

In the name of God



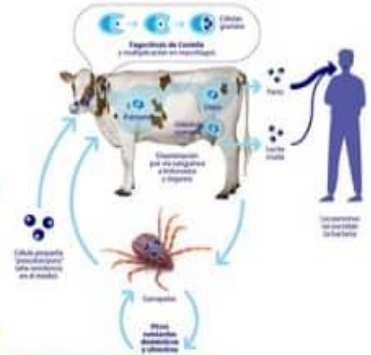


مرکز تحقیقات بیماری های نوپدید و بازپدید

بیست و دومین جلسه بررسی مقالات علمی

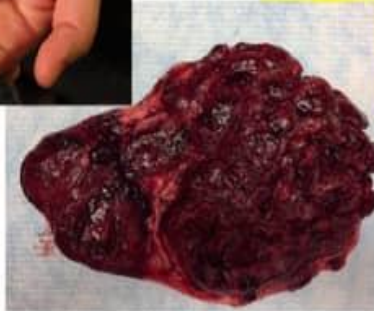
در حوزه بیماری های نوپدید و بازپدید

عنوان ارائه:



کوکسیلا بورنتی بعنوان یک عامل سقط عفونی در زنان

برگزار کننده: مرکز تحقیقات بیماری های نوپدید و بازپدید و آزمایشگاه مرجع کشوری طاعون، تولارمی و تب کیو انستیتو پاستور ایران



• مکان: کلاس یک، ساختمان آموزش، انستیتو پاستور ایران

• زمان: سه شنبه ۱۲ مهر ماه ۱۴۰۱، ساعت ۸:۳۰ الی ۱۰

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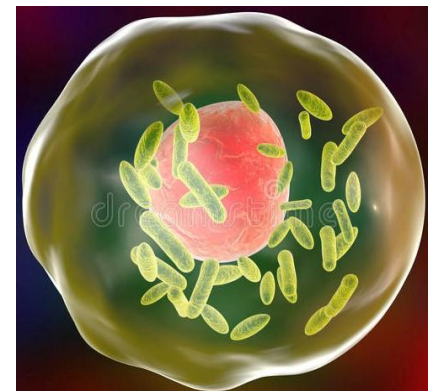
Title


Evidence of *Coxiella burnetii* infection among pregnant and aborted woman

- **Presenter: Mina Latifian**
- Department of Epidemiology and Biostatistics, Research Centre for Emerging and Reemerging Infectious Diseases, Pasteur Institute of Iran, Tehran, Iran

Q fever

- Q fever is known as a zoonotic disease worldwide except New Zealand.
- The infection causes by pleomorphic obligate gram-negative bacteria called *Coxiella burnetii* and was first described in Australia in 1935 after a febrile illness outbreak between slaughterhouse workers.



- 
- The host range of *C. burnetii* is diverse, including mammals (wild and domestic), birds, reptiles, and arthropods. Livestock such as cattle, sheep, and goats are the main reservoirs of this bacterium.
 - Although *C. burnetii* infection is usually asymptomatic or subclinical in animals, abortion, stillbirth, premature delivery, weak offspring, infertility, metritis, and mastitis have been reported in some.
 - Shedding of this bacterium into the environment could occur through milk, urine, feces, mucosal secretions, and birth fluids by infected animals.

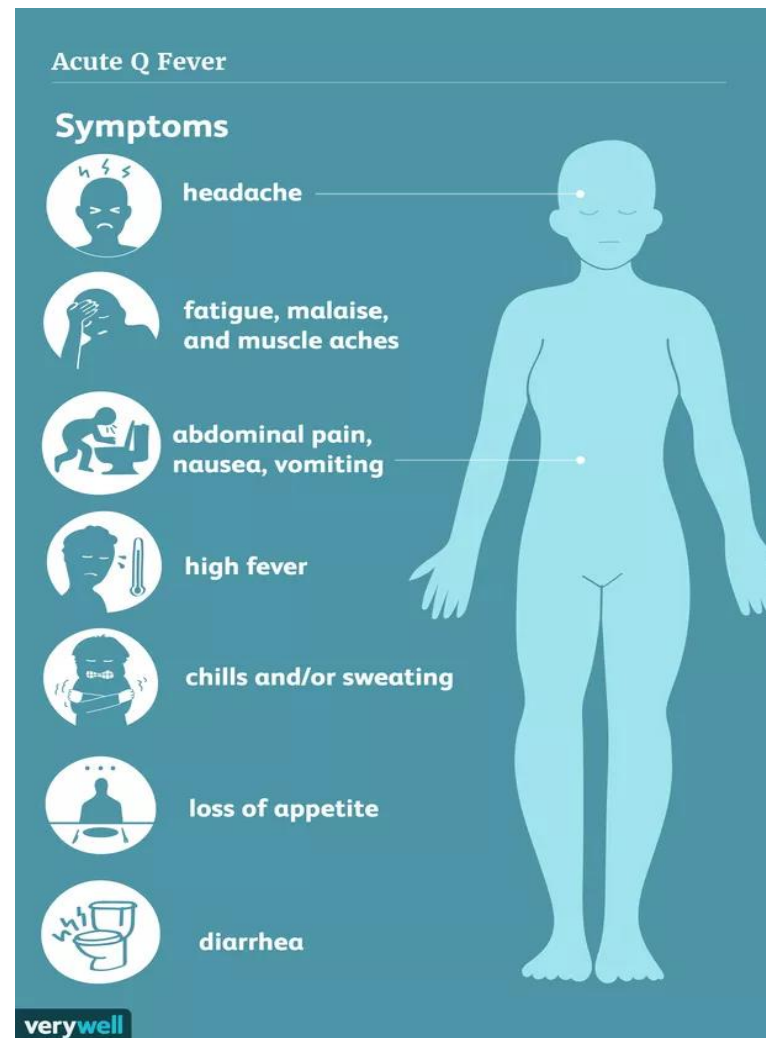
Transmission routes

- Inhalation of infected aerosol
- Consumption of contaminated dairy products
- Direct contact with parturient animals or their placentas
- Vertical transmission
- Person-to-person
- Tick bite



Type of infection

- Acute Q fever
- Chronic Q fever
- Fatigue syndrome





Q fever in pregnant women

- Until today, little data have been available on the incidence of Q fever in pregnant women and its complications in pregnancy.
- In 1958, Syrucek et al. isolated *C. burnetii* organisms from aborted human placentas.
- One of the first reports was the identification of Q fever infection during pregnancy in five pregnant women with abortion or premature delivery in France in 1990.

Q fever in pregnant women

- When pregnant women get Q fever, the bacteria colonize the uterus, mammary glands, and placenta, indicating that the infection can be transmitted through the placenta. *C. burnetii* can proliferate in trophoblast cells and cause an inflammatory reaction leading to placental necrosis and vasculitis, which can lead to miscarriage.



Gross view of placenta. Multiple foci of firm white tissue, flat or wedge shape (infract-like), involving maternal floor of placenta (yellow arrows).





Review

From *Coxiella burnetii* Infection to Pregnancy Complications: Key Role of the Immune Response of Placental Cells

Sandra Madariaga Zarza ^{1,2} , Soraya Mezouar ^{1,2,*}  and Jean-Louis Mege ^{1,2,3,†}

- ¹ Aix-Marseille University, MEPHI, IRD, APHM, 13005 Marseille, France; szarza90@gmail.com (S.M.Z.); jean-louis.mege@univ-amu.fr (J.-L.M.)
- ² Institute Hospitalo-Universitaire-Méditerranée Infection, 13005 Marseille, France
- ³ Unité Fonctionnelle Immunologie, Assistance Publique Hôpitaux de Marseille, 13005 Marseille, France
- * Correspondence: soraya.mezouar@univ-amu.fr; Tel.: +33-413-732-051
- † These authors had equal contribution.

A laboratory setting with a pipette on the left and several test tubes in a rack on the right, all set against a blurred green background.

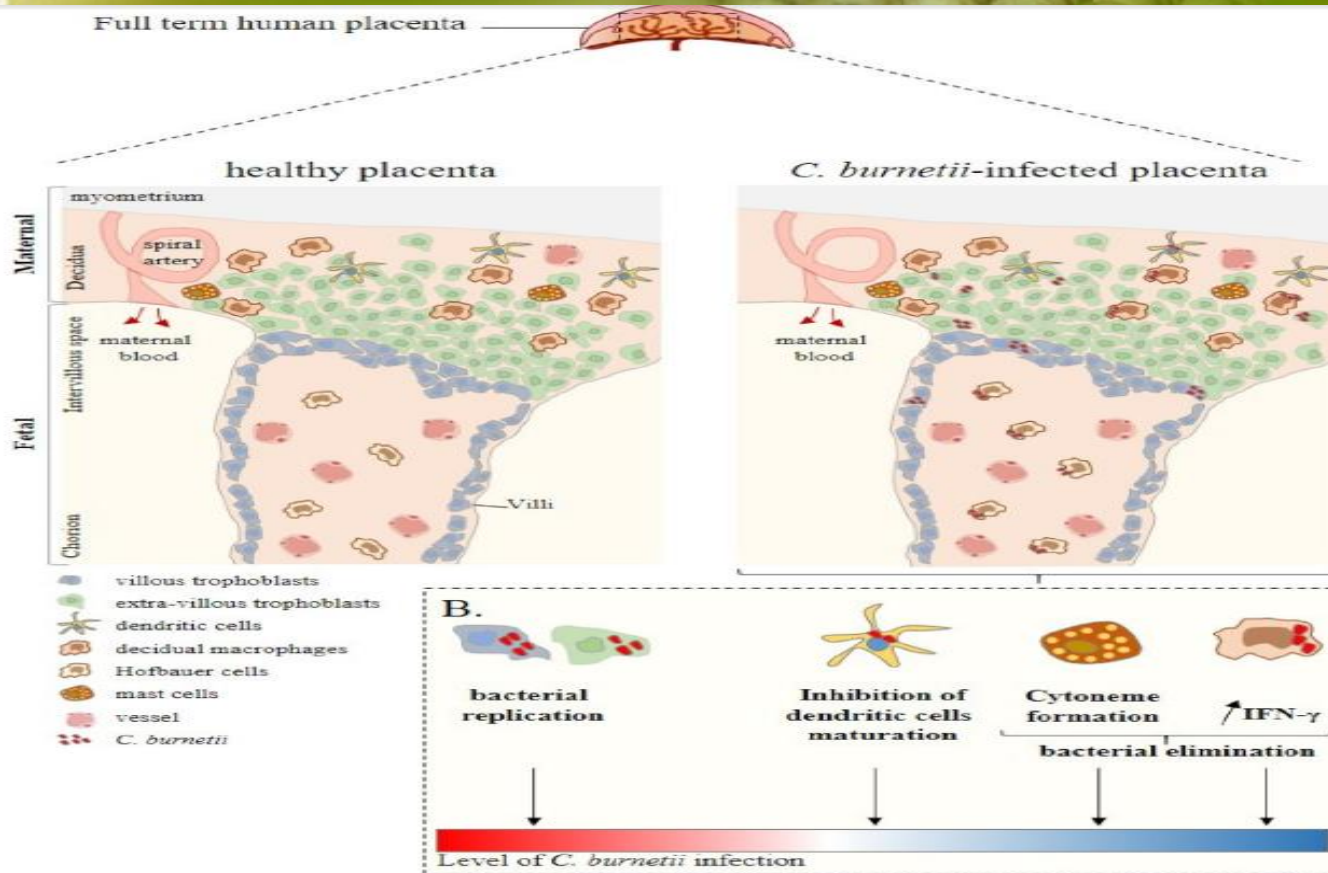
Q fever in pregnant women

- Pregnancy is an extraordinary situation in which the mother's immune system must tolerate a semi-allograft, the foetus.
- Consequently, this environment of immunosuppression secondary to pregnancy causes increased sensitivity to certain virus, parasites, or bacteria (such as *Brucella abortus* or *C. burnetii*), impairing pathogen clearance and increasing disease severity.
- Indeed, Q fever during pregnancy presents important risks for both the mother and the foetus. The placenta is a nutrient tissue at the maternal–foetal interface involved in both foetal growth and foetal tolerance.



Q fever in pregnant women

- The placenta is a complex tissue formed by the chorion and the decidua, corresponding to the foetal and maternal tissues, respectively.
- Due to its intrinsic structure and plasticity during pregnancy, the placenta is essential for foetal growth.
- Chorionic villus units are composed of mesenchymal cells, decidual macrophages (maternal macrophages), Hofbauer cells (foetal macrophages), foetal vascular cells, and trophoblast.
- The decidua is rich in immune cells, including NK cells, macrophages, T and B lymphocytes, DCs and mast cells, with an over-representation of NK cells and macrophages.



Placenta cell responses against *C. burnetii* infection. (A) Schematic representation of a full-term human placenta showing the maternal (decidua, myometrium) and foetal (intervillous space, chorion) parts.

(B) Ex vivo experiments based on in vitro infection of isolated primary cells from healthy at term human placentas reported the infectious capability of trophoblasts, dendritic cells, and macrophages by *C. burnetii*.

Q fever in pregnant women

Species	Placenta Histology and Cellular infiltration	<i>Coxiella burnetii</i> Presence in Placenta
Human	Symptomatic woman	<u>Maternal part:</u>
		<ul style="list-style-type: none"> Necrosis intermixed with disintegrating immune cells, neutrophils and plasma cells
		<ul style="list-style-type: none"> Placenta positive for <i>C. burnetii</i>
	<u>Foetal part:</u>	
	<ul style="list-style-type: none"> Necrosis on villitis and perivillitis (nuclear debris) 	
	Asymptomatic woman	<u>Maternal part:</u>
		<ul style="list-style-type: none"> No foci of necrosis or active inflammation
		<ul style="list-style-type: none"> Not reported
	<u>Foetal part:</u>	
	<ul style="list-style-type: none"> Fibrotic chorion villi, loss of capillaries, stromal karyorrhexis and haemorrhages 	

A background image showing laboratory glassware, including a pipette on the left and several test tubes in a rack on the right, all set against a soft, greenish-yellow gradient.

Q fever in pregnant women

- Trophoblast cells make up the majority of cells in the placenta, and the rest of the cells are related to immune cells, macrophages, dendritic cells, and mast cells, respectively.
- Based on histological studies, it appears that the trophoblast cells of the cotyledonary region are the first cells targeted by *Coxiella burnetii*.
- Of course, it should be noted that the role of other cells has not been clearly defined in *Coxiella burnetii* infection, but many of these cells are very important for the adaptation of the immune system of the mother and the fetus during infection.



Q fever in pregnant women

- Q fever infection in pregnant women has been associated with miscarriage, preterm birth, or low birth weight, and infrequently with fetal death, or congenital malformations.
- The prevalence of Q fever severe obstetric complications, including spontaneous abortion, intrauterine growth retardation, fetal death and premature delivery were 26%, 5.3%, 5.3% and 44.7%, respectively.
- The outcome of Q fever in pregnancy depends on the trimester of pregnancy, and if a person becomes infected in the first trimester, the chances of miscarriage are greatly increased.



TUMS

[Iran J Public Health](#). 2016 Apr; 45(4): 523–530.

PMCID: PMC4888180

PMID: [27252922](#)

The First Serological Study of *Coxiella burnetii* among Pregnant Women in Iran

[Maryam KHAYYAT KHAMENEIE](#),¹ [Javad ASADI](#),^{2,*} [Mohammad KHALILI](#),³ and [Zeinab ABIRI](#)³

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The First Serological Study of <i>Coxiella burnetii</i> among Pregnant Women in Iran	2014	Iran (Ahvaz)	200	181 Normal Pregnancy	44	ELISA	Blood
				19 Abnormal Pregnancy			
	Iran (Parsabad)	200	111 Normal Pregnancy	73			
			89 Abnormal Pregnancy				



First Seroprevalence Study of *Coxiella burnetii* in Rural Pregnant Women in Contact with Livestock in Khorramabad

Eiman Azizyari Ghobadi¹, Amin Jaydari ^{1,*}, Soheila Akbari² and Khaterh Anbari³

¹Department of Pathobiology, Faculty of Veterinary Medicine, Lorestan University, Khorramabad, Iran

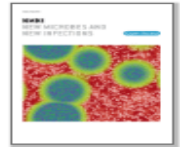
²Department of Obstetrics and Gynecology, Lorestan University of Medical Sciences, Khorramabad, Iran

³Department of Community Medicine, Lorestan University of Medical Sciences, Khorramabad, Iran

*Corresponding author: Department of Pathobiology, Faculty of Veterinary Medicine, Lorestan University, Khorramabad, Iran. Email: jaydari.a@lu.ac.ir



Received 2019 September 05; **Revised** 2019 October 11; **Accepted** 2019 October 15.

First Seroprevalence Study of <i>Coxiella burnetii</i> in Rural Pregnant Women in Contact with Livestock in Khorramabad	2016 - 2017	Iran (Khorramabad)	184 From rural pregnant	89 (19 Of them History of Abortion)	ELISA	Blood
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Original Article

Coxiella burnetii infection with women's febrile spontaneous abortion reported in Algiers

H. Ghaoui^{1, 3}  , I. Bitam^{1, 7}, K. Ait-Oudhia³, N. Achour⁴, A. Saad-Djaballah⁴, F.Z. Saadnia⁵, S. Kedjour⁶, P.-E. Fournier²

Coxiella burnetii infection with women's febrile spontaneous abortion reported in Algiers	2014 - 2015	Algiers	725	380 Febrile Spontaneous Abortion	4	PCR	Placenta
				345 Normal	0		



[Investigation of *Coxiella burnetii* prevalence in women who had miscarriage and their spouses by serological and molecular methods].

Eyigör M¹✉, Gültekin B, Telli M², Odabaşı AR, Yüksel H, Demircan Sezer S, Aydın N

Author information ▶

Mikrobiyoloji Bulteni. 01 Apr 2013, 47(2):324-331 Language:tur

DOI: 10.5578/mb.4543 PMID: 23621732

Investigation of <i>Coxiella burnetii</i> Prevalence in Women Who Had Miscarriage and Their Spouses by Serological and Molecular Methods	2012	Turkey	51	29 Abortion	0	PCR	Placenta
				22 Delivery	0		



University of Thi-Qar Journal Vol.12 No.4 DEC 2017

Web Site: <https://jutq.utq.edu.iq/index.php/main>

Email: journal@jutq.utq.edu.iq

Molecular Detection of *Coxiella burnetii* Among Aborted Women in Thi-Qar Province/ Iraq

<https://doi.org/10.32792/utq/utj/vol12/4/7>

Hekmat K. Ateya

College of Veterinary Medicine, Thi- Qar University, Iraq.

Molecular Detection of <i>Coxiella burnetii</i> Among Aborted Women in Thi-Qar Province	2014	Iraq	47 aborted women	8	PCR	Cord Blood
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ELSEVIER

American Journal of Obstetrics and Gynecology

Volume 189, Issue 1, July 2003, Pages 228-232



General Obstetrics and Gynecology Obstetrics

Coxiella burnetii seropositivity in parturient women is associated with adverse pregnancy outcomes ☆, ☆☆

Presented in part at the Thirty-Eighth Interscience Conference on Antimicrobial Agents and Chemotherapy, San Diego, Calif, September 24-27, 1998, as Abstract L-068.

Coxiella burnetii seropositivity in parturient women is associated with adverse pregnancy outcomes	1997 - 1998	France	246	153 Seropositive	0	PCR	Placenta
				93 Control	0		



- We search the literature that reported the prevalence of *C. burnetii* in woman with a history of abortion in the world from 1993 to 2021.
- Finally, 25 studies were included in this review.

	Group category	Country	Year	Method	Sample size	Sample type
1	Seroprevalence in pregnant women	Algeria	2014-2015	IFA	725	Blood
2		Iran	2016-2017	ELISA	184	Blood
3		England	2008	IFA	438	Blood
4		Iran	2014	ELISA	400	Blood
5		Netherlands	2007-2008	IFA	1174	Blood
6		France	2002-2003	IFA	376	Blood
7		Turkey	2012	IFA	100	Blood
8		Japan	1993-1998	IFA	200	Blood
9		France	2013	ELISA	179	Blood
10		Denmark	1996-2003	IFA	856	Blood
11		France	1996	IFA	12716	Blood
12		Spain	2009-2010	IFA	500	Blood
13		France	1997-1998	IFA	7658	Cord blood
14		France	2014	IFA	1112	Blood
15		Turkey	2009-2010	IFA	58	Blood
16		Germany	2003 & 2005	IFA	93	Blood
17		Thailand	2015-2016	ELISA	105	Blood

	Group category	Country	Year	Method	Sample size	Sample type
18	Molecular prevalence in pregnant women	Algeria	2014-2015	PCR	725	Placenta
19		Turkey	2012	PCR	51	Placenta
20		France	1997-1998	PCR	246	Placenta
21		Iraq	2014	PCR	47	Blood
22	Isolation	Germany	2003 & 2005	Culture	5	Placenta, Amniotic fluid & colostrum
23	Follow-up of pregnant women with Q fever	France	2006-2011	IFA & PCR	30	Blood & Placenta
24		India	2007	IFA, PCR & Culture	74	Blood, Genital swabs, Fecal swabs & Urine
25		Denmark	2007-2001	IFA & PCR	12	Urine, placenta, Bonemarrow, Milk & Blood
26		Netherlands	2011	IFA & PCR	9	Blood & Placenta
28		France	2007-2012	PCR & Culture	14	Placenta
29		France	1997	PCR & Culture	5	Blood, placenta & Fetal Tissue
30		France	1991-2005	PCR & Culture	53	Placenta & Fetal Tissue

Result

Study population	Subgroup	Number of studies	Sample size	Pooled estimate (95%CI)	I ²	p
Studies on pregnant women without defined previous infection						
Serology						
Total seroprevalence	Total	17	26874	11.10 (6.06-13.13)	98.81	<0.001
Prevalence based subgroup						
Income situation	High income	11	25302	11.56 (9.39-13.73)	97.18	<0.001
	Upper middle income	3	263	15.21 (7.40-23.11)	99.04	<0.001
	Lower middle income	3	1309	22.41 (0.00-47.73)	90.26	<0.001
Study year	Before 2010	20	22526	7.10 (6.08-8.12)	98.08	<0.001
	After 2010	5	3494	18.38 (9.60-27.16)	99.18	<0.001

Result

Study population	Subgroup	Number of studies	Sample size	Pooled Estimate (95%CI)	I ²	p
Molecular						
Total prevalence	Total	4	1069	0.30 (0.00-0.69)	73.42	0.01

Result

Study population	Subgroup	Number of studies	Sample size	Pooled estimate (95%CI)	I ²	p
Prevalence of <i>C.brunetti</i> in women with previous infection						
Serology	Total	6	183	79.23 (58.36-100.00)	98.09	<0.001
PCR	Total	7	197	13.97 (2.74-25.19)	74.56	<0.001
Culture	Total	5	55	35.61 (10.13-61.08)	80.15	<0.001

Result

	Number of studies	Sample size	Pooled prevalence in women with exposure	Sample size	Pooled prevalence In women without exposure	Pooled OR (95% CI)	I ²
Seroprevalence of coxiella brunetii in pregnant or parturated women							
Abortion history	10	2125	13.68 (10.35-17.02)	10772	12.66 (8.99-16.32)	1.58 (1.24-2.02)	35.78*
Risky population	7	11919	7.73 (4.82-10.64)	4066	6.90 (3.66-10.13)	1.86 (0.63-5.48)	87.94
Seroprevalence of coxiella brunetii in pregnant or parturated women with history of previous infection with coxiella brunetii							
Abortion history	2	512	0.80 (0.00-1.60)	264	0.00 (0.00-0.57)	2.81 (0.31-25.32)	0.36*



Discussion

- Infection with intracellular bacteria such as *Listeria* and *C. burnetii* can lead to adverse complications such as infertility, stillbirth, preterm delivery, ectopic pregnancy, intrauterine fetal demise, and low birth weight.
- These bacteria are food-borne and zoonotic pathogens that tend to embryonic units and lead to fatal diseases in the mother and fetus.



Discussion

- The prevalence of Q fever in pregnant women is generally unknown and occurs asymptotically in 90% of cases.
- To diagnose the disease in pregnant women, routine screening, especially in areas where the disease is endemic, is considered essential. Studies show that Q fever infection increases the risk of miscarriage in early pregnancy and premature fetal or intrauterine fetal death in late pregnancy.



Discussion

- Living in high-risk areas, as well as close contact with domestic animals and livestock, increases the risk of infection in pregnant women.
- May be living within 5 km of farms with infected goats and sheep is considered a high-risk area for the disease. Also, travel to these areas can cause infection in pregnant women.



Discussion

- Several methods have been proposed to identify *C. burnetii* in clinical specimens. These methods include molecular methods, serological methods (ELISA & IFA) and culture, which can be used to more quickly identify the disease and prevent its dangerous side effects.
- Acute Q fever is confirmed by a positive molecular test and an increase in Phase II IgM antibody titer or a quadruple increase in Phase II IgG titer. Chronic Q fever is also confirmed by a positive molecular test and an increase in IgG phase I titer.



Discussion

- In general, treating Q fever during pregnancy is associated with great challenges.
- Since doxycycline is a choice drug for the treatment of Q fever and this drug is contraindicated during pregnancy, as a result, the course of treatment with cotrimoxazole has been suggested since 1996.

The background of the slide features a soft-focus image of laboratory glassware. On the left, a pipette is visible, and on the right, a rack of several test tubes is shown. The overall color palette is a mix of light green and yellow, creating a clinical and scientific atmosphere.

Conclusion

- Because there is limited information about the mechanism of Q fever in pregnant women, screening of women who have occupational exposure to livestock and live in endemic areas with serological methods is essential.
- It is also necessary to follow up on the treatment of pregnant women who have a history of Q fever infection to control the disease and prevent chronic Q fever infection, as well as complications in subsequent pregnancies.



thank you

