criteria and findings of a panel of serological tests that accord with recently acquired infection are diagnostic for toxoplasmic lymphadenitis in older children and adults.[99] If needed, treatment is usually administered for 2–4 weeks followed by reassessment of the patient's condition. The combination of pyrimethamine, sulfadiazine, and folinic acid for 4–6 weeks is the most typical drug combination (table 3). Infections acquired by laboratory accident or transfusion of blood products are potentially most severe, and these patients should always be treated.

Maternal and fetal infection

Management of maternal and fetal infection varies considerably between different countries and centres within

the same country.[36] The antibody status of a pregnant woman should be obtained before or early in pregnancy. One in five pregnant women in the USA request termination of their pregnancy if they are told they have a recently acquired *T gondii* infection (based on positive tests for IgM antibodies) and that their offspring might be at risk for congenital infection.[95,118] However, 60% of these women are found to be chronically infected when tested at a reference laboratory.[118] Thus, confirmatory serological testing done at a reference laboratory, with correct interpretation by an expert, diminished the rate of unnecessary abortions by about 50% in women with positive IgM toxoplasma test results reported by outside laboratories.[95,118] Thus, positive IgM test results should always undergo confirmatory tests in a reference laboratory.[74,95] Serological tests for measurement of IgG (dye test, AC/HS), IgM, IgA, and IgE antibodies have been successfully used as a panel of confirmatory tests.[74,118]

Negative tests for IgM antibodies during the first two trimesters essentially rule out recently acquired infection, unless serum samples are obtained so early that an IgM antibody response is not yet detectable (very rare) or too late that the IgM antibodies have already become undetectable. Definitive diagnosis of acute infection or toxoplasmosis requires demonstration of a rise in titres in serial specimens (either conversion from a negative to a positive titre or a significant rise from a low to a higher titre), but this change is rarely shown in countries where systematic screening during pregnancy is not available.[118]

Treatment with spiramycin should be initiated as immediately as feasible after diagnosis of recently acquired maternal infection (table 3). Findings of European studies have suggested that the incidence of congenital toxoplasmosis does not seem to be lower in women who took spiramycin during pregnancy when compared with those who did not.[120–123] However, these data should not prompt any change in current policies of spiramycin administration to pregnant women suspected to have or diagnosed with recently acquired *T gondii* infection.[124] The studies included very few untreated women in their analysis and most untreated women were infected during the third trimester. The design of studies undertaken to date has not permitted a definitive conclusion about use of spiramycin. Until appropriately designed studies are done, authorities continue to recommend spiramycin (for the first and early second trimester) or pyrimethamine/sulfadiazine (for late second and third trimester) for women with suspected or confirmed acute *T gondii* infection acquired during gestation.[36,120,125] Since maternal infection does not necessarily result in fetal infection, suspected or established maternal infection acquired during gestation (based on ultrasonography or serology) must be confirmed by prenatal diagnosis by PCR of amniotic fluid. This test has an overall reported sensitivity of 64–98·8%.[31,32,34,126] In case of a negative PCR result, pregnant women should receive spiramycin prophylaxis until the 17th week of pregnancy and have monthly ultrasound examinations for the entire pregnancy.[81]

Spiramycin is continued throughout pregnancy in the USA and France. In Austria and Germany, spiramycin prophylaxis is followed by a 4-week course of pyrimethamine plus sulfadiazine at 17 weeks of gestation; this approach seems to reduce the rate of clinical signs in the fetus (Prusa A-R, Universitätsklinik für Kinder- und Jugendheilkunde, Wien, Austria, personal communication). In case of a positive PCR result or very highly probable infection of the fetus (ie, acquisition of maternal infection in late second or third trimesters), treatment consists of pyrimethamine/ sulfadiazine—in some countries this regimen is alternated with spiramycin.[15] Prenatal treatment with pyrimethamine/ sulfadiazine of women suspected or confirmed to have fetal infection reduces sequelae of the disease in the newborn.[122]

Antitoxoplasma treatment should be continued throughout pregnancy (table 3). Folinic acid is added to regimens to reduce bone-marrow suppression; careful monitoring for haematotoxicity is mandatory. Ultrasound should be done at least monthly until term if the initial examination revealed no abnormalities; the presence of hydrocephalus has been used as an indication for termination of the pregnancy.

In most countries, treatment of the fetus is followed by treatment of the newborn throughout the first year of life.[15,82] However, lengths of treatment protocols vary greatly between centres in European countries.[123]

Chorioretinitis

The decision to treat active toxoplasmic chorioretinitis should be made based on results of an examination done by an ophthalmologist familiar with the disease. Low titres of IgG antibody are usual in patients with active chorioretinitis because of reactivation of congenital *T gondii* infection; IgM antibodies generally are not detected. Patients with chorioretinitis due to postnatally acquired disease usually have serological findings consistent with infection acquired in the recent past.[75] Most ophthalmologists would recommend treatment if they record severe inflammatory responses, proximity of retinal lesions to the fovea or optic disk, or both.[127]

Nine drugs (or commercially available combinations) have been used in 24 different regimens as treatments for typical cases of recurrent toxoplasmic chorioretinitis.[127] The combination of pyrimethamine, sulfadiazine, and prednisone is the most typically used regimen (table 3). Clindamycin or trimethoprim/ sulfamethoxazole for a minimum of 3 weeks has also been used with favourable clinical results. Because toxoplasmic chorioretinitis can be self-limited in immunocompetent individuals, many clinicians may not treat small peripheral retinal lesions that are not immediately vision-threatening. The rate of recurrent toxoplasmic chorioretinitis can be greatly reduced with a long-term intermittent regimen of trimethoprim/ sulfamethoxazole.[128] In some patients, the morphology of retinal lesions can be non-diagnostic, response to treatment can be suboptimum, or both. In such cases, detection of an abnormal *T gondii*-specific antibody response in ocular fluids (Goldman-Witmer coefficient) and demonstration of the parasite by PCR have been used successfully to establish diagnosis.

Infection in the immunocompromised host

Toxoplasma encephalitis, generalised infection

Transplant recipients who are most likely to acquire *T gondii* infection via the allograft (ie, heart, lung, heart-lung, and kidney) need to be tested—as well as the donor—for baseline toxoplasma IgG antibodies. A seropositive donor (D+) and seronegative recipient (R–) represent the highest risk for disease in these patients; trimethoprim/sulfamethoxazole prophylaxis is highly effective in this setting. Recipients from D–/R–, D–/R+, or D+/R+ pairs rarely develop toxoplasmosis. Serological results indicating apparent reactivation (rising IgG and IgM titres) in the absence of clinically apparent infection, and results consistent with chronic infection in the presence of toxoplasmosis, can be seen and could be misleading.[129] Thus, for immunocompromised patients in

Future areas of work in *T gondii* infection and toxoplasmosis

Clinical management

Diagnosis

- Avidity testing using recombinant antigens
- Amniocentesis and PCR techniques
- Congenital disease in newborns with negative IgM and IgA

Treatment, prophylaxis, screening

- Clinical trials comparing different drug regimens and strategies in different clinical settings—eg, eye disease and congenital toxoplasmosis or prevention of multiple episodes of recurrent episodes of chorioretinitis
- Prophylaxis and treatment of disease in bone-marrow transplant recipients
- Effectiveness of prevention strategies in pregnancy
- Cost-effectiveness of routine serological screening programmes during pregnancy to prevent congenital disease
- Susceptibility of the host to infection—eg, HLA types

Basic research

Strains of T gondii

- Phylogeny
- Sequencing
- Mutants

Sources of infection

- Relative importance of different sources of transmission—eg, meat vs cats vs water
- Genotyping of strains in serum samples with peptides

Interaction of T gondii with immune cells—eg, antigen-presenting cells

- Dendritic cells
- Immune activation vs evasion
- Immune response in specific compartments—eg, eye and brain

Animal models of eye disease

- Vaccination

Proteins

- Strategies (DNA, adjuvants, mucosal)

whom toxoplasmosis is suspected, additional diagnostic methods—including PCR amplification of *T gondii* DNA or isolation of the parasite from blood or body fluids that could contain the parasite, and histological examination of tissues—are strongly recommended.

Pre-emptive antiparasitic treatment should be considered for all symptomatic seropositive immunocompromised patients suspected to have toxoplasmosis. When clinical manifestations suggest involvement of the brain, spinal cord, or both, neuroimaging studies such as CT or MRI are mandatory. These studies should be considered even if neurological examination does not indicate focal deficits. Empiric anti-*T gondii* treatment is an accepted practice for patients with multiple ring enhancing brain lesions (usually established by MRI), positive IgG antibody titres against *T gondii*, and advanced immunodeficiency; a clinical and radiological response to specific anti-*T gondii* treatment is judged supportive of the diagnosis of CNS toxoplasmosis. Patients with cerebral toxoplasmosis usually improve by more than 50% of their baseline neurological examination by 7–10 days.[80]

Monotherapy has no role in treatment of toxoplasmosis in immunocompromised patients. The most typically used and successful regimen continues to be the combination of pyrimethamine/sulfadiazine and folinic acid (table 3).[130] Clindamycin can be used instead of sulfadiazine in patients intolerant to sulfonamides. Treatment is recommended for 4–6 weeks after resolution of all signs and symptoms (sometimes for several months or longer). Trimethoprim/sulfamethoxazole appears to be equivalent to pyrimethamine/sulfadiazine in patients with AIDS.[131] Atovaquone in combination with either pyrimethamine or sulfadiazine has sufficient activity to be considered for treatment of acute toxoplasmic encephalitis in patients with a Karnofsky performance status score—a combined measure of the ability to work, undertake normal activities without assistance, and to care for personal needs—of more than 30.[132] The role of other drugs in the treatment of toxoplasmosis in immunocompromised patients, including clarithromycin, azithromycin, or dapsone, has not been well established.[78] If these drugs have to be used as a last resort, they should always be given in combination with other drugs (preferably pyrimethamine).

After treatment of the acute phase (primary or induction treatment) in immunocompromised patients, maintenance therapy (secondary prophylaxis) should be started, usually with the same regimen that was used in the acute phase but at half doses. Currently, maintenance treatment should be continued for the life of the patient or until underlying immunosuppression has ceased. In patients with AIDS, primary and secondary prophylaxis are generally discontinued when the patient's CD4 count has returned to more than 200 cells per µL and HIV PCR peripheral blood viral load has been reasonably controlled for at least 6 months.[133]

Prevention

Public-health measures to prevent *T gondii* infection are a possible approach to diminish burden of disease in human beings and animals. Wide differences exist in public-health policies to prevent congenital infection; however, data for the efficacy of such policies are scarce.[134] Systematic serological screening of all pregnant women is undertaken only in France and Austria.[42,135] Uncertainty about incidence of congenital infection, cost-effectiveness, difficulties with sensitivity and specificity of serological tests, and findings suggesting absence of spiramycin effectiveness have hampered attempts to implement screening programmes in several countries.[134,136] Neonatal screening has been implemented in several countries (eg, Denmark) or areas such as Massachusetts, USA;[26,28,137,138] through these programmes as many as 80% of infected newborns have been identified.

An effective vaccine against human *T gondii* infection is a desirable but elusive target. Only the attenuated live S48 strain of the parasite has been licensed for use in sheep in Europe and New Zealand.[139] Most research is now focused on vaccine candidates that can induce protective Th1 and humoral (including IgA) responses—both systemic and at the intestinal mucosa level—with the hope to mimic the lifelong immunity conferred by natural infection. Vaccine approaches have included use of purified or recombinant *T gondii* surface antigens,[140,141] live attenuated or mutant strains of the parasite,[11] or DNA with plasmids encoding colony-stimulating factors.[142]

Outlook

Despite great progress in clinical and basic science research, many unresolved issues in toxoplasmosis remain to be addressed. These topics encompass important clinical issues such as epidemiology, diagnosis and treatment, and prevention (screening) strategies (panel).[143]

Conflict of interest statement

None declared.

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References

1 Cornelissen AW, Overdulve JP, van der Ploeg M. Determination of nuclear DNA of five eucoccidian parasites, *Isospora (Toxoplasma) gondii*, *Sarcocystis ovuni*, *Eimeria tenella*, *E acervulina* and *Plasmodium berghei*, with special reference to gamontogenesis and meiosis in I. (*T.*) *gondii*. *Parasitology* 1984; **88:** 531–53.

2 Frenkel JK. Toxoplasmosis: parasite life cycle pathology and immunology. In: Hammond DM, Long PL, eds. The Coccidia. Baltimore: University Park Press, 1973: 343–410.

3 Dubey JP, Miller NL, Frenkel JK. The *Toxoplasma gondii* oocyst from cat feces. *J Exp Med* 1970; **132:** 636–62.

4 Dobrowolski JM, Sibley LD. *Toxoplasma* invasion of mammalian cells is powered by the actin cytoskeleton of the parasite. *Cell* 1996; **84:** 933–39.

5 Sibley LD, Boothroyd JC. Virulent strains of *Toxoplasma gondii* comprise a single clonal lineage. *Nature* 1992; **359:** 82–85.

6 Howe DK, Sibley DL. *Toxoplasma gondii* comprises three clonal lineages: correlation of parasite genotype with human disease. *J Infect Dis* 1995; **172:** 1561–66.

7 Ajzenberg D, Cogne N, Paris L, et al. Genotype of 86 *Toxoplasma gondii* isolates associated with human congenital toxoplasmosis, and correlation with clinical findings. *J Infect Dis* 2002; **186:** 684–89.

8 Kong JT, Grigg ME, Uyetake L, Parmley S, Boothroyd JC. Serotyping of *Toxoplasma gondii* infections in humans using synthetic peptides. *J Infect Dis* 2003; **187:** 1484–95.

9 Grigg ME, Bonnefoy S, Hehl AB, Suzuki Y, Boothroyd JC. Success and virulence in Toxoplasma as the result of sexual recombination between two distinct ancestries. *Science* 2001; **294:** 161–65.

10 Su C, Evans D, Cole RH, Kissinger JC, Ajioka JW, Sibley LD. Recent expansion of Toxoplasma through enhanced oral transmission. *Science* 2003; **299:** 414–16.

11 Fox BA, Bzik DJ. De novo pyrimidine biosynthesis is required for virulence of *Toxoplasma gondii*. *Nature* 2002; **415:** 926–29.

12 Meissner M, Schluter D, Soldati D. Role of *Toxoplasma gondii* myosin A in powering parasite gliding and host cell invasion. *Science* 2002; **298:** 837–40.

13 Desmonts G, Couvreur J, Alison F, Baudelot J, Gerbeaux J, Lelong M. Etude epidemiologique sur la toxoplasmose: l'influence de la cuisson des viandes de boucherie sur la frequence de l'infectin humaine. *Rev Fr Etud Clin Biol* 1965; **10:** 952–58.

14 Cook AJ, Gilbert RE, Buffolano W, et al. Sources of toxoplasma infection in pregnant women: European multicentre case-control study. *BMJ* 2000; **321:** 142–47.

15 Remington JS, McLeod R, Thulliez P, Desmonts G. Toxoplasmosis. In: Remington JS, Klein J, eds. Infectious diseases of the fetus and newborn infant, 5th edn. Philadelphia: WB Saunders, 2001: 205–346.

16 Dubey JP, Gamble HR, Hill D, Sreekumar C, Romand S, Thulliez P. High prevalence of viable *Toxoplasma gondii* infection in market weight pigs from a farm in Massachusetts. *J Parasitol* 2002; **88:** 1234–38.

17 Teutsch SM, Juranek DD, Sulzer A, Dubey JP, Sikes RK. Epidemic toxoplasmosis associated with infected cats. *N Engl J Med* 1979; **300:** 695–99.

18 Bowie WR, King AS, Werker DH, et al. Outbreak of toxoplasmosis associated with municipal drinking water. *Lancet* 1997; **350:** 173–77.

19 Bahia-Oliveira LM, Jones JL, Azevedo-Silva J, Alves CC, Orefice F, Addiss DG. Highly endemic, waterborne toxoplasmosis in north Rio de Janeiro state, Brazil. *Emerg Infect Dis* 2003; **9:** 55–62.

20 Brooks RG, Remington JS. Transplant-related infections. In: Bennett JV, Brachman PS, eds. Hospital infections, 2nd edn. Boston: Little, Brown and Co, 1986: 581–618.

21 Israelski DM, Remington JS. Toxoplasmosis in the non-AIDS immunocompromised host. In: Remington J, Swartz M, eds. Current clinical topics in infectious diseases. London: Blackwell Scientific Publications, 1993: 322–56.

22 Ruiseanen SA. The importance of trophozoites in transmission of toxoplasmosis: survival and pathogenity of *Toxoplasma gondii* trophozoites in liquid media. *Med Hypotheses* 1978; **4:** 367–75.

23 Siegel SE, Lunde MN, Gelderman AH, et al. Transmission of toxoplasmosis by leukocyte transfusion. *Blood* 1971; **37:** 388–94.

24 Kayhoe DE, Jacobs L, Beye HK, McCullough NB. Acquired toxoplasmosis: observations on two parasitologically proved cases treated with pyrimethamine and triple sulfonamides. *N Engl J Med* 1957; **257:** 1247–54.

25 Remington JS, Gentry LO. Acquired toxoplasmosis: infection versus disease. *Ann NY Acad Sci* 1970; **174:** 1006–17.

26 Guerina N, Hsu H-W, Meissner H, et al. Neonatal serologic screening and early treatment for congenital *Toxoplasma gondii* infection. *N Engl J Med* 1994; **330:** 1858–63.

27 Jenum PA, Stray-Pedersen B, Melby KK, et al. Incidence of *Toxoplasma gondii* infection in 35,940 pregnant women in Norway and pregnancy outcome for infected women. *J Clin Microbiol* 1998; **36:** 2900–06.

28 Lebech M, Andersen O, Christensen NC, et al. Feasibility of neonatal screening for toxoplasma infection in the absence of prenatal treatment. *Lancet* 1999; **353:** 1834–37.

29 Gavinet MF, Robert F, Firtion G, et al. Congenital toxoplasmosis due to maternal reinfection during pregnancy. *J Clin Microbiol* 1997; **35:** 1276–77.

30 Vogel N, Kirisits M, Michael E, et al. Congenital toxoplasmosis transmitted from an immunologically competent mother infected before conception. *Clin Infect Dis* 1996; **23:** 1055–60.

31 Hohlfeld P, Daffos F, Costa J-M, Thuylliez P, Forestier F, Vidaud M. Prenatal diagnosis of congenital toxoplasmosis with polymerase-chain-reaction test on amniotic fluid. *N Engl J Med* 1994; **331:** 695–99.

32 Romand S, Wallon M, Franck J, Thulliez P, Peyron F, Dumon H. Prenatal diagnosis using polymerase chain reaction on amniotic fluid for congenital toxoplasmosis. *Obstet Gynecol* 2001; **97:** 296–300.

33 Dunn D, Wallon M, Peyron F, Petersen E, Peckham C, Gilbert R. Mother-to-child transmission of toxoplasmosis: risk estimates for clinical counselling. *Lancet* 1999; **353:** 1829–33.

34 Daffos F, Forestier F, Capella-Pavlovsky M, et al. Prenatal management of 746 pregnancies at risk for congenital toxoplasmosis. *N Engl J Med* 1988; **318:** 271–75.

35 Wilson CB, Remington JS, Stagno S, Reynolds DW. Development of adverse sequelae in children born with subclinical congenital Toxoplasma infection. *Pediatrics* 1980; **66:** 767–74.

36 Wallon M, Liou C, Garner P, Peyron F. Congenital toxoplasmosis: systematic review of evidence of efficacy of treatment in pregnancy. *BMJ* 1999; **318:** 1511–14.

37 European Collaborative Study and Research Network on Congenital Toxoplasmosis. Low incidence of congenital toxoplasmosis in children born to women infected with human immunodeficiency virus. *Eur J Obstet Gynecol Reprod Biol* 1996; **68:** 93–96.

38 Minkoff H, Remington JS, Holman S, Ramirez R, Goodwin S, Landesman S. Vertical transmission of toxoplasma by human immunodeficiency virus-infected women. *Am J Obstet Gynecol* 1997; **176:** 555–59.

39 Jones JL, Kruszon-Moran D, Wilson M, McQuillan G, Navin T, McAuley JB. *Toxoplasma gondii* infection in the United States: seroprevalence and risk factors. *Am J Epidemiol* 2001; **154:** 357–65.

40 Forsgren M, Gille E, Ljungstrom I, Nokes DJ. *Toxoplasma gondii* antibodies in pregnant women in Stockholm in 1969, 1979, and 1987. *Lancet* 1991; **337:** 1413–14.

41 Smith KL, Wilson M, Hightower AW, et al. Prevalence of *Toxoplasma gondii* antibodies in US military recruits in 1989: comparison with data published in 1965. *Clin Infect Dis* 1996; **23:** 1182–83.

42 Aspock H, Pollak A. Prevention of prenatal toxoplasmosis by serological screening of pregnant women in Austria. *Scand J Infect Dis Suppl* 1992; **84:** 32–37.

43 Liesenfeld O. Immune responses to *Toxoplasma gondii* in the gut. *Immunobiology* 1999; **201:** 229–39.

44 Su C, Howe DK, Dubey JP, Ajioka JW, Sibley LD. Identification of quantitative trait loci controlling acute virulence in *Toxoplasma gondii*. *Proc Natl Acad Sci USA* 2002; **99:** 10753–58.

45 Suzuki Y, Wong S-Y, Grumet FC, et al. Evidence for genetic regulation of susceptibility to toxoplasmic encephalitis in AIDS patients. *J Infect Dis* 1996; **173:** 265–68.

46 Roberts C, Cruickshank S, Alexander J. Sex-determined resistance to *Toxoplasma gondii* is associated with temporal differences in cytokine production. *Infect Immun* 1995; **63:** 2549–55.

47 Barragan A, Sibley LD. Transepithelial migration of *Toxoplasma gondii* is linked to parasite motility and virulence. *J Exp Med* 2002; **195:** 1625–33.

48 Morrissette NS, Sibley LD. Cytoskeleton of apicomplexan parasites. *Microbiol Mol Biol Rev* 2002; **66:** 21–38.

49 Karsten V, Qi H, Beckers CJ, et al. The protozoan parasite *Toxoplasma gondii* targets proteins to dense granules and the vacuolar space using both conserved and unusual mechanisms. *J Cell Biol* 1998; **141:** 1323–33.

50 Shaw MK, Roos DS, Tilney LG. Acidic compartments and rhoptry formation in *Toxoplasma gondii*. *Parasitology* 1998; **117** (Pt 5): 435–43.

51 Nielsen H, Christiansen L, Buus S, Fomsgaard A, Petersen E,

Lauemoller S. Complete protection against lethal *Toxoplasma gondii* infection in mice immunized with a plasmid encoding the SAG1 gene. *Infect Immun* 1999; **67:** 6358–63.
52 Bhopale GM. Development of a vaccine for toxoplasmosis: current status. *Microbes Infect* 2003; **5:** 457–62.
53 Chardes T, Buzoni-Gatel D, Lepage A, Bernard F, Bout D. *Toxoplasma gondii* oral infection induces specific cytotoxic CD8α/β+ Thy-1+ gut intraepithelial lymphocytes, lytic for parasite-infected enterocytes. *J Immunol* 1994; **153:** 4596–603.
54 Reis e Sousa C, Hieny S, Scharton-Kersten T, et al. In vivo microbial stimulation induces rapid CD40 ligand-independent production of interleukin 12 by dendritic cells and their redistribution to T cell areas. *J Exp Med* 1997; **186:** 1819–29.
55 Bliss SK, Marshall AJ, Zhang Y, Denkers EY. Human polymorphonuclear leukocytes produce IL-12, TNF-alpha, and the chemokines macrophage-inflammatory protein-1 alpha and -1 beta in response to *Toxoplasma gondii* antigens. *J Immunol* 1999; **162:** 7369–75.
56 Denkers EY, Gazzinelli RT. Regulation and function of T-cell-mediated immunity during *Toxoplasma gondii* infection. *Clin Microbiol Rev* 1998; **11:** 569–88.
57 Luder CG, Lang T, Beuerle B, Gross U. Down-regulation of MHC class II molecules and inability to up-regulate class I molecules in murine macrophages after infection with *Toxoplasma gondii*. *Clin Exp Immunol* 1998; **112:** 308–16.
58 Luder CG, Lang C, Giraldo-Velasquez M, Algner M, Gerdes J, Gross U. Toxoplasma gondii inhibits MHC class II expression in neural antigen-presenting cells by down-regulating the class II transactivator CIITA. *J Neuroimmunol* 2003; **134:** 12–24.
59 Nash PB, Purner MB, Leon RP, Clarke P, Duke RC, Curiel TJ. *Toxoplasma gondii*-infected cells are resistant to multiple inducers of apoptosis. *J Immunol* 1998; **160:** 1824–30.
60 Montoya JG, Lowe KE, Clayberger C, et al. Human CD4+ and CD8+ T lymphocytes are both cytotoxic to *Toxoplasma gondii*-infected cells. *Infect Immun* 1996; **64:** 176–81.
61 Suzuki Y, Orellana MA, Schreiber RD, Remington JS. Interferon-γ: the major mediator of resistance against *Toxoplasma gondii*. *Science* 1988; **240:** 516–18.
62 Scalise F, Gerli R, Castellucci G, et al. Lymphocytes bearing the γδ T-cell receptor in acute toxoplasmosis. *Immunology* 1992; **76:** 668–70.
63 de Paoli P, Basaglia G, Gennari D, Crovatto M, Modolo M, Santini G. Phenotypic profile and functional characteristics of human gamma and delta t cells during acute toxoplasmosis. *J Clin Microbiol* 1992; **30:** 729–31.
64 Chardes T, Bourguin I, Mevelec M-N, Dubremetz J-F, Bout D. Antibody responses to *Toxoplasma gondii* in sera, intestinal secretions, and milk from orally infected mice and characterization of target antigens. *Infect Immun* 1990; **58:** 1240–46.
65 Mineo J, McLeod R, Mack D, et al. Antibodies to *Toxoplasma gondii* major surface protein (SAG-1, P30) inhibit infection of host cells and are produced in murine intestine after peroral infection. *J Immunol* 1993; **150:** 3951–64.
66 Dorfman RF, Remington JS. Value of lymph-node biopsy in the diagnosis of acute acquired toxoplasmosis. *N Engl J Med* 1973; **289:** 878–81.
67 Weiss L, Chen Y, Berry G, Strickler J, Dorfman R, Warnke R. Infrequent detection of *Toxoplasma gondii* genome in toxoplasmic lymphadenitis: a polymerase chain reaction study. *Hum Pathol* 1992; **23:** 154–58.
68 Holland GN, O'Connor GR, Belfort R Jr, Remington JS. Toxoplasmosis. In: Pepose JS, Holland GN, Wilhelmus KR, eds. Ocular infection and immunity. St. Louis: Mosby Yearbook, 1996: 1183–223.
69 Montoya JG, Jordan R, Lingamneni S, Berry GB, Remington JS. Toxoplasmic myocarditis and polymyositis in patients with acute acquired toxoplasmosis diagnosed during life. *Clin Infect Dis* 1997; **24:** 676–83.
70 Luft BJ, Conley F, Remington JS, et al. Outbreak of central-nervous-system toxoplasmosis in western Europe and North America. *Lancet* 1983; **1:** 781–84.
71 Frenkel JK. Pathology and pathogenesis of congenital toxoplasmosis. *Bull N Y Acad Med* 1974; **50:** 182–91.
72 Luft BJ, Remington JS. Toxoplasmic encephalitis in AIDS. *Clin Infect Dis* 1992; **15:** 211–22.
73 Mariuz P, Bosler EM, Luft BJ. Toxoplasma pneumonia. *Semin Respir Infect* 1997; **12:** 40–43.
74 Montoya JG. Laboratory diagnosis of *Toxoplasma gondii* infection and toxoplasmosis. *J Infect Dis* 2002; **185** (suppl 1): S73–82.
75 Montoya JG, Remington JS. Toxoplasmic chorioretinitis in the setting of acute acquired toxoplasmosis. *Clin Infect Dis* 1996; **23:** 277–82.
76 Holland GN. Reconsidering the pathogenesis of ocular toxoplasmosis. *Am J Ophthalmol* 1999; **128:** 502–05.
77 Burnett AJ, Shortt SG, Isaac-Renton J, King A, Werker D, Bowie WR. Multiple cases of acquired toxoplasmosis retinitis presenting in an outbreak. *Ophthalmology* 1998; **105:** 1032–37.
78 Liesenfeld O, Wong SY, Remington JS. Toxoplasmosis in the setting of AIDS. In: Bartlett JG, Merigan TC, Bolognesi D, eds. Textbook of AIDS medicine, 2nd edn. Baltimore: Williams & Wilkins, 1999: 225–59.
79 Porter SB, Sande M. Toxoplasmosis of the central nervous system in the Acquired Immunodeficiency Syndrome. *N Engl J Med* 1992; **327:** 1643–48.
80 Luft BJ, Hafner R, Korzun AH, et al. Toxoplasmic encephalitis in patients with the acquired immunodeficiency syndrome. *N Engl J Med* 1993; **329:** 995–1000.
81 Gay-Andrieu F, Marty P, Pialat J, Soumies G, Drier de Laforte T, Peyron F. Fetal toxoplasmosis and negative amniocentesis: necessity of an ultrasound follow-up. *Prenat Diagn* 2003; **23:** 558–60.
82 McAuley J, Boyer KM, Patel D, et al. Early and longitudinal evaluations of treated infants and children and untreated historical patients with congenital toxoplasmosis: the Chicago collaborative treatment trial. *Clin Infect Dis* 1994; **18:** 38–72.
83 Swisher CN, Boyer K, McLeod R. Congenital toxoplasmosis. *Semin Pediatr Neurol* 1994; **1:** 4–25.
84 Cazenave J, Cheyrou A, Blouin P. Use of polymerase chain reaction to detect *Toxoplasma*. *J Clin Pathol* 1991; **44:** 1037.
85 Fuentes I, Rodriguez M, Domingo CJ, Del Castillo F, Juncosa T, Alvar J. Urine sample used for congenital toxoplasmosis diagnosis by PCR. *J Clin Microbiol* 1996; **34:** 2368–71.
86 Sabin AB, Feldman HA. Dyes as microchemical indicators of a new immunity phenomenon affecting a protozoan parasite (toxoplasma). *Science* 1948; **108:** 660–63.
87 Walton BC, Benchoff BM, Brooks WH. Comparison of the indirect fluorescent antibody test and methylene blue dye test for detection of antibodies to *Toxoplasma gondii*. *Am J Trop Med Hyg* 1966; **15:** 149–52.
88 Balsari A, Poli G, Molina V, et al. ELISA for toxoplasma antibody detection: a comparison with other serodiagnostic tests. *J Clin Pathol* 1980; **33:** 640–43.
89 Hedman K, Lappalainen M, Seppala I, Makela O. Recent primary Toxoplasma infection indicated by a low avidity of specific IgG. *J Infect Dis* 1989; **159:** 736–39.
90 Liesenfeld O, Montoya JG, Kinney S, Press C, Remington JS. Effect of testing for IgG avidity in the diagnosis of *Toxoplasma gondii* infection in pregnant women: experience in a US reference laboratory. *J Infect Dis* 2001; **183:** 1248–53.
91 Montoya JG, Liesenfeld O, Kinney S, Press C, Remington JS. VIDAS test for avidity of Toxoplasma-specific immunoglobulin G for confirmatory testing of pregnant women. *J Clin Microbiol* 2002; **40:** 2504–08.
92 Dannemann BR, Vaughan WC, Thulliez P, Remington JS. Differential agglutination test for diagnosis of recently acquired infection with *Toxoplasma gondii*. *J Clin Microbiol* 1990; **28:** 1928–33.
93 Jenum PA, Stray-Pedersen B, Gundersen A-G. Improved diagnosis of primary *Toxoplasma gondii* infection in early pregnancy by determination of antitoxoplasma immunoglobulin G activity. *J Clin Microbiol* 1997; **35:** 1972–77.
94 Lappalainen M, Koskela P, Koskiniemi M, et al. Toxoplasmosis acquired during pregnancy: improved serodiagnosis based on avidity of IgG. *J Infect Dis* 1993; **167:** 691–97.
95 Liesenfeld O, Press C, Montoya JG, et al. False-positive results in immunoglobulin M (IgM) toxoplasma antibody tests and importance of confirmatory testing: the Platelia toxo IgM test. *J Clin Microbiol* 1997; **35:** 174–78.
96 Naot Y, Desmonts G, Remington JS. IgM enzyme-linked immunosorbent assay test for the diagnosis of congenital Toxoplasma infection. *J Pediatr* 1981; **98:** 32–36.
97 Siegel JP, Remington JS. Comparison of methods for quantitating antigen-specific immunoglobulin M antibody with a reverse enzyme-linked immunosorbent assay. *J Clin Microbiol* 1983; **18:** 63–70.
98 Wilson M, Remington JS, Clavet C, et al. Evaluation of six commercial kits for detection of human immunoglobulin M antibiodies to *Toxoplasma gondii*. *J Clin Microbiol* 1997; **35:** 3112–15.
99 Montoya JG, Remington JS. Studies on the serodiagnosis of toxoplasmic lymphadenitis. *Clin Infect Dis* 1995; **20:** 781–90.
100 Roberts A, Hedman K, Luyasu V, et al. Multicenter evaluation of strategies for serodiagnosis of primary infection with *Toxoplasma gondii*. *Eur J Clin Microbiol Infect Dis* 2001; **20:** 467–74.
101 Desmonts G, Naot Y, Remington JS. Immunoglobulin M-immunosorbent agglutination assay for diagnosis of infectious diseases: diagnosis of acute congenital and acquired Toxoplasma infections. *J Clin Microbiol* 1981; **14:** 486–91.
102 Stepick-Biek P, Thulliez P, Araujo FG, Remington JS. IgA antibodies for diagnosis of acute congenital and acquired toxoplasmosis. *J Infect Dis* 1990; **162:** 270–73.

103 Decoster A, Slizewicz B, Simon J, et al. Platelia-toxo IgA, a new kit for early diagnosis of congenital toxoplasmosis by detection of anti-P30 immunoglobulin A antibodies. *J Clin Microbiol* 1991; **29:** 2291–95.

104 Pinon JM, Dumon H, Chemla C, et al. Strategy for diagnosis of congenital toxoplasmosis: evaluation of methods comparing mothers and newborns and standard methods for postnatal detection of immunoglobulin G, M, and A antibodies. *J Clin Microbiol* 2001; **39:** 2267–71.

105 Wong SY, Hadju M-P, Ramirez R, Thulliez P, McLeod R, Remington JS. The role of specific immunoglobulin E in diagnosis of acute toxoplasma infection and toxoplasmosis. *J Clin Microbiol* 1993; **31:** 2952–59.

106 Pinon JM, Touhas D, Marx C, et al. Detection of specific immunoglobulin E in Patients with toxoplasmosis. *J Clin Microbiol* 1990; **28:** 1739–43.

107 de Boer JH, Verhagen C, Bruinenberg M, et al. Serologic and polymerase chain reaction analysis of intraocular fluids in the diagnosis of infectious uveitis. *Am J Opthalmol* 1996; **121:** 650–58.

108 Grover CM, Thulliez P, Remington JS, Boothroyd JD. Rapid prenatal diagnosis of congenital Toxoplasma infection by using polymerase chain reaction and amniotic fluid. *J Clin Microbiol* 1990; **28:** 2297–301.

109 Montoya JG, Parmley S, Liesenfeld O, Jaffe GJ, Remington JS. Use of the polymerase chain reaction for diagnosis of ocular toxoplasmosis. *Ophthalmology* 1999; **106:** 1554–63.

110 Brezin AP, Egwuagu CE, Burnier M, et al. Identification of *Toxoplasma gondii* in paraffin-embedded sections by the polymerase chain reaction. *Am J Ophthalmol* 1990; **110:** 599–604.

111 Dupouy-Camet J, Lavareda de Souza L, Maslo C, et al. Detection of *Toxoplasma gondii* in venous blood from AIDS patients by polymerase chain reaction. *J Clin Microb* 1993; **31:** 1866–69.

112 Mele A, Paterson PJ, Prentice HG, Leoni P, Kibbler CC. Toxoplasmosis in bone marrow transplantation: a report of two cases and systematic review of the literature. *Bone Marrow Transplant* 2002; **29:** 691–98.

113 Costa JM, Ernault P, Gautier E, Bretagne S. Prenatal diagnosis of congenital toxoplasmosis by duplex real-time PCR using fluorescence resonance energy transfer hybridization probes. *Prenat Diagn* 2001; **21:** 85–88.

114 Filisetti D, Gorcii M, Pernot-Marino E, Villard O, Candolfi E. Diagnosis of congenital toxoplasmosis: comparison of targets for detection of *Toxoplasma gondii* by PCR. *J Clin Microbiol* 2003; **41:** 4826–28.

115 Fardeau C, Romand S, Rao NA, et al. Diagnosis of toxoplasmic retinochoroiditis with atypical clinical features. *Am J Ophthalmol* 2002; **134:** 196–203.

116 Hitt JA, Filice GA. Detection of *Toxoplasma gondii* parasitemia by gene amplification, cell culture, and mouse inoculation. *J Clin Microbiol* 1992; **30:** 3181–84.

117 Conley FK, Jenkins KA, Remington JS. *Toxoplasma gondii* infection of the central nervous system: use of the peroxidase-antiperoxidase method to demonstrate toxoplasma in formalin fixed, paraffin embedded tissue sections. *Hum Pathol* 1981; **12:** 690–98.

118 Liesenfeld O, Montoya JG, Tathineni NJ, et al. Confirmatory serologic testing for acute toxoplasmosis and rate of induced abortions among women reported to have positive Toxoplasma immunoglobulin M antibody titers. *Am J Obstet Gynecol* 2001; **184:** 140–45.

119 Wong S, Remington JS. Toxoplasmosis in pregnancy. *Clin Infect Dis* 1994; **18:** 853–62.

120 Gilbert RE, Gras L, Wallon M, Peyron F, Ades AE, Dunn DT. Effect of prenatal treatment on mother to child transmission of *Toxoplasma gondii*: retrospective cohort study of 554 mother-child pairs in Lyon, France. *Int J Epidemiol* 2001; **30:** 1303–08.

121 Gilbert R, Dunn D, Wallon M, et al. Ecological comparison of the risks of mother-to-child transmission and clinical manifestations of congenital toxoplasmosis according to prenatal treatment protocol. *Epidemiol Infect* 2001; **127:** 113–20.

122 Foulon W, Villena I, Stray-Pedersen B, et al. Treatment of toxoplasmosis during pregnancy: a multicenter study of impact on fetal transmission and children's sequelae at age 1 year. *Am J Obstet Gynecol* 1999; **180** (2 Pt 1): 410–15.

123 Gilbert R, Gras L. Effect of timing and type of treatment on the risk of mother to child transmission of *Toxoplasma gondii*. *BJOG* 2003; **110:** 112–20.

124 Thulliez P. Efficacy of prenatal treatment for toxoplasmosis: a possibility that cannot be ruled out. *Int J Epidemiol* 2001; **30:** 1315–16.

125 Gras L, Gilbert RE, Ades AE, Dunn DT. Effect of prenatal treatment on the risk of intracranial and ocular lesions in children with congenital toxoplasmosis. *Int J Epidemiol* 2001; **30:** 1309–13.

126 Forestier F, Hohlfeld P, Sole Y, Daffos F. Prenatal diagnosis of congenital toxoplasmosis by PCR: extended experience. *Prenat Diagn* 1998; **18:** 407–09.

127 Holland GN, Lewis KG. An update on current practices in the management of ocular toxoplasmosis. *Am J Ophthalmol* 2002; **134:** 102–14.

128 Silveira C, Belfort R Jr, Muccioli C, et al. The effect of long-term intermittent trimethoprim/sulfamethoxazole treatment on recurrences of toxoplasmic retinochoroiditis. *Am J Ophthalmol* 2002; **134:** 41–46.

129 Luft BJ, Billingham M, Remington JS. Endomyocardial biopsy in the diagnosis of toxoplasmic myocarditis. *Transplant Proc* 1986; **18:** 1871–73.

130 Montoya JG, Remington JS. *Toxoplasma gondii*. In: Mandell GL, Bennett JE, Dolin R, eds. Principles and practice of infectious diseases. Philadelphia: Churchill Livingstone, 2000: 2858–88.

131 Torre D, Casari S, Speranza F, et al. Randomized trial of trimethoprim-sulfamethoxazole versus pyrimethamine-sulfadiazine for therapy of toxoplasmic encephalitis in patients with AIDS. *Antimicrob Agents Chemother* 1998; **42:** 1346–49.

132 Chirgwin K, Hafner R, Leport C, et al. Randomized phase II trial of atovaquone with pyrimethamine or sulfadiazine for treatment of toxoplasmic encephalitis in patients with acquired immunodeficiency syndrome: ACTG 237/ANRS 039 Study. *Clin Infect Dis* 2002; **34:** 1243–50.

133 Kaplan JE, Masur H, Holmes KK. Guidelines for preventing opportunistic infections among HIV-infected persons, 2002: recommendations of the US Public Health Service and the Infectious Diseases Society of America. *MMWR Recomm Rep* 2002; **51** (RR-8): 1–52.

134 Eskild A, Oxman A, Magnus P, Bjorndal A, Bakketeig LS. Screening for toxoplasmosis in pregnancy: what is the evidence of reducing a health problem? *J Med Screen* 1996; **3:** 188–94.

135 Desmonts G. Prevention de la toxoplasmose: remarques sur l'experience poursuivie en France. *Prog Clin Biol Res* 1985; **163B:** 333.

136 McCabe R, Remington JS. Toxoplasmosis: the time has come. *N Engl J Med* 1988; **318:** 313–15.

137 Kimball AC, Kean BH, Fuchs F. Congenital toxoplasmosis: a prospective study of 4,048 obstetric patients. *Am J Obstet Gynecol* 1971; **111:** 211–18.

138 Petersen E, Eaton RB. Control of congenital infection with *Toxoplasma gondii* by neonatal screening based on detection of specific immunoglobulin M antibodies eluted from phenylketonuria filter-paper blood-spot samples. *Acta Paediatr Suppl* 1999; **88:** 36–39.

139 Buxton D, Innes EA. A commercial vaccine for ovine toxoplasmosis. *Parasitology* 1995; **110:** 11–16.

140 Bulow R, Boothroyd JC. Protection of mice from fatal *Toxoplasma gondii* infection by immunization with p30 antigen in liposomes. *J Immunol* 1991; **147:** 3496–500.

141 Petersen E, Nielsen HV, Christiansen L, Spenter J. Immunization with *E coli* produced recombinant *T gondii* SAG1 with alum as adjuvant protect mice against lethal infection with *Toxoplasma gondii*. *Vaccine* 1998; **16:** 1283–89.

142 Ismael AB, Sekkai D, Collin C, Bout D, Mevelec MN. The MIC3 gene of *Toxoplasma gondii* is a novel potent vaccine candidate against toxoplasmosis. *Infect Immun* 2003; **71:** 6222–28.

143 Liesenfeld O, Remington JS. Toxoplasmosis. In: Martens M, Faro S, Soper D, eds. Infectious diseases in women. Philadelphia: WB Saunders, 2001: 57–79.

CLINICAL PRACTICE INVITED ARTICLE
Ellie J. C. Goldstein, Section Editor

Management of *Toxoplasma gondii* Infection during Pregnancy

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Acute infection with *Toxoplasma gondii* during pregnancy and its potentially tragic outcome for the fetus and newborn continue to occur in the United States, as well as worldwide, despite the fact that it can be prevented. The infection can be acquired through ingestion of infected, undercooked meat or contaminated food or water. Transmission to the fetus occurs almost solely in women who acquire their primary infection during gestation and can result in visual and hearing loss, mental and psychomotor retardation, seizures, hematological abnormalities, hepatosplenomegaly, or death. Systematic education and serological screening of pregnant women are the most reliable and currently available strategies for the prevention, diagnosis, and early treatment of the infection in the offspring; this is largely because toxoplasmosis in pregnant women most often goes unrecognized. Treatment of the infection in the fetus and infant during the first year of life has been demonstrated to significantly improve the clinical outcome.

Toxoplasma gondii infection acquired by pregnant women during gestation and its transmission to the fetus continue to be the cause of tragic yet preventable disease in the offspring [1]. In addition to the unfortunate outcome for infants and children are the emotional and economic burdens faced by the parents and society. It has been estimated that 500–5000 infants each year are born with congenital toxoplasmosis in the United States [2]. Although the majority of infants appear to be healthy at birth, significant long-term sequelae may become obvious only months or years later.

T. gondii infection is acquired primarily through ingestion of cysts in infected, undercooked meat or oocysts that may contaminate soil, water, and food. Meat (primarily pork and lamb) is an important source of the infection in humans in the United States [3]. However, the frequency at which the source is meat versus ingestion of oocysts among different populations and geographical areas in the United States is unknown. Recent studies have identified water as a potential source of the infection in both humans and animals [4–8].

The purpose of this review is to provide an update on the diagnosis and management of toxoplasmosis during pregnancy in the United States. A more comprehensive review of the subject can be found elsewhere [1].

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CLINICAL MANIFESTATIONS DURING PREGNANCY

Transmission to the fetus occurs predominantly in women who acquire their primary infection during gestation. In rare cases, congenital transmission has occurred in chronically infected women whose infection was reactivated because of their immunocompromised state (e.g., from AIDS or treatment with corticosteroids for their underlying disease).

Most pregnant women with acute acquired infection do not experience obvious symptoms or signs [1, 9]. A minority may experience malaise, low-grade fever, and lymphadenopathy. Rarely, pregnant women will present with visual changes due to toxoplasmic chorioretinitis [10] as a result of recently acquired infection or reactivation of a chronic infection. A recent study revealed that 52% of mothers who gave birth to congenitally infected offspring could not recall experiencing an infection-related illness during pregnancy or an identifiable epidemiological risk factor [9]. In severely immunocompromised, chronically infected pregnant women (e.g., patients with AIDS and those receiving high-dose immunosuppressive therapy, including organ transplant recipients, patients with malignancies, and patients with connective tissue disorders), reactivation of

latent *T. gondii* infection resulted in congenital transmission of the parasite to the fetus [11–13].

SPECIAL CONSIDERATIONS IN THE FETUS AND NEWBORN RELATED TO MATERNAL INFECTION

The frequency of vertical transmission increases with the gestational age (table 1) [1, 14]. In contrast, severe clinical signs in the infected infant are more commonly observed in offspring of women whose infection was acquired early in gestation (table 1).

Occasionally, the diagnosis of the infection in a pregnant woman is first considered when ultrasonographic findings reveal the presence of fetal abnormalities [1]. In other cases, it is first considered in a mother whose newborn has clinical manifestations of the infection.

DIAGNOSIS DURING PREGNANCY

Serological tests and PCR are used in an attempt to diagnose toxoplasmosis in pregnant women (table 2) [1]. Transmission of the parasite to the fetus frequently occurs in pregnant women who have no history of illness during gestation or exposure to undercooked meat or to cats [9]. Therefore, the decision to perform *T. gondii* serological tests during pregnancy should not be based solely on clinical (e.g., presence or absence of symptoms) or epidemiological (i.e., history of exposure to *T. gondii*) grounds [1, 9].

Systematic serological screening for *T. gondii* IgG and IgM antibodies in all pregnant women as early in gestation as feasible (ideally during the first trimester) and in seronegative women each month or trimester thereafter would be optimal. Such screening allows for detection of seroconversion and early initiation of treatment. Although screening is rarely performed in the United States, such screening is mandated by law in some countries (e.g., France and Austria), to facilitate early detection of recently acquired infection. Although we support the use of systematic serological screening during pregnancy, we acknowledge that factors such as cost, demographic characteristics, availability of appropriate tests, and the relatively low incidence of acute infection must be taken into consideration. An additional consideration is the recent controversy about the effectiveness of treatment during gestation in an attempt to prevent transmission to the fetus.

Serological tests. The detection (and quantification) of *T. gondii* antibodies in serum is used to establish whether a pregnant woman has been infected and, if so, to determine whether the infection was acquired recently or in the distant past. If serological test results suggest a recently acquired infection, an effort is made to determine whether the infection was likely acquired during gestation or shortly before conception. If so, the fetus is at risk.

In the United States, physicians most often submit only a single serum sample for serological testing, and from the results for that specimen, they expect a diagnosis. Thus, seroconversion is rarely demonstrable in the United States. Only approximately one-third of the samples submitted to our serology laboratory are obtained from women in their first trimester [1]. Serological test results of serum samples obtained later in gestation are frequently difficult to interpret. The earlier the serum sample is obtained, the more likely the results will prove clinically helpful. Testing of a serum sample drawn after the second trimester most often will not be able to exclude that an infection was acquired earlier in the pregnancy.

For serological diagnosis, IgG, IgM, IgA, and IgE antibodies; IgG avidity; and the differential agglutination (AC/HS) tests have been employed successfully in an attempt to distinguish the acute versus the chronic stage of the infection [15]. Except for measurement of IgG and IgM antibodies, most of these tests are performed only in reference laboratories (e.g., in the United States, at the Palo Alto Medical Foundation Toxoplasma

Table 1. Risk of *Toxoplasma gondii* congenital infection (transmission) and development of clinical signs in offspring before age 3 years, according to gestational age at maternal seroconversion.

Gestational age at maternal seroconversion, weeks	Risk of congenital infection (95% CI), %	Development of clinical signs in the infected offspring (95% CI), %	Risk of development of clinical signs when infection status is unknown,[a] %
13	6 (3–9)	61 (34–85)	4
26	40 (33–47)	25 (18–33)	10
36	72 (60–81)	9 (4–17)	7

NOTE. This analysis was performed with 603 women whose *T. gondii* infection was documented to have occurred during gestation. Anti-*Toxoplasma* treatment was administered to 504 (84%) of the women. Data are from [14].

[a] Risk of development of clinical signs of infection in a child whose mother was known to have been infected during gestation but in whom congenital infection has not been established yet (values are obtained by multiplying the risk of congenital infection by the risk of signs among congenitally infected children).

Table 2. Laboratory tests available for diagnosis of toxoplasmosis during pregnancy and the distinguishing features between serological testing at nonreference laboratories and at Palo Alto Medical Foundation Toxoplasma Serology Laboratory (PAMF-TSL).

Diagnostic tests	Use	Available tests	Storage of serum samples	Assistance to clinicians
Serological tests				
At nonreference or commercial laboratory	Useful for initial screening because only ~10% of pregnant women in the US are seropositive	IgG: positive or negative results are usually reliable; IgM: negative results are most often reliable, and positive or equivocal results require confirmatory testing at reference laboratory	Samples are usually discarded after testing and are not available for future parallel testing	Usually not available
At reference laboratory (PAMF-TSL[a])	Particularly useful for pregnant women with positive or equivocal IgM test results	IgG (dye test), IgM, IgA, IgE, AC/HS, avidity, agglutination	Samples are stored for ≥1 year for potential future parallel testing	Provided by physician consultants
Amniotic fluid PCR	Should be performed at 18 weeks of gestation or as soon as feasible thereafter for pregnant women with suspected or proven toxoplasmosis during pregnancy; 35-multicopy B1 gene is commonly used as the target	…	…	…
Ultrasound	Should be performed (ideally every month) for pregnant women with suspected or proven *T. gondii* infection acquired during pregnancy	…	…	…

[a] http://www.pamf.org/serology/; telephone number (650) 853-4828; e-mail, toxolab@pamf.org.

Serology Laboratory [PAMF-TSL]; Palo Alto, CA; http://www.pamf.org/serology/; telephone number (650) 853-4828; e-mail, toxolab@pamf.org). Currently, the IgG avidity test is not commercially available in the United States. Ongoing studies at PAMF-TSL are in progress with the VIDAS IgG avidity kit (bioMérieux), which is widely used in western Europe. An avidity test is also available at FOCUS Laboratories (Cypress, CA).

Serological testing for both IgG and IgM antibodies at clinical, nonreference laboratories should be performed initially. In the vast majority of cases, testing early in gestation can establish either that infection has not occurred, by the absence of both IgG and IgM antibodies, or that infection was acquired in the distant past, by positive IgG and negative IgM antibody test results (table 3). Additional assistance with confirmatory testing in reference laboratories is required primarily for patients with positive or equivocal IgM antibody test results. A reference laboratory such as PAMF-TSL often can determine whether a patient with a positive IgM antibody test result acquired the infection recently or in the distant past.

Physicians and laboratory personnel should realize the significant and often unfortunate delays that may occur between the date that the serological tests are ordered and the date that the results are actually reported back to the health care provider and the patient. This is particularly the case when results obtained at nonreference laboratories require confirmatory testing at a reference laboratory.

Appropriate interpretation of serological test results can best be achieved when adequate clinical information (i.e., gestational age, reason for testing, and presence of abnormal clinical or laboratory findings in the mother or the fetus) is made available to experienced consultants. Too frequently, serological tests are requested, but information about the patient is not provided. Lack of clinical information often results in suboptimal interpretation of results and limits the ability to provide appropriate recommendations.

It needs to be emphasized that a positive IgM antibody test result at any time before or during gestation does not necessarily mean a recently acquired infection [16–18]. IgM antibodies may persist for ⩾1 year following acute infection, and most positive IgM antibody test results are obtained in pregnant women who acquired their infection in the more distant past and beyond the period of fetal risk. These patients are chronically infected. Recently, we examined 100 consecutive serum samples submitted to PAMF-TSL because of a positive IgM antibody test result at an outside clinical laboratory. Confirmatory testing at PAMF-TSL revealed that 62% of these serum samples were negative for IgM antibody. This percentage is essentially the same as that we reported 7 years ago [19]. Additional testing confirmed that infection in such cases was acquired in the more distant past rather than recently. The greatest value of a positive IgM antibody test result is that it raises the question of a recently acquired infection, thereby necessitating confirmatory testing in a reference laboratory.

Figure 1 shows interpretation of results of serological tests performed at clinical laboratories. Serological testing for both IgG and IgM antibodies at clinical (nonreference) laboratories should be performed initially. Negative results of *Toxoplasma* IgG and IgM antibody tests, as well as positive results of IgG tests, tend to be accurate. Initial screening and testing for toxoplasmosis can be accomplished by these laboratories (table 3).

Figure 2 shows the procedure for confirmatory testing of positive IgM test results at a reference laboratory. A battery of serological tests is usually required in an attempt to establish whether a positive or equivocal IgM test result is clinically relevant (i.e., whether it is indicative of an infection acquired during gestation) [17]. It is noteworthy that only ~40% of positive IgM test results obtained at nonreference laboratories

Table 3. Interpretation of results of serological tests for toxoplasmosis performed at clinical (nonreference) laboratories.

IgG test result	IgM test result	Clinical relevance
Negative	Negative	Interpreted to indicate that the woman has not been infected with *Toxoplasma gondii*. Serial testing during pregnancy is advised. If such women acquire primary infection during gestation, they are at risk of transmitting the infection to their fetus.
Positive	Negative	During the first or second trimester, most often reflects an infection acquired before the present pregnancy[a]
Negative	Positive or equivocal	IgM antibodies are detected early in the acute infection. Because they may persist for prolonged periods, IgM antibodies may be detected in pregnant women who were infected in the distant past and before gestation. Therefore, a positive (or equivocal) IgM test result should be followed by confirmatory testing at a *Toxoplasma* reference laboratory[b] [17]
Positive	Positive or equivocal	Same as above

[a] In the third trimester, this result is more difficult to interpret. Although it is most consistent with an infection acquired before pregnancy, in some patients, this result may reflect an infection that was acquired early in gestation and that was accompanied by an increase in the IgM titer and a decrease to nondetectable levels within a relatively brief period of time.

[b] For example, the Palo Alto Medical Foundation Toxoplasma Serology Laboratory, telephone number (650) 853-4828; e-mail, toxolab@pamf.org.

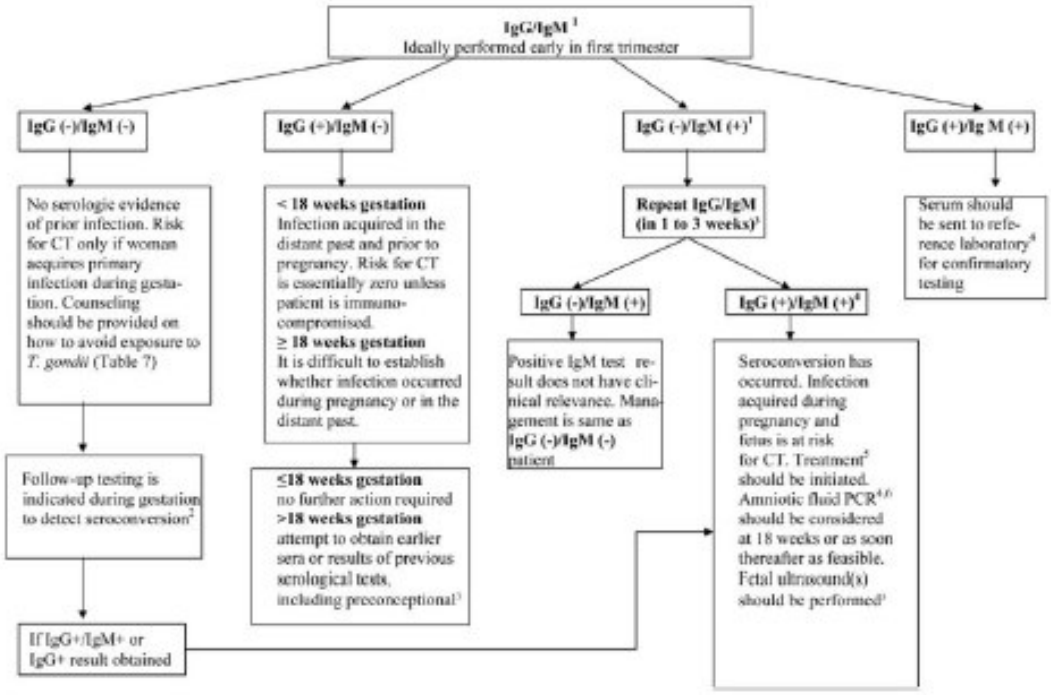

Figure 1. Guidelines for serological testing and management of toxoplasmosis during pregnancy on the basis of initial results obtained from *Toxoplasma gondii* IgG and IgM antibody tests performed at clinical (nonreference) laboratories. [1]Initial serological screening with IgG and IgM tests usually can be reliably performed at nonreference laboratories. Certain laboratories or clinicians may choose to send serum samples at this initial stage directly to a reference laboratory; interpretation of results obtained in a reference laboratory usually will be the same as that shown here for nonreference laboratories. [2]The interval for serological screening varies by the center and country where systematic serological screening is performed (e.g., every month in France). Systematic serological screening to detect early infection acquired during gestation is not performed in the United States. [3]Consider consultation with a physician expert in management of toxoplasmosis during pregnancy (e.g., at Palo Alto Medical Foundation Toxoplasma Serology Laboratory [PAMF-TSL], telephone number (650) 853-4828, or US [Chicago, IL] National Collaborative Treatment Trial Study, telephone number (773) 834-4152). [4]Consider sending samples to a reference laboratory such as PAMF-TSL [17]. [5]Treatment with spiramycin or with pyrimethamine, sulfadiazine, and folinic acid (see text and table 6). [6]Amniotic fluid PCR should be performed at 18 weeks of gestation (not before) or later. In patients at >18 weeks of gestation, the risk of the procedure should be carefully weighed against the potential benefit of diagnosing fetal infection (see text and tables 2 and 5). CT, congenital toxoplasmosis.

in the United States were found for patients who had acquired their primary (acute) infection in the recent past [19].

Confirmatory testing of a positive IgM test result by the use of additional tests in various combinations has been validated by reference laboratories in Europe and the United States (tables 2 and 4) [15, 20, 21]. An example is the battery of tests (*Toxoplasma* serological profile [TSP]) used at PAMF-TSL. The TSP comprises the dye test (which measures primarily IgG antibodies); IgM, IgA, and IgE ELISAs; and the AC/HS test [1]. The methods used for demonstration of IgM, IgA, and IgE antibodies at the PAMF-TSL were developed by that laboratory and are not available elsewhere. In addition to the reporting of serological test results, consultants at PAMF-TSL offer medical interpretation of results and are available to assist clinicians in management of their patients' conditions.

The TSP has been used successfully at PAMF-TSL in attempts to determine whether a pregnant woman acquired her infection during or before gestation. This distinction is important with regard to decisions about prenatal drug intervention(s) and additional diagnostic tests, such as PCR and ultrasound. In addition, correct interpretation of the TSP results and their communication to the patient's physician by an expert were reported to decrease the rate of unnecessary abortions by ~50% among women in the United States for whom positive IgM test results had been reported by outside laboratories [19].

A *Toxoplasma* IgG avidity test has also been used at PAMF-TSL since July 2000. It is used only in conjunction with the AC/HS test and, when indicated, with other tests in the TSP [22, 23]. High-avidity IgG antibodies develop at least 12–16 weeks (depending on the test method used) after infection. The presence of high-avidity antibodies in the TSP indicates that infection was acquired >16 weeks earlier [22, 24, 25]. Thus, in a pregnant woman in the first months of gestation, regardless of the IgM antibody test result, a high-avidity IgG test result indicates that the fetus is essentially not at risk for congenital toxoplasmosis. A high-avidity IgG test result is especially useful

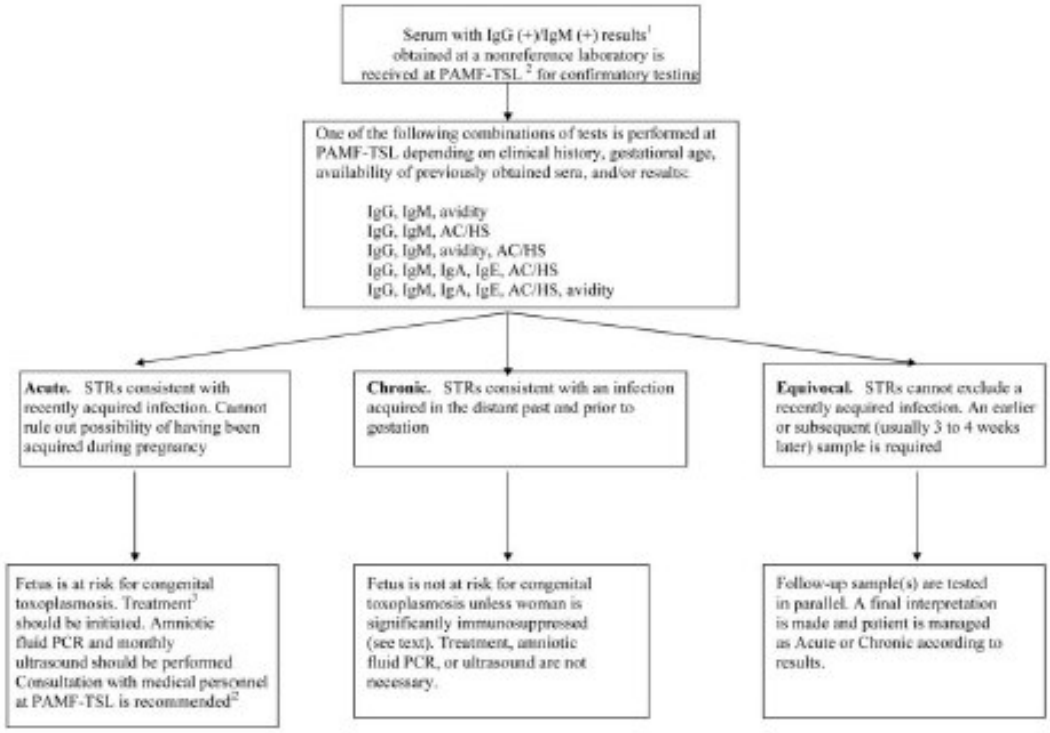

Figure 2. Serological testing and management of toxoplasmosis during pregnancy on the basis of results obtained at the Palo Alto Medical Foundation Toxoplasma Serology Laboratory (PAMF-TSL), telephone number (650) 853-4828. [1]A serum sample with positive results of IgG and IgM antibody tests is the most common reason for requesting confirmatory testing at PAMF-TSL. [2]PAMF-TSL or US (Chicago, IL) National Collaborative Treatment Trial Study, telephone number (773) 834-4152. [3]Treatment with spiramycin or with pyrimethamine, sulfadiazine, and folinic acid (see text and table 6). AC/HS, differential agglutination test; STRs, serological test results at PAMF-TSL; TSP, *Toxoplasma* serological panel.

when only a single sample of serum has been obtained in which *T. gondii* IgM antibodies are present and for which the AC/HS test (or the TSP) reveals an acute or equivocal pattern. For pregnant women beyond 16 weeks of gestation, a high-avidity test result may be helpful in establishing that the infection was acquired at least 12–16 weeks earlier in gestation; in this scenario, the transmission rate would be lower [14], the potential for fetal damage would be greater (table 1) [14], and the negative predictive value of the amniotic fluid PCR would be greater (table 5) [26] than if the infection was acquired later in gestation. Of special note is that low-avidity or equivocal test results can persist for many months or a year or more after the primary infection and, for this reason, must not be used alone to determine whether the infection was recently acquired [22, 27]. In fact, in serum samples with low- or borderline-avidity antibodies and negative IgM antibody test results or a TSP reflecting an infection acquired in the distant past, the IgG avidity test is not useful and, if used alone, can potentially be misleading [28].

Confirmatory testing with the TSP and the avidity method during the first 16 weeks of gestation has the potential to decrease the need for follow-up serum samples and thereby reduce costs, to make the need for PCR of amniotic fluid and for treatment with spiramycin for the mother unnecessary, to remove the pregnant woman's anxiety associated with further testing, and to decrease unnecessary abortions. Final interpretation of results of serological tests performed at PAMF-TSL yields 3 possibilities: (1) results are consistent with a recently acquired infection, and thus the possibility that the patient acquired her infection during gestation or shortly before conception cannot be excluded; (2) results are consistent with an infection acquired in the distant past and before pregnancy; or (3) results are equivocal, which usually requires a follow-up serum sample for parallel testing (figure 2 and table 4).

PCR. Amplification of *T. gondii* DNA in amniotic fluid at 18 weeks of gestation (the optimal time) or later has been used successfully for prenatal diagnosis of congenital toxoplasmosis [26, 29, 30]. Its sensitivity and specificity for amniotic fluid obtained before 18 weeks of gestation have not been studied; in addition, the procedure done early in gestation is associated with a higher risk to the fetus and likely is less useful. A definitive study of the routine use of PCR of amniotic fluid obtained at 18 weeks of gestation or later was reported in France to have an overall sensitivity of 64% for the diagnosis of congenital infection in the fetus, a negative predictive value of 88%, and a specificity and positive predictive value of 100% (i.e., a

Table 4. Examples of final interpretation of results of confirmatory tests performed at Palo Alto Medical Foundation Toxoplasma Serology Laboratory (PAMF-TSL) on serum samples that had positive results of IgM antibody tests at clinical laboratories.

Patient (weeks of gestation)	Clinical (nonreference) laboratory results of IgG/IgM tests	PAMF-TSL results for test						Interpretation
		IgG (dye test), IU/mL	IgM	IgA	IgE	AC/HS[a] pattern	Avidity	
A (11)	+/+	8000	+	+	+	Acute	Low	Consistent with recently acquired infection
B (9)	+/+	256	+	–	–	Equivocal	High	Consistent with infection acquired in the distant past (i.e., ≥6 months ago)
C (12)	+/+	4096	–	–	–	Nonacute	Low	Consistent with infection acquired in the distant past
D (12)	+/equivocal	1024	+	+	–	Equivocal	Low	Cannot exclude recently acquired infection; test of earlier or subsequent sample is required for further clarification

[a] Differential agglutination.

positive result signifies infection of the fetus) (table 5) [26]. Gestational age had a significant influence on the sensitivity and negative predictive values [26]. Sensitivity was statistically significantly higher when maternal infection occurred at 17–21 weeks of gestation, compared with when infection occurred before 17 weeks or after 21 weeks of gestation ($P < .02$) [26]. However, the negative predictive value of PCR of amniotic fluid from women who acquired the infection early in gestation (e.g., before week 7 of gestation) was ~100% because of the very low transmission rate during that time in gestation [26]. Romand et al. [31] also demonstrated that the parasite load in amniotic fluid is an independent risk factor for severity of fetal infection, in addition to the gestational age. Maternal infections acquired before 20 weeks of gestation with a parasite load >100 parasites per mL of amniotic fluid was associated with the highest risk of severe outcome in the fetus. In clinical practice, amniocentesis has essentially replaced fetal blood sampling for diagnosis of congenital toxoplasmosis, because of its inherently lower risk and higher sensitivity [1, 30].

Table 5. Rates of congenital transmission in 270 women and the sensitivity and negative predictive value (NPV) of amniotic fluid PCR for prenatal diagnosis of congenital toxoplasmosis, according to gestational age at which maternal infection was acquired.

Gestational age at maternal infection,[a] weeks	No. of infected[b] fetuses/total no. of fetuses (%)	Amniotic fluid PCR	
		Sensitivity, %	NPV, %
≤6	0/14 (0)	NA	100
7–11	7/50 (14)	28.6	89.6
12–16	7/61 (11)	57.1	94.7
17–21	14/66 (21)	92.9	98.1
22–26	16/36 (44)	62.5	76.9
27–31	19/30 (63)	68.4	64.7
≥32	12/13 (92)	50	14.3
Total	75/270 (28)	NA	NA

NOTE. The positive predictive value was 100%, regardless of gestational age. Data are from [26]. NA, not applicable.

[a] Maternal infection was diagnosed by seroconversion in the 270 women; 261 (97%) were given treatment with spiramycin.

[b] Congenital infection was diagnosed by the persistence of *Toxoplasma* IgG antibodies after 1 year of life.

PCR techniques for detection of *T. gondii* DNA in amniotic fluid or other samples are not standardized, and there is no consensus on the best protocol to use [26, 29, 31–34]. The specimen should be sent to a laboratory experienced in performing this assay on amniotic fluid and that has proper validation and quality-control data and experience in interpretation of its results.

Amniotic fluid examination by PCR should be considered for pregnant women (without a contraindication for the procedure) who (1) have serological test results diagnostic or highly suggestive of an infection acquired during gestation or shortly before conception; (2) have evidence of fetal damage by ultrasonographic examination (e.g., ventriculomegaly or hepatic or brain calcifications); or (3) are significantly immunosuppressed and thus at risk of reactivation of their latent infection (with the exception of women with AIDS). Amniocentesis may be less advisable for patients coinfected with *T. gondii* and HIV, because of the risk of infecting the fetus with HIV during the amniocentesis. PCR also may be useful for demonstration of parasite DNA in fetal tissues and placenta [35].

Ultrasound. Ultrasound is recommended for women with suspected or diagnosed acute infection acquired during or shortly before gestation. Ultrasound may reveal the presence of fetal abnormalities, including hydrocephalus, brain or hepatic calcifications, splenomegaly, and ascites [1].

The clinical outcome of congenitally infected children whose mothers had acquired the infection during the first trimester of pregnancy, whose fetal ultrasound findings were normal, and who received spiramycin during gestation was recently reported. Although these children were expected to have severe damage (table 1), their 2-year follow-up revealed that their outcomes did not differ significantly from those of infected

children born to mothers who had acquired the infection during the second and third trimesters (table 1) [36]. The authors concluded that, in such circumstances, termination of pregnancy was not indicated. However, appropriate treatment was essential, and prenatal ultrasound findings should be free of any anomaly [36]. In addition to ultrasound, CT has been used to search for brain calcifications, and MRI for other abnormalities in the fetus.

Histological analysis and attempts to isolate the parasite. Occasionally, placental or fetal tissues from pregnant women suspected of having acquired acute infection during gestation are available to attempt to determine whether vertical transmission of the parasite has occurred. *T. gondii* cysts may be visualized in these tissues with the Wright-Giemsa stain, but immunoperoxidase staining using *T. gondii*–specific antibodies is more sensitive [37]. Isolation of the parasite can be attempted by inoculation of tissues into tissue culture or mice [1].

APPROACH FOR PATIENTS WITH SUSPECTED OR DIAGNOSED *T. GONDII* INFECTION ACQUIRED DURING GESTATION

Once it has been established that serological test results are consistent with a recently acquired infection and that acquisition of the infection during the first 18 weeks of gestation or shortly before conception cannot be excluded, an attempt to prevent vertical transmission of the parasite through treatment with spiramycin is recommended for the mother by many investigators in the United States and Europe (figure 3). If fetal infection is confirmed by a positive result of PCR of amniotic fluid at 18 weeks of gestation or later, treatment with pyrimethamine, sulfadiazine, and folinic acid is recommended (if the patient is already receiving spiramycin, the recommendation is to switch to this combination). In some centers in Europe, this switch takes place as early as week 14–16 [38].

Because of the high transmission rates observed after 18 weeks of gestation, treatment with pyrimethamine, sulfadiazine, and folinic acid is also used for patients who have acquired the infection after 18 weeks of gestation, in an attempt to prevent fetal infection from occurring and, if transmission has occurred, to provide treatment for the fetus (figure 3). Pyrimethamine is not used earlier because it is potentially teratogenic.

Spiramycin. The use of the macrolide antibiotic spiramycin has been reported to decrease the frequency of vertical transmission [30, 39–42]. However, carefully designed, prospective studies that demonstrate this effect have not been performed. The protection has been reported to be more distinct in women infected during their first trimester [39, 40, 42]. In studies using historical controls, the incidence of congenital infection was reduced by ~60% [39, 40, 42]. Spiramycin does not readily cross the placenta and thus is not reliable for treatment of infection in the fetus. There is no evidence that spiramycin is teratogenic (table 6). The drug is administered until delivery even in those patients with negative results of amniotic fluid PCR, because of the theoretical possibility that fetal infection can occur later in pregnancy from a placenta that was infected earlier in gestation [42]. For pregnant women in whom the possibility of fetal infection is high or fetal infection has been established, treatment with spiramycin should be switched after the 18th week of gestation to treatment with pyrimethamine, sulfadiazine, and folinic acid. In some centers, change to such treatment occurs earlier (e.g., at 14–16 weeks of gestation) [38].

Spiramycin is not commercially available in the United States. It can be obtained at no cost and after consultation (with PAMF-TSL, telephone number (650) 853-4828, or the US [Chicago, IL] National Collaborative Treatment Trial Study [NCCTS], telephone number (773) 834-4152) through the US Food and Drug Administration, telephone number (301) 796-1600. It is administered orally at a dosage of 1.0 g (or 3 million U) every 8 h (total dosage of 3 g or 9 million U per day). Through this program, Sanofi-Aventis, for many years, has kindly been providing spiramycin to pregnant women in the United States at no cost.

In recent years, the effectiveness of spiramycin to prevent congenital toxoplasmosis has become controversial [38, 43]. Members of the European Multicentre Study on Congenital Toxoplasmosis (EMSCOT) have raised the question as to the value of such treatment [38, 43]. These investigators have stated repeatedly that carefully designed studies are necessary to clarify whether spiramycin is efficacious in prevention of congenital toxoplasmosis. We agree with that specific statement. Recent data from the EMSCOT investigators suggest that spiramycin may be more efficacious when administered early after seroconversion [43]. The studies supporting both positions (for and against the recommendation of spiramycin treatment) primarily suffer from a lack of randomization and necessary controls in their design and from small sample sizes for the group of untreated women [30, 38–43]. The data provided to date have not ruled out a potential benefit from spiramycin [44]. It has been suggested, and we agree, that only a large, randomized, controlled clinical trial would provide clinicians and patients with valid evidence of the potential benefit of prenatal treatment with spiramycin [43]. Until there is further clarification on this subject, we continue to recommend spiramycin treatment for women with suspected or confirmed acute *T. gondii* infection acquired during the first 18 weeks of gestation [1].

Pyrimethamine, sulfadiazine, and folinic acid. Until further information is available, we consider it justifiable to recommend the combination of pyrimethamine, sulfadiazine, and folinic acid as treatment for pregnant women who acquire the infection after 18 weeks of gestation and for those in whom

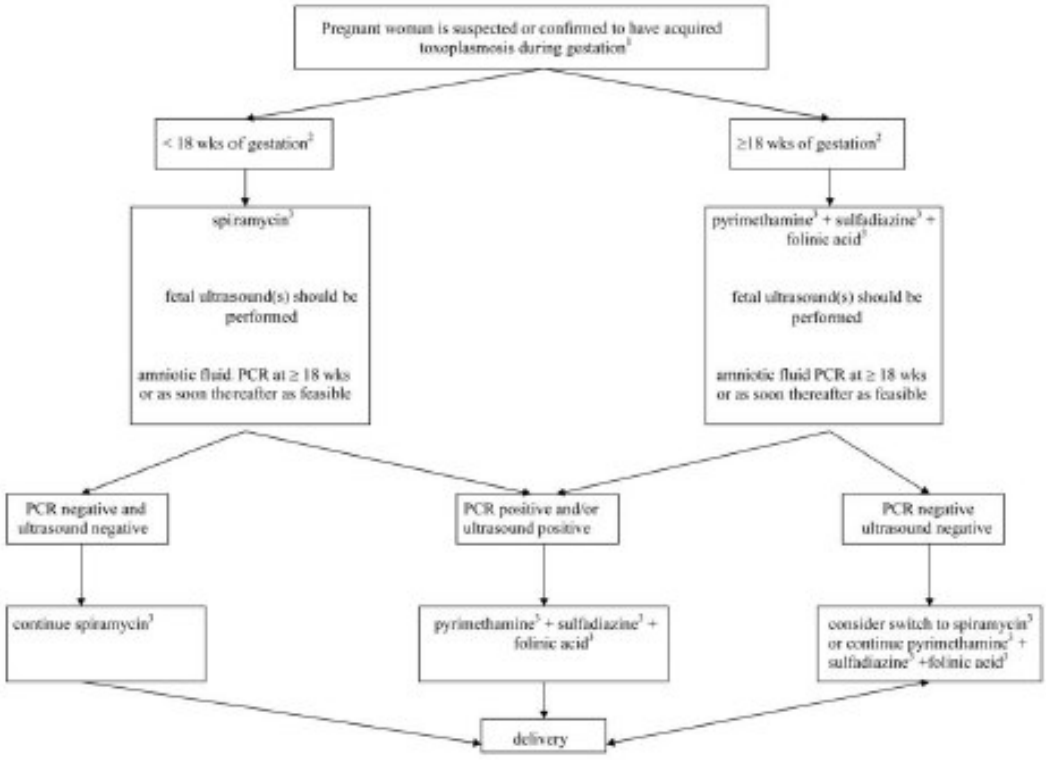

Figure 3. Approach for pregnant women who are suspected or confirmed to have toxoplasmosis acquired during gestation. [1]Consultation with a reference laboratory or physician expert in toxoplasmosis is suggested (i.e., Palo Alto Medical Foundation Toxoplasma Serology Laboratory, telephone number (650) 853-4828, or US [Chicago, IL] National Collaborative Treatment Trial Study, telephone number (773) 834-4152). [2]Gestational age at which maternal infection was suspected or confirmed to have been acquired (or the best estimate); this is not the gestational age at which the patient consulted with or was seen by the health care provider. [3]For dosages and comments, see table 6. Folic acid should not be used as a substitute for folinic acid. wks, Weeks.

fetal infection has been confirmed (i.e., by positive result of amniotic fluid PCR) or is highly suspected (e.g., because of fetal abnormalities consistent with congenital toxoplasmosis detected by ultrasound examination) (table 6) [1, 45]. This drug regimen is used in an attempt to treat the infection in the fetus and, in some instances, with the hope of preventing transmission, especially in those women for whom amniocentesis for PCR testing cannot be performed and whose infection was acquired after 18 weeks of gestation [46]. Pyrimethamine is potentially teratogenic and should not be used in the first trimester of pregnancy. The drug produces reversible, usually gradual, dose-related depression of the bone marrow. All patients who receive pyrimethamine should have complete blood cell counts frequently monitored. Folinic acid (not folic acid) is used for reduction and prevention of the hematological toxicities of the drug.

We suggest that each case involving a pregnant woman suspected of having or given the diagnosis of acute *T. gondii* infection acquired during gestation be discussed with an expert in the management of toxoplasmosis (in the United States, e.g., PAMF-TSL or NCCTS).

APPROACH FOR OTHERWISE IMMUNOCOMPETENT PATIENTS WITH *T. GONDII* INFECTION MOST LIKELY ACQUIRED ≥6 MONTHS BEFORE GESTATION

Because the incidence of congenital toxoplasmosis in the offspring of women who are known to have been infected before gestation or whose serological test results reveal infection acquired in the distant past (before gestation) has been shown to be extremely low (approaching zero), use of treatment with spiramycin or with pyrimethamine, sulfadiazine, and folinic acid and prenatal diagnosis of fetal infection are not indicated unless the mother is immunocompromised.

APPROACH FOR IMMUNOCOMPROMISED PATIENTS WITH *T. GONDII* INFECTION ACQUIRED BEFORE GESTATION

Women who are coinfected with HIV and *T. gondii* and who have developed AIDS are at risk of reactivating their *T. gondii* infection, developing severe toxoplasmosis (i.e., toxoplasmic encephalitis, pneumonia, etc.), and/or transmitting the parasite

Table 7. Measures to prevent primary *Toxoplasma gondii* infection during pregnancy.

Prevention measures
Cook meat to "well done" or thoroughly to 67°C (153°F). Meat should not be "pink" in the center.
Note that meat that is smoked, cured in brine, or dried may still be infectious
Avoid mucous membrane contact when handling raw meat
Wash hands carefully after contact with raw meat
Kitchen surfaces and utensils that have come in contact with raw meat should be washed wearing gloves
Refrain from skinning or butchering animals
Avoid contact with materials potentially contaminated with cat feces, especially when handling cat litter or gardening. Wearing gloves is recommended when these activities cannot be avoided.
Disinfect emptied cat-litter box with near-boiling water for 5 min before refilling
Wash fruits and vegetables before consumption
Avoid drinking water potentially contaminated with oocysts

to their offspring [1, 11]. Fortunately, such transmission is surprisingly rare [1, 11]. At present, data are insufficient to define the effectiveness of treatment intended to prevent vertical transmission of *T. gondii* in an HIV-infected woman. Until more data become available, we suggest that *Toxoplasma*-seropositive pregnant women whose CD4 cell count is <200 cells/mm^3 receive trimethoprim-sulfamethoxazole (80 mg trimethoprim and 400 mg sulfamethoxazole in a single-strength tablet, 1 tablet per day; this treatment is commonly used to prevent *Pneumocystis* pneumonia in such patients) in an attempt to prevent both reactivation of their *Toxoplasma* infection and transmission of the parasite to their offspring. Trimethoprim is usually avoided in the first trimester, because it is a folic acid antagonist. For women whose CD4 cell count is >200 cells/mm^3 and for non–HIV infected, immunocompromised women, spiramycin treatment is suggested for the duration of the pregnancy. Unfortunately, there are no studies to determine whether these strategies are effective.

Performance of amniotic fluid PCR may not be advisable for HIV-infected women because of the risk of facilitating the transmission of HIV to the fetus during the procedure. Amniotic fluid PCR should be considered for non–HIV infected, immunocompromised pregnant women who are chronically infected with *T. gondii* (as well as those who acquire the infection during pregnancy). Monthly ultrasound examinations should be considered as well for all immunocompromised pregnant women chronically infected with *T. gondii*.

APPROACH FOR PREGNANT WOMEN WITH TOXOPLASMIC CHORIORETINITIS

Pregnant women given a diagnosis of toxoplasmic chorioretinitis should have serological evaluation to establish whether the infection was acquired recently or in the distant past. Pregnant women with toxoplasmic chorioretinitis as a result of reactivation of a latent infection (acquired before gestation) do not appear to have a higher risk for transmission of the parasite to their offspring than that of pregnant women who were infected before gestation and who do not have active ocular toxoplasmosis [10]. Those with toxoplasmic chorioretinitis, considered to be a manifestation of recently acquired infection [47], should be given treatment for the infection, for both the eye disease and the risk of transmission of the infection to their fetus. In this scenario, the reader is referred to the approach described above in the Approach for Patients with Suspected or Diagnosed *T. gondii* Infection Acquired during Gestation section.

APPROACH FOR PATIENTS WITH RECENTLY ACQUIRED *T. GONDII* INFECTION WHO WANT TO KNOW WHEN IT IS SAFE TO BECOME PREGNANT

After a nonpregnant woman of childbearing age receives a diagnosis of a recently acquired *T. gondii* infection, the question frequently arises as to when they can safely become pregnant, with regard to the risk of congenital transmission of the parasite. It should be understood that there are no definitive data on this subject. Our advice has been conservative; we recommend that such women wait 6 months (from the date that the acute infection was diagnosed or documented) before attempting to become pregnant. Each case should be considered separately and, preferably, in consultation with an expert.

PREVENTION

Primary prevention. Educational materials that contain messages on how to prevent pregnant women from becoming infected have resulted in reduced rates of seroconversion (table 7) [48–50]. Educational measures should be in written form (e.g., books, magazines, or simple handouts), available in different languages, and integrated into existing prenatal programs, visits, and classes. Ultimately, it is the responsibility of health care policy makers and physicians to educate both pregnant women and women who are considering becoming pregnant, with regard to preventive measures. The need to take

Table 6. Medicines used for pregnant women who have suspected or confirmed *Toxoplasma gondii* infection acquired during gestation.

Treatment	Dosage	Comments
Spiramycin	1 g (3 million U) every 8 h (for a total of 3 g or 9 million U per day)	Not teratogenic; does not treat infection in the fetus; indicated for pregnant women suspected of having acquired the infection at <18 weeks of gestation. Spiramycin treatment should be continued until delivery in women with low suspicion of fetal infection or those with documented negative results of amniotic fluid PCR and negative findings on ultrasounds at follow-up. Available in the United States only through the Investigational New Drug process at the FDA. Prior consultation with medical consultants[a] is required.
Pyrimethamine, sulfadiazine, and folinic acid	Pyrimethamine: 50 mg every 12 h for 2 days followed by 50 mg daily; sulfadiazine: initial dose of 75 mg/kg, followed by 50 mg/kg every 12 h (maximum, 4 g/day); folinic acid[b] (leucovorin): 10–20 mg daily (during and 1 week after completion of pyrimethamine therapy)	Pyrimethamine is teratogenic; therefore, this combination should not be used before week 18 of gestation (in some centers in Europe, it is used as early as week 14–16). Indicated for women suspected of having acquired infection at ≥18 weeks of gestation and those with documented fetal infection (positive result of amniotic fluid PCR) or abnormal ultrasound findings suggestive of congenital toxoplasmosis, given when patient is at ≥18 weeks of gestation

NOTE. FDA, US Food and Drug Administration.

[a] Palo Alto Medical Foundation Toxoplasma Serology Laboratory, telephone number (650) 853-4828, or US (Chicago, IL) National Collaborative Treatment Trial Study, telephone number (773) 834-4152.

[b] Folic acid should not be used as a substitute for folinic acid.

these preventive measures continually must be reinforced throughout pregnancy for seronegative women. [48, 51]. Table 7 lists the measures that can be taken in an attempt to prevent *T. gondii* infection. Physicians are urged to make such written information available to their pregnant patients. Written materials are available through the March of Dimes and in a free, downloadable format at http://www.toxoplasmosis.org/.

Most important is to inform these women that all meat be prepared "well done" (not "pink" in the center). Meat should be heated throughout to at least 67°C (153°F). Freezing to at least −20°C (−4°F) for 24 h and thawing also kills *T. gondii* cysts [3, 52]. The process of curing meat does not necessarily result in a product free of parasite cysts [53].

Secondary prevention (serological screening). In addition to implementation of primary preventive measures in seronegative women, it is important to identify those women who acquire *T. gondii* infection during gestation, and if fetal infection is detected by prenatal testing, therapeutic options, including termination of pregnancy and antibiotic treatment of the fetus in utero, should be discussed with the patient. Women and their partners have the right to know whether their fetus is at risk for congenital toxoplasmosis or whether their fetus has already been infected. Congenital toxoplasmosis will continue to go largely undiagnosed in the United States in the absence of universal screening programs to detect acute *T. gondii* infection acquired during gestation and in the absence of effective and more widely distributed educational programs [1, 9, 54].

As an alternative, in the states of Massachusetts, New Hampshire, and Vermont, a secondary prevention program that performs *Toxoplasma* serological testing in all newborns has been underway for several years [55, 56]. Although postnatal screening of newborns identifies some subclinically infected infants, it has the potential to miss those infected late in the third trimester but who have not yet formed antibodies, as well as infants infected early in gestation who are negative for IgM and IgA antibodies. Postnatal screening programs do not allow for measures that attempt to prevent congenital infection.

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References

1. Remington JS, McLeod R, Thuilliez P, Desmonts G. Toxoplasmosis. In: Remington JS, Klein JO, Wilson CB, Baker C, eds. Infectious diseases of the fetus and newborn infant. 6th ed. Philadelphia: Elsevier Saunders, **2006**:947–1091.
2. Roberts T, Frenkel JK. Estimating income losses and other preventable costs caused by congenital toxoplasmosis in people in the United States. J Am Vet Med Assoc **1990**; 196:249–56.
3. Dubey JP, Hill DE, Jones JL, et al. Prevalence of viable *Toxoplasma gondii* in beef, chicken, and pork from retail meat stores in the United States: risk assessment to consumers. J Parasitol **2005**; 91:1082–93.
4. Bowie WR, King AS, Werker DH, et al. Outbreak of toxoplasmosis associated with municipal drinking water. Lancet **1997**; 350:173–7.
5. Miller MA, Gardner IA, Kreuder C, et al. Coastal freshwater runoff is a risk factor for *Toxoplasma gondii* infection of southern sea otters (*Enhydra lutris nereis*). Int J Parasitol **2002**; 32:997–1006.
6. Bahia-Oliveira LM, Jones JL, Azevedo-Silva J, Alves CC, Orefice F, Addiss DG. Highly endemic, waterborne toxoplasmosis in north Rio de Janeiro state, Brazil. Emerg Infect Dis **2003**; 9:55–62.
7. de Moura L, Bahia-Oliveira LM, Wada MY, et al. Waterborne toxoplasmosis, Brazil, from field to gene. Emerg Infect Dis **2006**; 12:326–9.
8. Lin YL, Liao YS, Liao LR, Chen FN, Kuo HM, He S. Seroprevalence and sources of *Toxoplasma* infection among indigenous and immigrant pregnant women in Taiwan. Parasitol Res **2008**; published online Mar 8.
9. Boyer KM, Holfels E, Roizen N, et al. Risk factors for *Toxoplasma gondii* infection in mothers of infants with congenital toxoplasmosis: implications for prenatal management and screening. Am J Obstet Gynecol **2005**; 192:564–71.

10. Garweg JG, Scherrer J, Wallon M, Kodjikian L, Peyron F. Reactivation of ocular toxoplasmosis during pregnancy. BJOG **2005**; 112:241–2.
11. Mitchell CD, Erlich SS, Mastrucci MT, Hutto SC, Parks WP, Scott GB. Congenital toxoplasmosis occurring in infants perinatally infected with human immunodeficiency virus 1. Pediatr Infect Dis J **1990**; 9:512–8.
12. Remington JS, McLeod R, Desmonts G. Toxoplasmosis. In: Remington JS, Klein JO, eds. Infectious diseases of the fetus and newborn infant. 4th ed. Philadelphia: W. B. Saunders, **1995**:140–267.
13. Wechsler B, Le Thi Huong D, Vignes B, Piette JC, Chomette G, Godeau P. Toxoplasmose et lupus: revue de la litterature a propos de 4 observations. Ann Med Interne (Paris) **1986**; 137:324–30.
14. Dunn D, Wallon M, Peyron F, Petersen E, Peckham C, Gilbert R. Mother-to-child transmission of toxoplasmosis: risk estimates for clinical counselling. Lancet **1999**; 353:1829–33.
15. Montoya JG. Laboratory diagnosis of *Toxoplasma gondii* infection and toxoplasmosis. J Infect Dis **2002**; 185(Suppl 1):S73–82.
16. Liesenfeld O, Press C, Montoya JG, et al. False-positive results in immunoglobulin M (IgM) toxoplasma antibody tests and importance of confirmatory testing: the Platelia Toxo IgM test. J Clin Microbiol **1997**; 35:174–8.
17. Public Health Service, Department of Health and Human Services; US Food and Drug Administration. FDA public health advisory: limitations of toxoplasma IgM commercial test kits. Rockville, MD: Department of Health and Human Services; US Food and Drug Administration, **1997**:3.
18. Wilson M, Remington JS, Clavet C, et al. Evaluation of six commercial kits for detection of human immunoglobulin M antibodies to *Toxoplasma gondii*. J Clin Microbiol **1997**; 35:3112–5.
19. Liesenfeld O, Montoya JG, Tathineni NJ, et al. Confirmatory serologic testing for acute toxoplasmosis and rate of induced abortions among women reported to have positive *Toxoplasma* immunoglobulin M antibody titers. Am J Obstet Gynecol **2001**; 184:140–5.
20. Lappalainen M, Hedman K. Serodiagnosis of toxoplasmosis: the impact of measurement of IgG avidity. Ann Ist Super Sanita **2004**; 40:81–8.
21. Roberts A, Hedman K, Luyasu V, et al. Multicenter evaluation of strategies for serodiagnosis of primary infection with *Toxoplasma gondii*. Eur J Clin Microbiol Infect Dis **2001**; 20:467–74.
22. Hedman K, Lappalainen M, Seppala I, Makela O. Recent primary *Toxoplasma* infection indicated by a low avidity of specific IgG. J Infect Dis **1989**; 159:736–9.
23. Lappalainen M, Koskela P, Koskiniemi M, et al. Toxoplasmosis acquired during pregnancy: improved serodiagnosis based on avidity of IgG. J Infect Dis **1993**; 167:691–97.
24. Pelloux H, Brun E, Vernet G, et al. Determination of anti–*Toxoplasma gondii* immunoglobulin G avidity: adaptation to the Vidas system (bioMérieux). Diagn Microbiol Infect Dis **1998**; 32:69–73.
25. Lappalainen M, Koskiniemi M, Hiilesmaa V, et al. Outcome of children after maternal primary *Toxoplasma* infection during pregnancy with emphasis on avidity of specific IgG. Pediatr Infect Dis J **1995**; 14: 354–61.
26. Romand S, Wallon M, Franck J, Thulliez P, Peyron F, Dumon H. Prenatal diagnosis using polymerase chain reaction on amniotic fluid for congenital toxoplasmosis. Obstet Gynecol **2001**; 97:296–300.
27. Montoya JG, Huffman HB, Remington JS. Evaluation of the immunoglobulin G avidity test for diagnosis of toxoplasmic lymphadenopathy. J Clin Microbiol **2004**; 42:4627–31.
28. Montoya JG, Liesenfeld O, Kinney S, Press C, Remington JS. VIDAS test for avidity of *Toxoplasma*-specific immunoglobulin G for confirmatory testing of pregnant women. J Clin Microbiol **2002**; 40:2504–8.
29. Grover CM, Thulliez P, Remington JS, Boothroyd JD. Rapid prenatal diagnosis of congenital *Toxoplasma* infection by using polymerase chain reaction and amniotic fluid. J Clin Microbiol **1990**; 28:2297–301.
30. Hohlfeld P, Daffos F, Costa J-M, Thulliez P, Forestier F, Vidaud M. Prenatal diagnosis of congenital toxoplasmosis with polymerase-chain-reaction test on amniotic fluid. N Engl J Med **1994**; 331:695–9.
31. Romand S, Chosson M, Franck J, et al. Usefulness of quantitative polymerase chain reaction in amniotic fluid as early prognostic marker of fetal infection with *Toxoplasma gondii*. Am J Obstet Gynecol **2004**; 190:797–802.
32. Costa JM, Dardé ML, Assouline B, Vidaud M, Bretagne S. Microsatellite in the beta-tubulin gene of *Toxoplasma gondii* as a new genetic marker for use in direct screening of amniotic fluids. J Clin Microbiol **1997**; 35:2542–5.
33. Chabbert E, Lachaud L, Crobu L, Bastien P. Comparison of two widely used PCR primer systems for detection of *Toxoplasma* in amniotic fluid, blood, and tissues. J Clin Microbiol **2004**; 42:1719–22.
34. Bretagne S. Molecular diagnostics in clinical parasitology and mycology: limits of the current polymerase chain reaction (PCR) assays and interest of the real-time PCR assays. Clin Microbiol Infect **2003**; 9: 505–11.
35. Fricker-Hidalgo H, Brenier-Pinchart MP, Schaal JP, Equy V, Bost-Bru C, Pelloux H. Value of *Toxoplasma gondii* detection in one hundred thirty-three placentas for the diagnosis of congenital toxoplasmosis. Pediatr Infect Dis J **2007**; 26:845–6.
36. Berrebi A, Bardou M, Bessieres MH, et al. Outcome for children infected with congenital toxoplasmosis in the first trimester and with normal ultrasound findings: a study of 36 cases. Eur J Obstet Gynecol Reprod Biol **2007**; 135:53–7.
37. Conley FK, Jenkins KA, Remington JS. *Toxoplasma gondii* infection of the central nervous system: use of the peroxidase-antiperoxidase method to demonstrate *Toxoplasma* in formalin fixed, paraffin embedded tissue sections. Hum Pathol **1981**; 12:690–8.
38. Gilbert R, Gras L, European Multicentre Study on Congenital Toxoplasmosis. Effect of timing and type of treatment on the risk of mother to child transmission of *Toxoplasma gondii*. BJOG **2003**; 110:112–20.
39. Desmonts G, Couvreur J. Congenital toxoplasmosis: a prospective study of the offspring of 542 women who acquired toxoplasmosis during pregnancy. In: Thalhammer O, Pollak A, Baumgarten K, eds. Perinatal medicine: proceedings of the 6th European Congress, Vienna. Stuttgart, Germany: Georg Thieme Publishers, **1979**:51–60.
40. Forestier F. Les foetopathies infectieuses: prevention, diagnostic prenatal, attitude pratique. Presse Med **1991**; 20:1448–54.
41. Hohlfeld P, Daffos F, Thulliez P, et al. Fetal toxoplasmosis: outcome of pregnancy and infant follow-up after in utero treatment. J Pediatr **1989**; 115:765–9.
42. Couvreur J, Desmonts G, Thulliez P. Prophylaxis of congenital toxoplasmosis: effects of spiramycin on placental infection. J Antimicrob Chemother **1988**; 22:193–200.
43. Thiebaut R, Leproust S, Chene G, Gilbert R. Effectiveness of prenatal treatment for congenital toxoplasmosis: a meta-analysis of individual patients' data. Lancet **2007**; 369:115–22.
44. Thulliez P. Commentary: efficacy of prenatal treatment for toxoplasmosis: a possibility that cannot be ruled out. Int J Epidemiol **2001**; 30:1315–6.
45. Kieffer F, Wallon M, Garcia P, Thulliez P, Peyron F, Franck J. Risk factors for retinochoroiditis during the first 2 years of life in infants with treated congenital toxoplasmosis. Pediatr Infect Dis J **2008**; 27: 27–32.
46. Foulon W, Villena I, Stray-Pedersen B, et al. Treatment of toxoplasmosis during pregnancy: a multicenter study of impact on fetal transmission and children's sequelae at age 1 year. Am J Obstet Gynecol **1999**; 180: 410–5.
47. Montoya JG, Remington JS. Toxoplasmic chorioretinitis in the setting of acute acquired toxoplasmosis. Clin Infect Dis **1996**; 23:277–82.
48. Foulon W, Naessens A, Lauwers S, De Meuter F, Amy JJ. Impact of primary prevention on the incidence of toxoplasmosis during pregnancy. Obstet Gynecol **1988**; 72:363–6.
49. Baril L, Ancelle T, Goulet V, Thulliez P, Tirard-Fleury V, Carme B. Risk factors for Toxoplasma infection in pregnancy: a case-control study in France. Scand J Infect Dis **1999**; 31:305–9.
50. Gollub EL, Leroy V, Gilbert R, Chene G, Wallon M. Effectiveness of health education on *Toxoplasma*-related knowledge, behaviour, and risk of seroconversion in pregnancy. Eur J Obstet Gynecol Reprod Biol **2008**; 136:137–45.

51. Wong S, Remington JS. Toxoplasmosis in pregnancy. Clin Infect Dis **1994**; 18:853–62.
52. Dubey JP, Lindsay DS, Speer CA. Structures of *Toxoplasma gondii* tachyzoites, bradyzoites, and sporozoites and biology and development of tissue cysts. Clin Microbiol Rev **1998**; 11:267–99.
53. Geurina NG, Hsu HW, Meissner HC, et al.; New England Regional Toxoplasma Working Group. Neonatal serologic screening and early treatment for congenital *Toxoplasma gondii* infection. N Engl J Med **1994**; 330:1858–63.
54. McCabe R, Remington JS. Toxoplasmosis: the time has come. N Engl J Med **1988**; 318:313–5.
55. Schmidt DR, Hogh B, Andersen O, Fuchs J, Fledelius H, Petersen E. The national neonatal screening programme for congenital toxoplasmosis in Denmark: results from the initial four years, 1999–2002. Arch Dis Child **2006**; 91:661–5.
56. Guerina N, Hsu H-W, Meissner H, et al. Neonatal serologic screening and early treatment for congenital *Toxoplasma gondii* infection. N Engl J Med **1994**; 330:1858–63.