



# LISTERIA MONOCYTOGENES AS THE POSSIBLE CAUSE OF THE SPONTANEOUS ABORTION IN FEMALE OF THE FERTILE AGE

MUFIDA ALJIČEVIĆ\*, EDINA BEŠLAGIĆ, ŠUKRIJA ZVIZDIĆ,  
SADETA HAMZIĆ, SABINA MAHMUTOVIĆ

Department of Microbiology, Faculty of Medicine, University of Sarajevo,  
Čekaluša 90, 71000 Sarajevo, Bosnia and Herzegovina

\* Corresponding author

## ABSTRACT

*Listeria monocytogenes* is a Gram-positive, weakly pathogenic bacterium able to grow also at the temperature of 4°C. A man most often gets affected by consuming contaminated food and water. Animals can carry bacteria although they have not to appear ill, then their meat and milk products are the source of infection of human being. The disease most often attacks with the weak immune system, newborns and pregnant women. That what is significant, listeria penetrates through the placenta and can lead to the fatal infection, which is characteristic by disseminated granulomatosis lesions of a newborn and micro abscess on the placenta. In a newborn can provoke the sepsis with the mortality of 50%. By the examination are encircled two groups of the reproductive age-totally 60. From these 30 had one or more spontaneous abortion, and 30 had no spontaneous abortion. By the serologic reaction the agglutination is discovered the presence of the antibodies in serum of the. The positive serologic answer was found in the first group in 18 (60%) and in that another group in 8 participants (26, 70%).

**KEY WORDS:** serologic response, *Listeria monocytogenes*

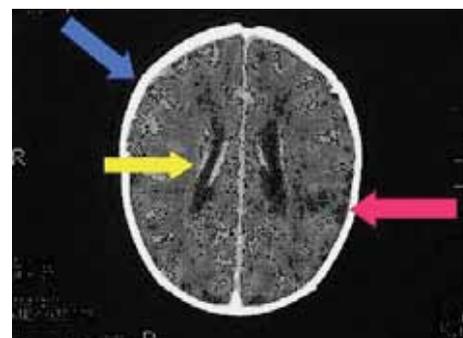
## INTRODUCTION

Listeriosis is the disease caused by bacteria *Listeria monocytogenes* and that most often by the consuming of food contaminated by this bacterium (1). The persons with weakened immune system, the newborn and fetus are most sensitive to this infection. The pregnant women are exceptionally highly risk group because the infection regularly gets transfer on the fetus causing abortion, birth of dead child, premature birth or birth of a child with the infantile listeriosis of various clinical manifestations (2, 3). According to CDC the pregnant women are about 20 times more sensitive to listeriosis than in the adult healthy persons (4). *Listeria* is Gram-positive bacteria of the chop stick form, movable and is to be found in earth and water. It is very capable for survival because it grows at the temperature below 3°C and all to about 40°C, and overcome also the harmful effect of cooling drying and heating (5). Thanks to that it can get multiplied in food which is kept in fridge. Animals can be also carriers of *listeria* so by consuming of meat, meat products and milk of the contaminated animals, can be affected also the human being. Vegetables, except carrot and tomato, also can be contaminated by this bacterium from earth of fertilizer (6). The brought in organism *listeria* by food can do the invasion onto the gastrointestinal epithelial over the intact gastrointestinal tract. After that *listeria* being phagocytes by monocytes, macrophage or polymorph nuclear leukocytes. The pathogenesis of this bacterium is based on the characteristic of *listeria* to survive and get multiply in the host phagocytes. As an intercellular microorganism which localized in the lymph tissue of the intensive goes into blood, liver and other organs cre-

ating microabscesses in them. The intracellular growth in phagocytes enables the migration to *listeria* through the placenta to fetus (7). The cause is about 10% of the neonatal sepsis (8). In humans, the association of a *Listeria* infection in pregnancy and severe disease in fetus was first described in 1936 (9). As intracellular pathogen possesses the specific mechanism then to this gets multiplied in the cells of the infected host. It can manipulate the expression of the gene in host cell. Protein (Act A) that is to be found on the surface of the bacterial cell induces the polymerization of actins in human cells into long active fibers through cytoplasm. Thanks to that *listeria* moves directly from one to another host cell avoiding the numerous defensive mechanisms, and simultaneously by its toxins damages the host cell what represents also the additional protection (7). The infective dosage of *Listeria monocytogenes* is not determined, but it is considered that in persons with the weakened immune system less than 1000 cells can be provoked the disease (10,11). Listeriosis in pregnant women shows regularly the tendency to chronicity. In women the cause can persist long enough saprophytically and that it only during the pregnancy gets activated, that is that it becomes virulent. It is observed that it in women who had the spontaneous abortion more times the presence of the *listeria* on the genital organs (12). In the infections during the pregnancy the infection of a mother does not need to be clinically visible or may appear as the febrile disease similar to flue (13). That what is significant, *listeria* penetrates the placenta and can lead to the foetus infections which are characterization by the granulomatosis lesions in a newborn and macro abscesses on the placenta (Figure 1). Infections during pregnancy can lead to premature delivery, infections of the new-



FIGURE 1. Placenta with the numerous granulomatose abscesses. (17)  
/ Professor P. Berche ( Faculty of Medicine Necker-Enfants Malades, Paris V) 10. 09. 2002. /



■ edema  
■ periventricular enhancement suggests ventriculitis  
■ diffuse parenchymal hypodensity

FIGURE 2. CT-x ray of the baby brain which is 2 weeks old with the listeriosis meningitis (18).

born, or even stillbirth. The incubation lasts 3-45 days, and the transplacental or intrapartally affected newborn has three clinical entities: granulomatosis infantiseptica – most often die under the septic picture of the respiratory distress syndrome (*listeria* visible in meconium and numerous microabscesses and granulomas, specially in the liver and spleen), then early occurred newborn listeriosis in the first 5 days of life which the mortality of about 50% and late occurred 2-4 weeks after the birth under the clinical picture of the pus meningitis (Figure 2). The serologic diagnosis is not specific, bases on the four times greater antibodies titer increase which connects the complement (IgG). They become positive between the seventh and ninth day of the disease and exist 3-4 weeks. The antibiotics therapy /Erythromycin/ lasts 7-10 days, but by this are not root out the microorganisms in the convalescent they can be persisted also by months. The mortality is above 50% in the premature infected in utero, 30% in those with the early neonatal sepsis, and 15% in later neonatal meningitis. As the consequence of listeriosis can to occur hydrocephalus, the mental retardation and other. When in the clinical picture there is sepsis, septic shock, meningitis or difficult neonatal infections which brought to death of the dead embryo, then should think of the listeriosis. Although listeriosis of a pregnant woman can cause difficult consequences obligatory should examine the mother serologically, and for the new pregnancy wait at least 6 months. Usually there is no danger of the repeat of same changes in the following pregnancy (14).

## OBJECTIVE

The aim of this examination is to determine the existence of the serologic response on *Listeria monocytogenes* in women of the fertile age, who had one or more spontaneous abortion.

## PATIENTS AND METHODS

By the examination are comprehended two groups of the examinees: the experimental and the control one with 30 examinees in each group – totally 60. The experimental group makes the examinees which in their anamnesis had one or more spontaneous abortions, and the control group makes the examinees which had no spontaneous abortion. In time taking blood of 30 examinees of the experimental group 9 of them were pregnancy, and 21 no, and in the control group one examines was not pregnant, while in the rest 29 are.

Blood was taken from the cubital vein in the amount of 5-7 ml by vein puncture by means of the “vacuuntainer” which in itself contains gel base for the serum separation. In the serum the examinees the antibody presence is being discovered by the serologic reaction of the agglutination to the *listeria* by means of the ready *listeria* antigens. The reaction of the agglutination /*Listeria* Gruber-Widal reaction/ we performed in the polystyrene microtitre plates, by the so-called micro-method. In order to get the titer of the antibodies were performed the dilution of the serum of 1:20 to 1:1280 according the principle of the double dilution. As a positive result was considered the titer of 1:320 and more, all below this was considered the negative result. The lower titers can be found in blood of healthy persons.

## RESULTS

From totally 30 patients of the experimental group in 18 (60, 00%) was found the positive serologic response. The value of the titer of 1:320 was found in 11 participants who in time of the examination were not pregnant. In the examinees which in the examination time were pregnant is the titer value of 1:320 was found in 5 participants, and the titer 1:640 was found in 2 participants. From totally 30 participants of the control group in 8 (26, 70%) was found the positive serologic response. In this group only one participant was not pregnant, and the rest 29 are. From these 29 participants 8 of them were positives, and 7 examinees with the titer height of 1: 320, 1 examine with titer height of 1: 640.

## DISCUSSION

Still from the ancient 1961 year there are doubts on the possibility of the transfer of *listeria* by food. In the beginning of 1980 year this doubt finally was proved when in Canada (New Scotia) occurred the epidemic of the listeriosis caused by sour cabbage. After that there were several reports about the epidemic and sporadic causes of the listeriosis cause by various kinds of food. From them on the listeriosis belongs to the so called foodborne diseases (14). Because the possible to cross the placenta transfer of the *listeria* on the embryo in the pregnant women who can carry the listeriosis infection asymptomatic, often this infection is fatal for the embryo. If the child gets born with the disseminated form of infection, in the untreated cases the mortality amounts even 100%. The incidence of the listeriosis in the developed countries is about 0, 2 to 0,

8 cases on 100,000 inhabitants yearly. The incidence is not high, but the mortality about 23%, therefore the listeriosis became the care of the public health (15). In the report of CDC from 1986 year was started in the publicity that in 6 regions of USA was 6,9 of cases occurred on the million of inhabitants. The mortality was 19, 1% and depended on the age of a pa-

tient and his/her immune state. The women who are 20-29 years old were the group of the same age group. This incidence in crease in young women is the reflection of the sensitivity increase during the pregnancy time. 21% of the pregnancy complicated by the infection of *Listeria monocytogenes* results with intrauterine embryo loss that is the fetus death (16).

## CONCLUSION

From 1998 year the registration of the listeriosis in EU countries. In us of the previous years in obligatory in each pregnant woman was about the examination also to listeria monocytogenes, in order to because of the war it was stopped by this. Therefore there are no data about the moment of the listeriosis in us. From the accepted results can be concluded that there is the serologic response to the Listerie monocytogenes in females of the fertile age, and that the number of the positive serologic response is greater in those examinees which had spontaneous abortions (one, two ore more) in the relation to those examinees who had not. The received results bring us to the conclusion that probably listeria monocytogenes is one of the causes of the spontaneous abortions in us.

## REFERENCES

- (1) Karakašević B. Mikrobiologija i parazitologija, Medicinska knjiga Beograd-Zagreb, 1987; 45: 847-851
- (2) Vazquez-Boland J., Kuhn M., Berche P. Listeria pathogenesis and molecular virulence determinants. Clin. Microbiol. Rev. 2001; 14: 584-640.
- (3) Kalenić S., Mlinarević-Missoni E. Medicinska bakteriologija i mikologija. Zagreb, 2001; 19: 253-255.
- (4) [http://www.inform.umd.edu/~/Listeria\\_the\\_organism\\_and\\_the\\_disease.htm](http://www.inform.umd.edu/~/Listeria_the_organism_and_the_disease.htm). Adams C. Listeria-the organism and the disease. Information paper. U.S. Department of Agriculture, Extension Service. [access: 24. 02.2002]
- (5) Seeliger H., Jones D. Bergey,s Manual of Systematic Bacteriology, Wiliam and Willkins. Baltimor, 1986; Vol. 2: 1235-1245.
- (6) Hof H., Nichterlein T. Aspects of diagnosis and research in medical microbiology, Biotest Bulletin, 1998; Vol 6: 21-32.
- (7) <http://www.sgi.co.yu/html/004/00404.html> Mačvanin M. Listerioza, fatalna infektivna bolest sa "bezazlenim simptomima". Aktualnosti iz nauke i tehnologije SciTech-Bakteriologija. [access: 09. 02.2005]
- (8) [http://www.medicina.hr/index/str\\_dod.asp?id=5](http://www.medicina.hr/index/str_dod.asp?id=5) Kuzmančić N. Listerioza, [access: 30.03. 2003 ]
- (9) Bille J., Rocourt J., Swaminathan B. Manual of Clinical Microbiology 2002; American Society for Microbiology, Chapter 38. pp.461-467.
- (10) <http://www.foodsafety.gov/~dms/Imr2qa.html> Center for Food Safety and Applied Nutrition.: Listeria. The bacterium, The disease. Listeria monocytogenes risk assessment questions and answers. [access: 21.10. 2003 ]
- (11) Teftedarija M., Đorđević D. Opšta i specijalna infektologija, Sarajevo, 1985; 148-151.
- (12) Miković, Ž. Infekcije u trudnoći. <http://users.verat.net/~mcdoc/skripta/predL.htm> [access: 12.05.2005.]
- (13) Čulić V. Dijagnostika i praćenje intrauterinih infekcija. Paediatr. Croat. 2004; 48 (Suppl. 1): 180-191.
- (14) Southwick F., Purich D. Intracellular pathogenesis of listeriosis. New Engl. J. Med. 1996; 334: 770-776
- (15) Evans A., Brachman P. Bacterial infections of humans. USA 1998; 21: 421-436.
- (16) Bešliagić E., Bašić F. Mikrobiologija-morfološki aspekti sa dijagnostikom. Sarajevo. 1998; 157-158.
- (17) <http://www.microbes-edu.org/etudiant/etudiants.html> Listeria monocytogenes Professor P. Berche ( Faculty of Medicine Necker-Enfants Malades, Paris V) [access: 25.04.2005.]
- (18) <http://www.uofodepteds.org/Presentations/Listeria /Alyson Shaw, PGY-3., Infectious Disease Rounds /> [access: 19.04.2002.]