

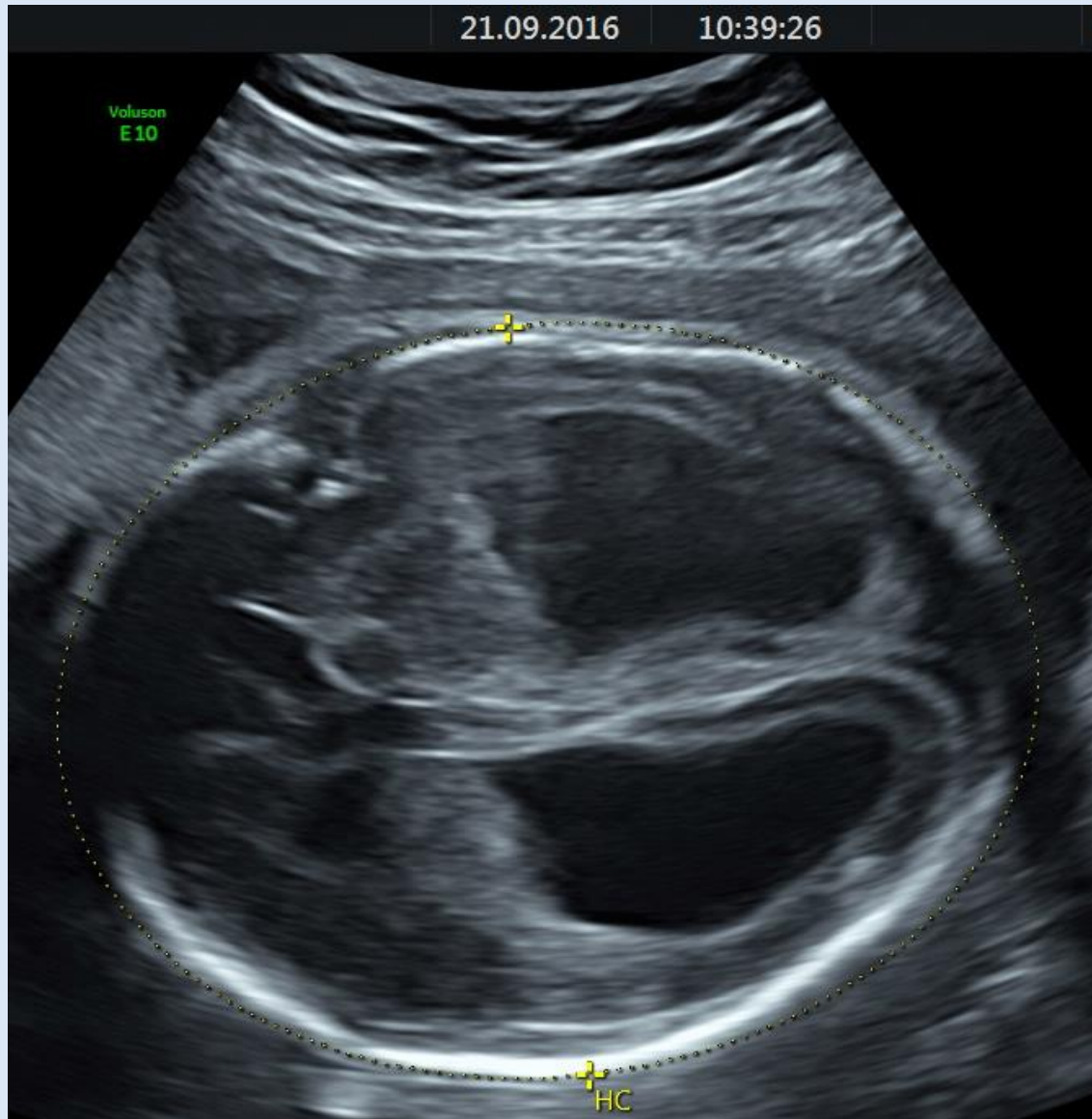
Update Toxoplasmose

M. Häusler

13. 12. 2016, Perinatologischen ARGE für Steiermark



Gestational toxoplasmosis - is an important health problem !



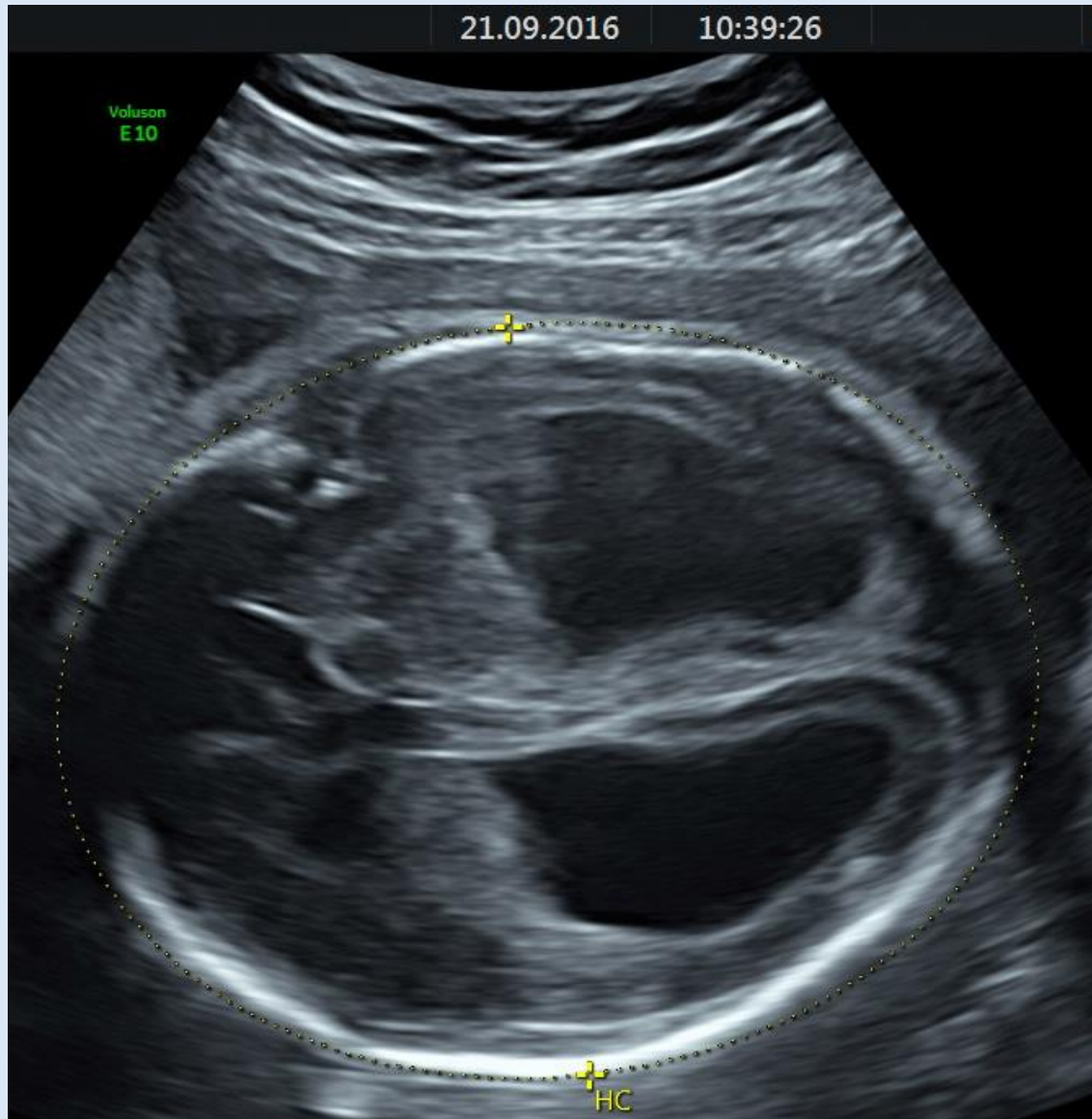
12+4 Toxo IgG neg.

25+2 IgG + IgM pos



MRI revealed
ventriculomegaly,
signal alteration in
the basal ganglia,
disseminated cystoid
cortical lesions

Gestational toxoplasmosis is an important health problem ... and preventable!



12+4 Toxo IgG neg.

25+2 IgG + IgM pos



MRI revealed
ventriculomegaly,
signal alteration in
the basal ganglia,
disseminated cystoid
cortical lesions

Prognosis, if Ultrasound Shows Pathology

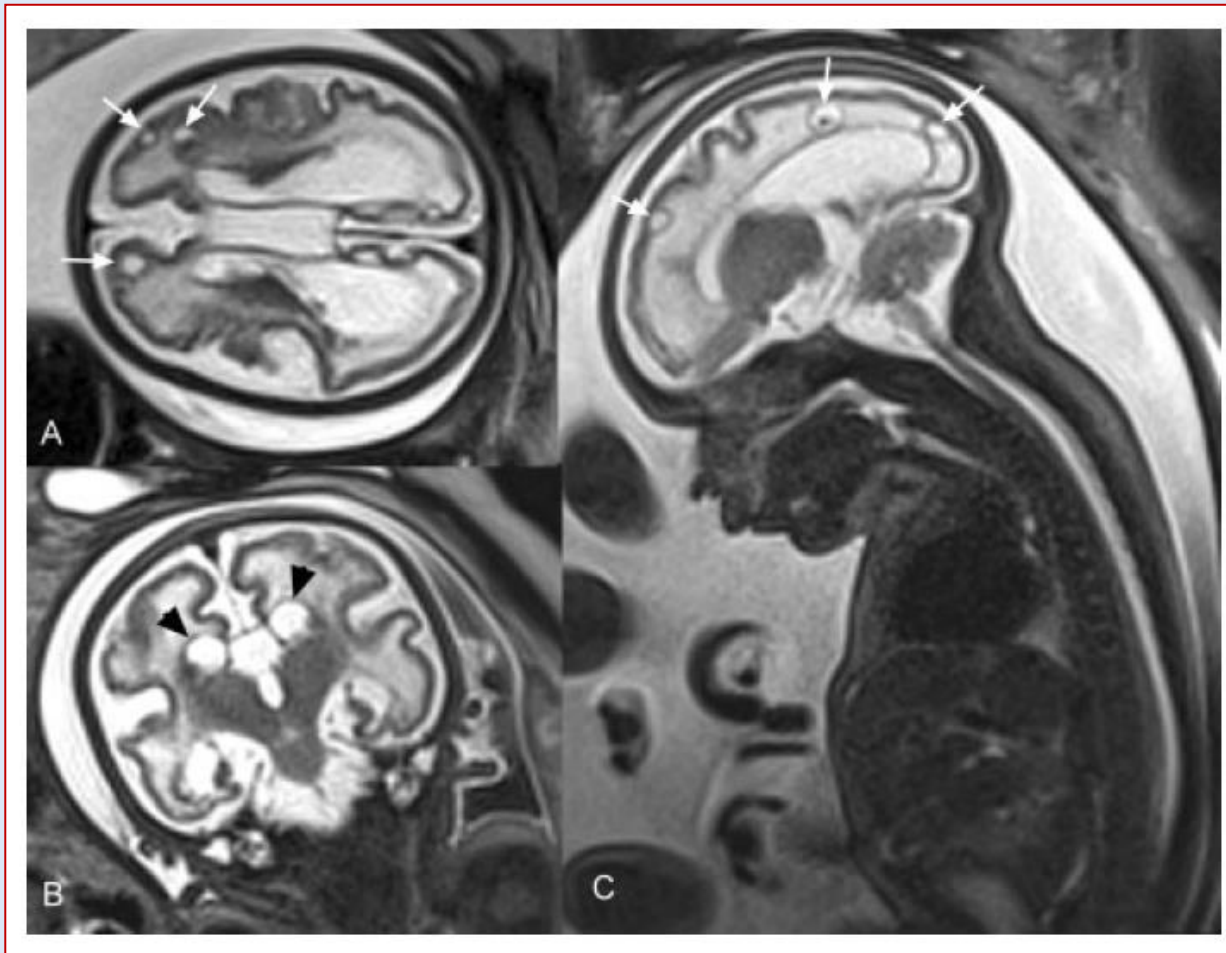


10 countries, Ultrasound
(and MRI)
8 cases,
24-34 weeks' gestation.
Ventriculomegaly and
echogenic foci

... the prognosis seems
to be correlated to the
extent of brain
involvement.

Malinger G, et al. PD **2011**;31:881-3

Gestational toxo infection and MRI



Malinger G, et al. PD **2011**;31:881-3

Toxoplasmosis is a treatable disorder



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Congenital Toxoplasmosis — A Prospective Study of 378 Pregnancies

Georges Desmonts, M.D., and Jacques Couvreur, M.D.

Desmonts GD, Couvreur J. N Engl J Med **1974**;290(20):1110-6


Toxoplasmosis is a treatable disorder

5 centers (Belgium, France, Norway, Finland ... all prenatal screening)
 n=140 congenital toxo infections / 19 with sequelae

	<i>Mothers (No.)</i>	<i>Global sequelae*</i>		<i>Severe sequelae*</i>	
		<i>No.</i>	<i>%</i>	<i>No.</i>	<i>%</i>
Prenatal treatment	119*	12	10	4	3.5
No prenatal treatment	25	7	28‡	5	20§
			p .026		p .007

Foulon W, et al. **1999**;180:410-4154:1721-31

Toxoplasmosis is a treatable disorder

Centre	Proportion of seroconverting women treated (%)	Estimated risk (%) of any manifestation by 3 years
Lyon	94	22
Austria	90	9 
Denmark	0	21
Netherlands	51	33

Gilbert R, Hayde M, et al. Epidemiol Infect 2001;127:113-120

The treatment scheme matters!

Toxoplasmosis is a treatable disorder

Prospective cohort study, 1996-2000, 10 centers
n=255 cases of congenital toxo infection

Prenatal treatment: France, Italy, Austria

No prenatal treatment: Sweden, Poland, Denmark

72% reduction of risk for intracranial lesions, if mothers
treated within 4 weeks of seroconversion ...
compared to untreated mothers

(p=0.52 „borderline significance“)

Graas L, Hayde M, et al. Acta Paed **2005**;94:1721-31



LABOR UNTERSUCHUNGEN SSW 25 -28

BIS SSW 16

Blutgruppe

A B AB 0

Rh-Faktor

pos. neg.

Since 1974 Mother-Child-Booklet

Röteln-Antikörper

neg. pos. Titer 1:

Lues Reaktion (TPHA)

neg. pos.

Toxoplasmose-Untersuchung:

pos. Vorbefund frühere SS nein ja Titer 1:

aktueller Befund neg. pos. Titer 1:

HIV durchgeführt

Erythrozytenanzahl:

Einheiten
oder
Hämatokrit: % Hämoglobin: g/dl

Datum:
Name des Labors, Unterschrift

andere durchgeführte Untersuchungen

HBs Antigen

neg. pos.
 weitere Abklärung veranlasst

nüchtern: 1h: 2h:

(kose)mg/dl

Erythrozytenanzahl:

Einheiten
oder
Hämatokrit: % Hämoglobin: g/dl

Datum:

> 40 Years of Toxoplasmosis Screening in Austria

Kontrollen, falls erforderlich:

Rh-Antikörper-Suchtest:

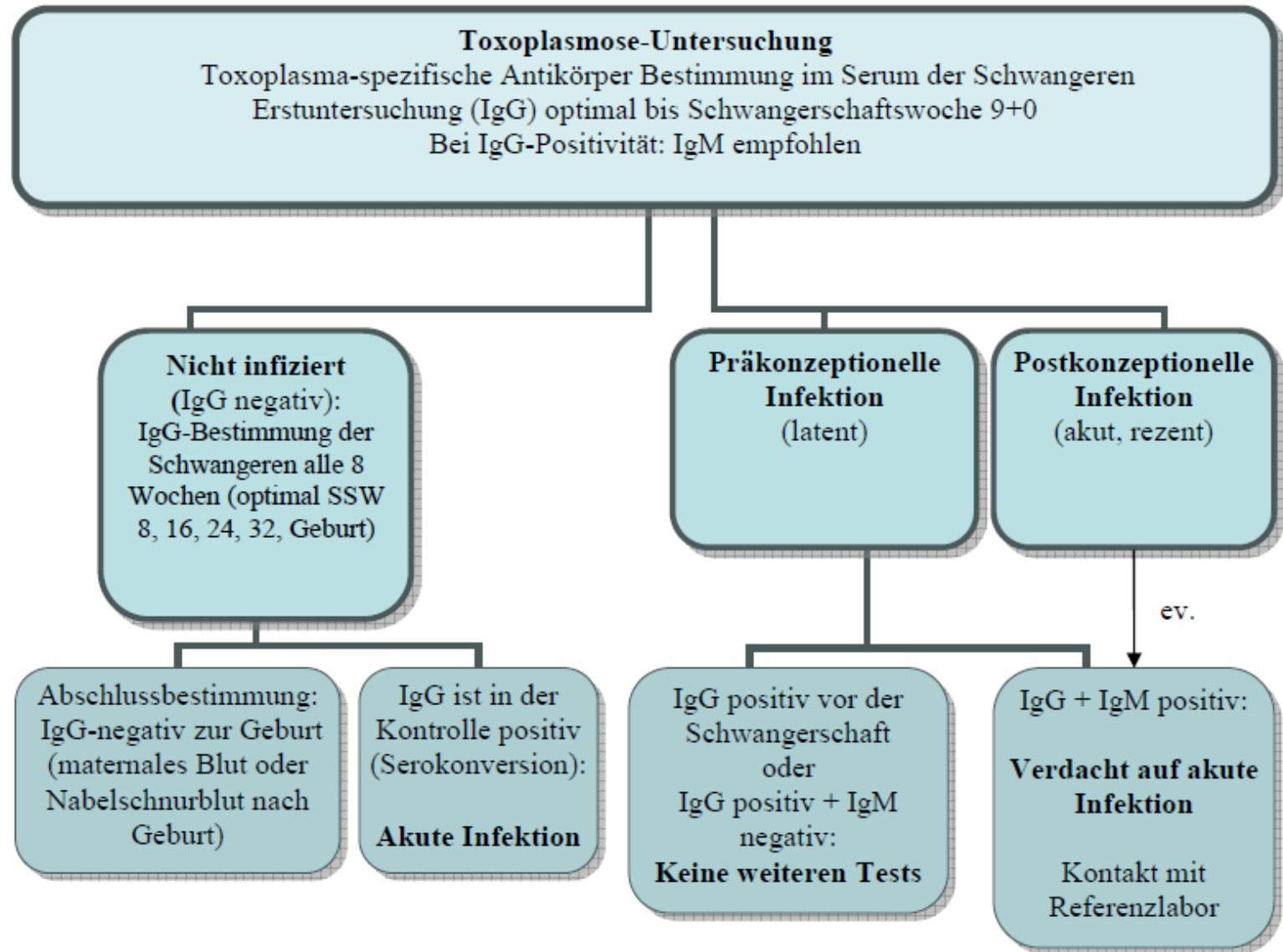
Datum, SSW + Tage	neg.	pos.	Titer (IE):
.....	<input type="checkbox"/>	<input type="checkbox"/>
.....	<input type="checkbox"/>	<input type="checkbox"/>
.....	<input type="checkbox"/>	<input type="checkbox"/>

Toxoplasmose-Kontrolluntersuchungen:

letzte Kontrolle nach SSW 32

Datum, SSW + Tage	neg.	pos.	Titer (IE):
.....	<input type="checkbox"/>	<input type="checkbox"/>
.....	<input type="checkbox"/>	<input type="checkbox"/>
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Anhang 1A. Österreichisches Toxoplasmose-Screening im Rahmen der Mutter-Kind-Pass-Untersuchung



How to get comprehensive data ?



Austrian Toxoplasmosis Registry since 1992

Nationwide data on
Serology mother /child,
Prenatal ultrasound,
Treatment,
Amniocentesis,
Clinical follow-up of infants



Prof. Michael Hayde





Austrian Toxoplasmosis Registry

Analysis 1992-2008

n=1,387.680 pregnancies

30-40%: infected prior to pregnancy, so ...

60-70% at risk for infection!

Gestational infection: 8,2 / 10.000 Life Births

Symptomatic congenital toxoplasmosis: 0,12 / 10.000 LB

Prusa, Hayde, et al. Clin Infect Dis **2015**;60(2):e4-e10

Gestational Toxoplasmosis is a treatable disorder - Austrian Data

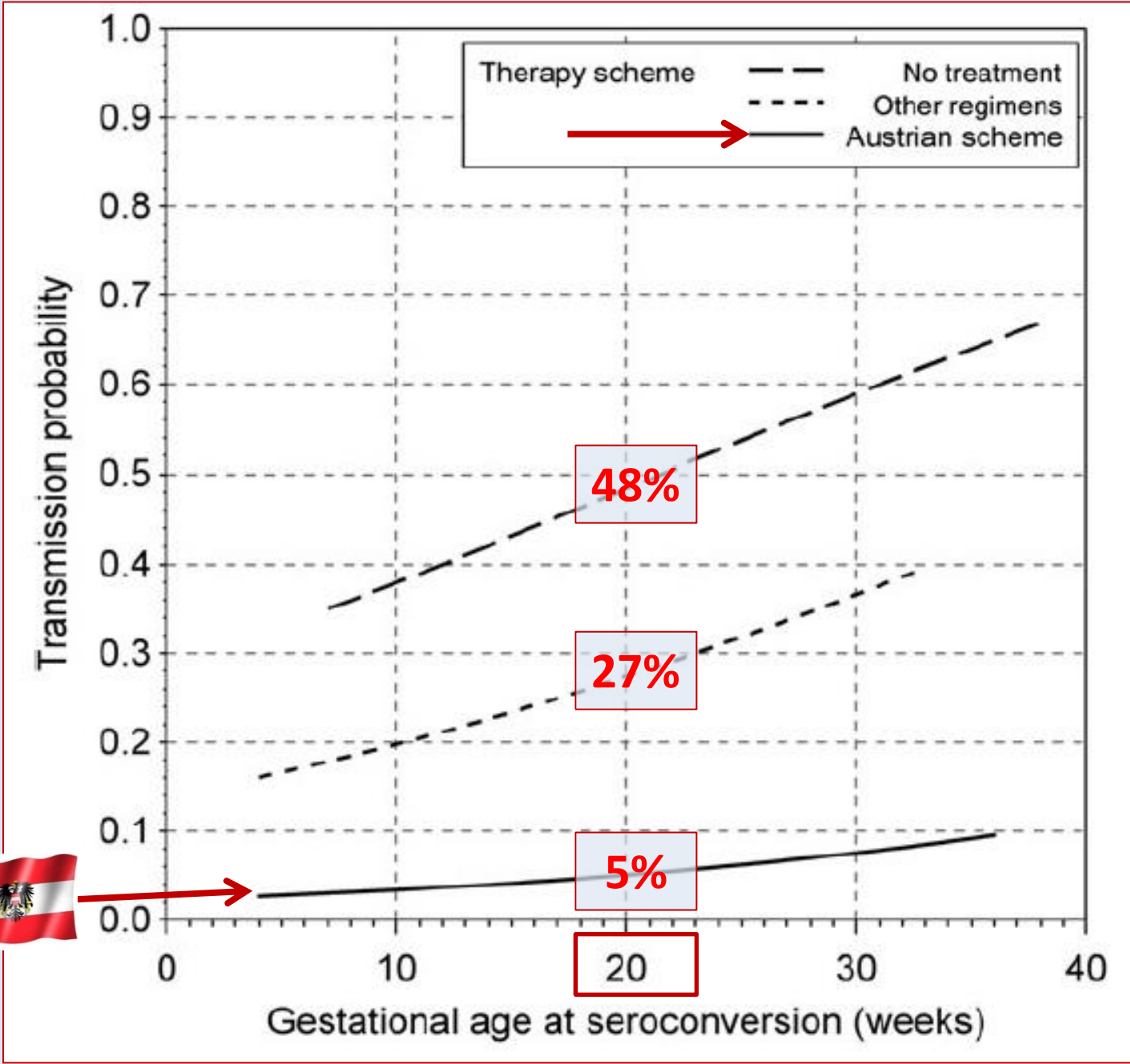


Table 1. Impact of Maternal Treatment on Maternofetal Transmission

Treatment	Transmission Rate, % (95% CI)
Austrian scheme	8.6 (6.9–10.4)
Other regimens	21.4 (13.4–29.3)
No treatment	50.8 (38.5–63.1)

p<.001

Prusa, Hayde, et al. Clin Infect Dis **2015**;60(2):e4-e10



EMSCOT Study

The **E**uropean **M**ulticentre **S**tudy on **C**ongenital **T**oxoplasmosis

14 europ. centers

n=293 conatally infected children

n= 9 cases with **severe neurological sequelae**

Any prenatal treatment = 3% severe neurological sequelae

No prenatal treatment = 12% severe neurological sequelae
= *OR 0,236*

EMSCOT Study. Cortina-Borja, et al. PLoS Med **2010**;7(10):1-11

EMSCOT Study

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Any prenatal treatment = 3% severe neurological sequelae

No prenatal treatment = 12% severe neurological sequelae
= *OR 0,236*

Conclusion:

Prenatal treatment substantially reduced the risk of
severe neurological sequelae

EMSCOT Study

The **E**uropean **M**ulticentre **S**tudy on **C**ongenital **T**oxoplasmosis

Number **N**eeded to **T**reat to prevent one case of
serious neurological sequelae:

After maternal infection at 10 weeks gest. = 3

at 20 weeks gest.= 18

at 30 weeks gest. = 6

EMSCOT Study. Cortina-Borja, et al. PLoS Med **2010**;7(10):1-11

Hydrocephalus in congenital toxo infection



Striking difference between



USA and France



31% vs. 0,3 – 0,8%

no screening vs. screening

**,,Congenital toxoplasmosis is no longer a severe disease in France, unlike what we still see in the United States“.*

Hutson SL, et al. Clin Infect Dis **2015** ;61:1831-34

Peyron F. Clin Infect Dis **2016**;62(6):811–2

* McLeod R, et al. Clin Infect Dis **2016**;62(6):812–4

*Is maternal toxo infection detectable
without screening?*

... by maternal symptoms?

Our study showed that <4% of women were identified by clinical symptoms or risk factors associated with acute infection.

Prusa, Hayde, et al. Clin Infect Dis **2015**;60(2):e4-e10

52% of mothers with congenitally infected infants do not recall an infection-related illness.

Boyer KM, et al. AJOG **2005**;192:564-571

Is maternal toxo infection detectable without screening?

No !

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52% of mothers with congenitally infected infants do not recall an infection-related illness.

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Maternal toxo infection is asymptomatic in most cases

No clinical symptoms!

*Is maternal toxo infection detectable
without screening?*

... by ultrasound?

Most affected fetuses appear sonographically normal.

Tercanli S, et al. Ther Umsch 2008; 65(11):667-74

*Is maternal toxo infection detectable
without screening?*

No !

Most affected fetuses appear sonographically normal.

Tercanli S, et al. Ther Umsch 2008; 65(11):667-74

But long-term sequelae will present years after birth

9/10 infected-asymptomatic-untreated newborns
will develop sequelae later in life!
= Mostly retinochorioiditis





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Rh-Antikörper-Suchtest:

Datum, SSW + Tage neg. pos. Titer (IE):

Toxoplasmose-Kontrolluntersuchungen:

letzte Kontrolle nach SSW 32

Datum, SSW + Tage neg. pos. Titer (IE):

Situation in Germany

(„Mutterschafts-Richtlinien“)

in der Fassung vom 10. Dezember 1985
(veröffentlicht im Bundesanzeiger Nr. 60 a vom 27. März 1986)

zuletzt geändert am 21. April 2016
veröffentlicht im Bundesanzeiger AT 19.07.2016 B5
in Kraft getreten am 20. Juli 2016

No toxo screening

„Cases of congenital infection have to be reported
to the Robert-Koch-Institute“

Underreporting: 9/10 children not detected

„Wild screening“ = depends on care givers.



Situation in Germany:
Nationwide Representative Survey
by the *Robert Koch Institute / Berlin*



1.3% of women aged 18–49 to seroconvert each year.



6.393 seroconversions annually during pregnancy in Germany

Wilking H, Seeber F, et al. *Scient. Reports* **2015**; 6(22551):1-9

Nationwide Representative Survey by the *Robert Koch Institute* Implications



6.393 seroconversions annually during pregnancy



3.200 infected children per year / 50% transmission rate/untreated /
(Lit: Thalhammer, Wallon, Prusa)



320 connatal damage / 10%



2.590 late sequelae (retinochorioiditis) (Lit: Buch HoYen)



Nationwide Representative Survey
by the *Robert Koch Institute*



Conclusion:

„*Toxoplasma gondii* infection in Germany
is highly prevalent“.

A high number of seroconversions during pregnancy pose
substantial risks for unborn children!“

Wilking H, Seeber F, et al. *Scient. Reports* **2015**; 6(22551):1-9



Matthias David · Andreas D. Ebert (Hrsg.)

Geschichte der Berliner Universitäts Frauenkliniken



Charité



Mandatory Toxo Screening in the DDR until 1989

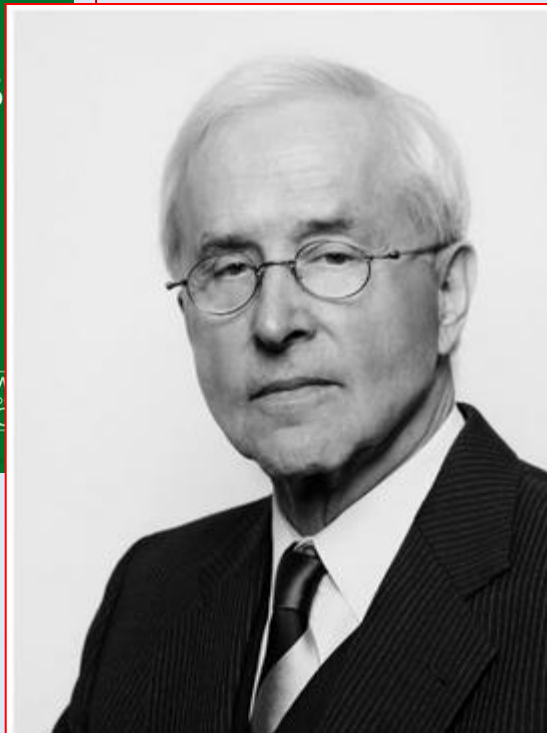


Abb. 7.16 Prof. P. Hengst.



Die geburtshilfliche Abteilung (► Abb.7.15), Ambulanz und der stationäre Bereich wurde von **Peter Hengst** geleitet. Sein wissenschaftliches Hauptinteresse galt den Infektionen durch **Toxoplasma** in der Schwangerschaft. Zu dieser Zeit wurde die Diagnostik der Toxoplasmaeinfektionen bei allen Schwangeren als Screening durchgeführt.



Situation in Switzerland



„Wild screening system“ for Toxo was abandoned 7 years ago

“A broad lack of evidence with regard to many aspects of congenital toxoplasmosis has been recognised.”

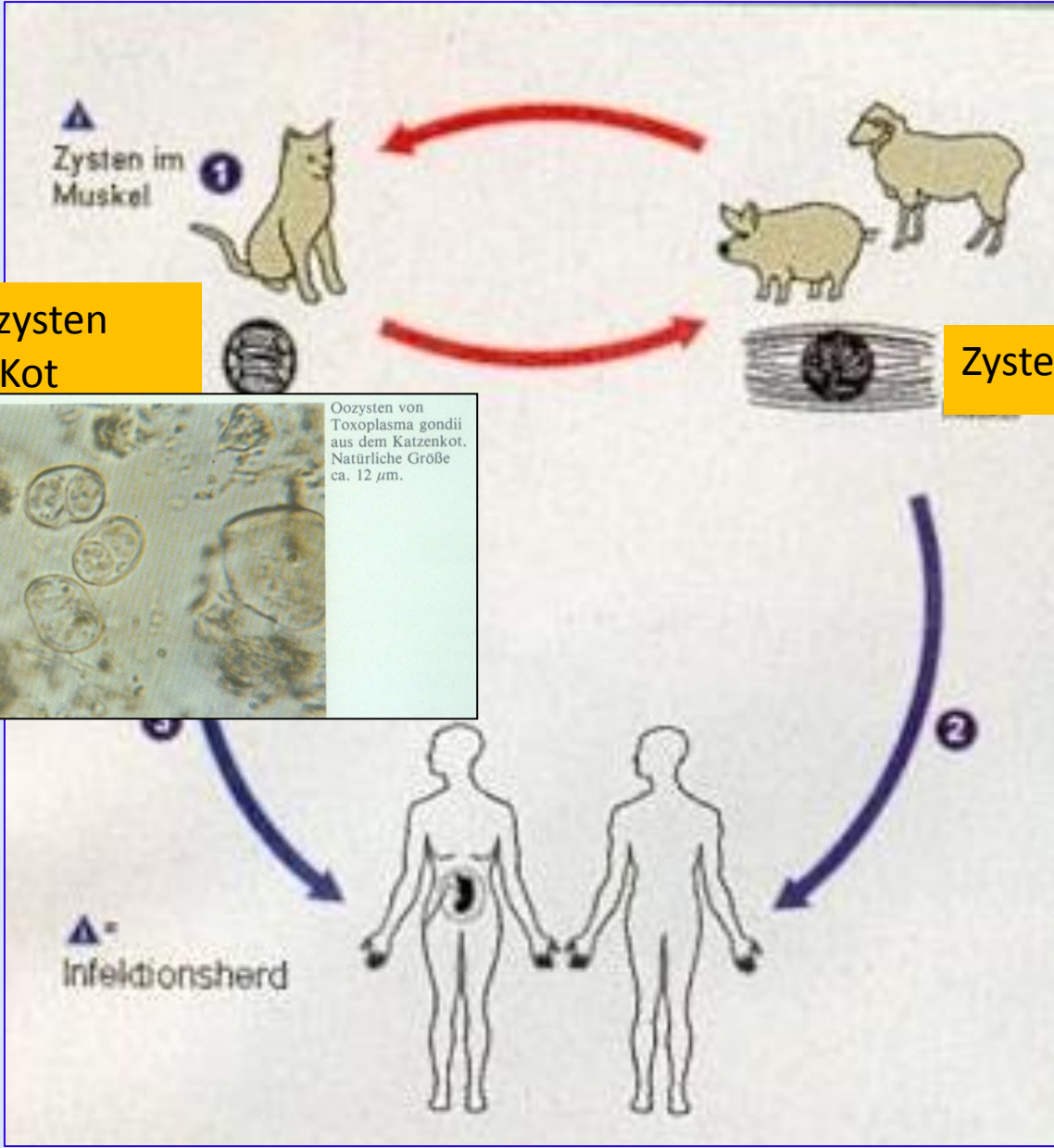
... a minor benefit cannot be ruled out with certainty.

Swiss Working Group on Congenital Toxoplasmosis
Swiss MedWeekly 2008;138(49–50)

Different Strains of *Toxoplasma gondii*

Finally, our results relate to the relatively benign type II strain of *T. gondii*, which predominates in Europe and North America. Trials are urgently needed to determine the most effective timing and type of prenatal treatment for the more virulent parasite strains that predominate in South America [31].

Gilbert RE, et al. PLoSNegl Trop Dis **2008**;2:e277



Oozysten
im Kot

Zysten im Muskel



Oozysten von *Toxoplasma gondii* aus dem Katzenkot. Natürliche Größe ca. 12 µm.



Dr.E.F.Karpf
Pathologie Graz

Toxo

Diagnostik

Zeigt die serologische Bestimmung positives IgG,
so ist zusätzlich eine IgM Bestimmung notwendig.

Ist **sowohl IgG als auch IgM positiv**,

so sind weitere Tests wie die **Avidität** durchzuführen.

IgG-Antikörper

Tiefe Avidität

Hohe Avidität

Antigen

Antigen

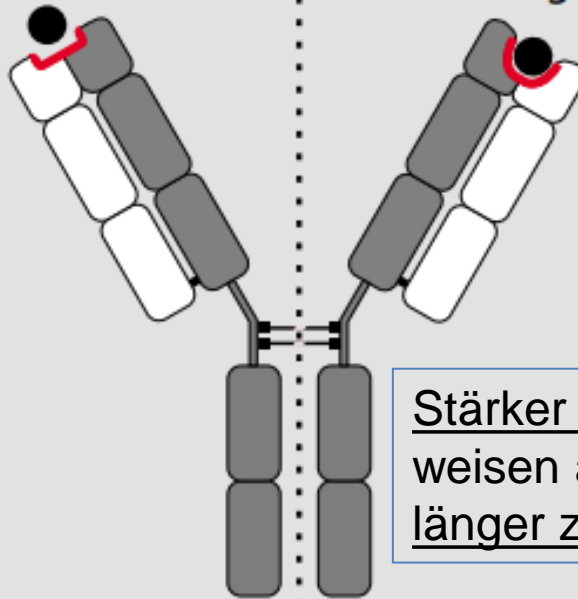
Schwache Bindung

Starke Bindung

Aviditäts Index < 0.3
Infekt < 4 Monate

Aviditäts Index ≥ 0.3
Infekt ≥ 4 Monate

Stärker bindende IgG-Antikörper weisen auf eine bereits länger zurückliegende Infektion hin.





Thank You

Therapie bei Erstinfektion - in der Schwangerschaft

Rovamycin^R

= Spiramycin

Sulfadiacin^R

Daraprim^R

Leucoverin^R

= Sulfadiacin

= Daraprim

= Folsäure

Toxo Screening – Cost Effective?

A cost-minimizing model for congenital toxoplasmosis in the United States compared the French protocol, vs. no systematic screening or perinatal treatment.

Thus, **cost savings of \$620 per child** are predicted with the implementation of a universal maternal screening program in the US population ..., or **nearly \$2.5 billion saved annually with screening compared to no maternal screening.**

Stillwaggon E, et al. PLoS Negl Trop Med. 2011 | Volume 5 | Issue 9 | e1333