University Of Medicine And Pharmacy “Gr. T. Popa”

PhD Thesis

Clinical and laboratory research in syphilitic infection associated with pregnancy

Abstract

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Iasi- 2012
Key words:
Syphilis, Congenital, pregnancy, infection, prevention
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**Study III: prospective study of children born to mothers diagnosed with syphilis over a period of six years (2005-2010)**

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**IV. DISCUSSION**

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ABBREVIATIONS
ANOVA = analysis of variance (method of statistical processing)
APGAR = muscular activity, Puls, G = reflexes, A = skin color, breathing
BCF = fetal heart rate
CDC = Centers for Disease Control and Prevention
CRL = crown-rump length
CTG = cardiotocography
DAT = Diameter Transverse Abdominal
DBP = biparietal diameter
DFA = Direct Fluorescent Antibody Test
DFO = Diameter Fronto-occipital
DSP = Departament of Public Health
DTT = Transversal diameter of the chest
EIA = enzyme-linked immunosorbent assay
ELISA = Enzyme Linked Immunosorbent Assay
EIA = Enzyme Linked Immunosorbent Assay
FDA = U.S. Food and Drug Administration
FTA-Abs = Fluorescent treponemal Antibody Absorption Test with
IDF = direct immunofluorescence
IFI = Indirect Immunofluorescence
Ig = Imunoglobuline (imunoglobulin G)
STI = ITS= sexually transmitted infections
LA = amniotic fluid
LCP = length of skull pelvis
LCR = CSF = cerebrospinal fluid
LF = length of the femur
MS = Ministry of Health
RPR = Rapid Plasma Reagin
TPHA = Treponema pallidum haemagglutination assay
TP-PA = Treponema pallidum particle agglutination assay
TRUST = Toluidine Red unheated serum test
EU = European Union
UV = Ultraviolet
VDRL = Venereal Disease Research Laboratory
I. Introduction

Syphilis is a systemic infectious diseases, non-immune complex, with chronic evolution, with variable clinical manifestations, "chameleon", imitating many skin problems caused by *Treponema pallidum* spp, which only affects some people and primates.

Syphilis was first described in Spain by Ruy Dias of Isla in Barcelona in 1493. It is assumed that Christopher Columbus and his crew brought syphilis from the America.

The first recorded epidemic of syphilis in Europe in 1495 among French troops besieging Naples.

It shows clinical signs and disease progression and susceptibility to penicillin is preservation of *Treponema pallidum* from 1943, currently being described as rarely resistant strains.

Syphilitic infection is of particular concern, both socially as the great infection by its manifestations primary-secondary, and from the individual.

Signs and symptoms of this disease have a polymorphism or marked absent in accordance with the state in which the presentation to the doctor for diagnosis.

Syphilis has been called "the great imitator" because of the often atypical clinical picture. In contrast with the clinical diagnosis that requires alertness and well-trained medical doctor who has to face such a patient, diagnosis is simple and effective, as is the treatment of this disease and serological testing.

Congenital syphilis is caused by the spirochaete passage through the placenta from an infected mother to fetus during intrauterine life is the result of inefficient filters serological or contamination during pregnancy, causing: death of the conceptus, abortifacient disease,
hypertrophy, fetal deaths perinatal, neonatal, fetal pathological changes: jaundice, bleeding, hepato-splenomegaly, changes in bone and teeth.

As can be transmitted to descendants, syphilis can have a negative influence on social and health status of future generations. Therefore patients should be educated, aware not to neglect medical advice when there is suspicion of infection, not to avoid the mandatory health checks of the Population surveillance scheme (clinical and serological regular employment, the prenup, during pregnancy, enrollment in some contests), sanitary police role in Romania being neutral in this respect since 1989.

A well-conducted epidemiological investigation may prevent onset congenital syphilis fetuses of couples with a past history risk, with the ability to seek treatment early and correct.

Once diagnosing the disease, it is the responsibility of specialists to establish a therapeutic algorithm correctly. A limit of medical practice in some cases makes it difficult to drive a full treatment according to patients, for various reasons. So it is necessary for doctors to develop their strategies, adapted to clinical and socio-educational reality existing to serve the interests of the patient.

The first part of the thesis was devoted to the general description of syphilitic infection, including elements of epidemiology, etiopathogenesis and clinical and paraclinical diagnosis, then an overview of current strategies of treatment.

The second part of this study assumed that fetal pain is still determined to a significant percentage of syphilitic infection transmitted from mother to child during pregnancy. Interdisciplinary study of co-opted specialists, obstetricians, dermatologists, neonatologists, infectious disease, radiology, laboratory and aims to identify and evaluate risk factors affecting survival and recovery of the child born of a mother with syphilis, summation and analysis of clinical and laboratory features maternal and congenital syphilis-related proposals to limit damage to the offspring obtained by T. pallidum in Romania in 2012.
II. PERSONAL CONTRIBUTIONS

PURPOSE OF RESEARCH
The study aims to establish the incidence of syphilis in pregnant women and infants in Iasi between the periods of 2003-2011, to identify and evaluate the risk factors affecting the survival of the child, description of clinical and laboratory features related to congenital syphilis and determination of treatment effectiveness in combating this condition.

OBJECTIVES OF WORK
Identification of cases of acquired syphilis in pregnant women investigated for a period of 9 years from 2003-2011.

- Assessment of epidemiological links locally and regionally.
- Identify efficiency of diagnostic methods currently used in Iasi.
- Tracking the effectiveness of specific regimens adopted by MS in Romania, which, when applied correctly in time, can lead to illness in both mother and infant, with or without squeal.
- Assessment of progress and outcome of cases, highlighting the possibility of general coordinates of the disease.

The first study involved an evaluation of 461 cases suspected and then confirmed pregnant with syphilis and their babies through a retro-prospective study over a period of nine years, between 2003 and 2011. The objective was to determine the incidence, area of origin, clinical and biological evaluation, registration of these cases by general practitioners or specialists, the correct application of treatment according to established WHO scheme adopted by the MS from Romania and periodic serological evaluations after treatment in the follow efficacy.

In the second study we focused on a group of 209 pregnant, aborted and puerperium diagnosed with syphilis in The Obstetrics and Gynecology Clinical Hospital "Cuza Voda" and Dermatology Clinic of Emergency County Hospital "St. Spiridon "from Iasi, in the period 2005-2010.
The objectives of this study were: epidemiological tracking of cases studied, applied laboratory conducting investigations to detect maternal and fetal infection (double test and triple test for fetal malformations, amniocentesis, the immediate effect of treatment over pregnant uterine contractions and the product of conception by cardiotocography, abdominal and pelvic ultrasound, serology, histopathology of the placenta and the product of abortion, psychological evaluation, the progress of pregnancy), differentiate infection from simple low positive serology in infants, children (due to the transplacental passage of antibodies from the mother only without actual infection with the spirochete), and assessing fetal risk of infection.

In the third study were followed for up to 6 years (2005-2010) 55 children born to mothers with syphilis from the Children's Hospital "St. Mary" in Iasi and 121 infants of mothers with syphilis in The Obstetrics and Gynecology Clinical Hospital "Cuza Voda" in Iasi, to detect the occurrence of early and late signs of disease and correlation with clinical data for clearly serologic diagnosis of congenital syphilis.

**Study I: retro-prospective study statistically for a period of 9 years (2003-2011) of pregnant women and newborns diagnosed with syphilis**

**MATERIALS AND METHODS**

Retro-prospective study was conducted by adding the statistical and correlation and forensic statistics obtained from the Service Communicable Disease Surveillance, Control in Science and DSP observation sheets of pregnant women and newborns diagnosed with syphilis during 2003-2011 in maternity hospitals in Iasi.

In the group of patients studied were included 922 patients: 461 puerperium diagnosed with syphilis and babies born to these mothers.

Diagnosing pregnant and confined women and the newborns was performed by clinical methods (inspection and palpation) and laboratory tests, respectively serology: RPR, VDRL, TPHA, ELISA IgM, ELISA IgG, FTA-Abs (IFI IgG, IFI IgM).
The data obtained were processed statistically using ANOVA and specific tests for correlation then plotted using Microsoft Office Excel 2007 software program.

RESULTS AND DISCUSSION

In Romania, the tendency is to decrease the incidence of syphilis from 2003 to today (15 new cases in 2009 inhabitants 0%000 till, 11 %000 in 2011), with reference to one of the highest rates of reduction in the number of syphilis cases (over 30% since 2006) in comparison with the EU, where the incidence of new cases of syphilis was 4.55 %o oo in 2009 and grew steady.

The data provided by DSP Iasi, about one quarter of women in Romania who were diagnosed with syphilis are pregnant.

The number of confirmed cases of congenital syphilis recorded in maternity hospitals in the county of Iasi, decreased dramatically during the period in which this phenomenon has been studied, this is consistent with fewer new cases of syphilis reported in the whole country.

Significant difference between the two populations is that since 2008 has not been confirmed or confirmed cases of congenital syphilis, because intensive work, the team of epidemiologists, physicians, dermatologists, obstetricians and GP’s.

None of the women with infants infected with congenital syphilis were not treated properly during pregnancy for this condition. It is noted that 41% cases from localities close to cities of Targu Frumos and Pascani, representing two major epidemiological outbreaks in Iasi region (Figure 1).

Of the 27 cases of children with congenital syphilis puerperium confirmed 15 cases were not have medical dispensary during pregnancy (Figure 2).

Four of the 12 cases pursued by family doctors throughout pregnancy have never performed laboratory tests.

This is unacceptable in a country where access to tests for syphilis serology is often facilitated by the free movement area of mobile laboratory teams (Figure 3).
Most newborns of mothers with syphilis (78% cases) were confirmed with congenital syphilis because of increased antibody titer greater than or equal to 4 times the maternal antibody titer by quantitative VDRL testing or positivity tests: ELISA-IgM or FTA-IgM Abs (figure 4).

Of the 27 pregnant women diagnosed with syphilis who had infants with confirmed congenital syphilis, 12 patients (44% cases) said they had at least one miscarriage and stillbirth birth history (Figure 5).

Percentage distribution according to application or not a treatment for syphilis, the number of pregnant women who had infants with confirmed congenital syphilis is represented in Figure 6.

Whereas the fact that more and more parents misunderstand to exercise parenting, women's refusing some medical advice, fair treatment while refusing to tel o ask sexual partners to be investigated and treated, it is necessary to reestablish police service for health (dissolved after 1989) to activate by the Departments of Public Health and can carry out medical act on the parents for the child's interest.

Figure 1. Percentage distribution of pregnant women who had infants with confirmed congenital syphilis (between 2003-2011) according to the place of residence

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Figure 2. Percentage distribution of pregnant women who had medical dispensary - taken / not taken into medical records of family doctors.

Figure 3. Percentage distribution of serologic evaluation for syphilis during pregnancy.
Figure 4. Percentage distribution of cases of congenital syphilis confirmed by the presence / absence of clinical signs

Figure 5. Percentage distribution of pregnant women who had infants with confirmed congenital syphilis, according to the presence / absence of pathological obstetrical history
Study II: Prospective study on the epidemiology, clinical and laboratory investigations for a period of six years (2005-2010) of pregnant and confined women diagnosed with syphilis and their product design

MATERIALS AND METHODS
Total study consisted of 209 pregnant, aborted pregnancies and puerperium diagnosed with syphilis.

Pregnancies were taken between a period of 6 years from 2005 to 2010 in Dermatology Clinic and in Cuza Voda Hospital Obstetrics and Gynecological Clinic. 2011 year was dedicated for statistics interpretation (epidemiology, clinics, paraclinics and treatment).

Current cases have been studied based on clinical examination and some imaging Investigations carried out by PhD student.

Pregnant women and newborns for study were provided free of charge: initial clinical examination and paraclinical confirmation of diagnosis, initiation of therapy and its proper, complete treatment performance monitoring and controls and periodical evaluations.
Composition of study group:
From 209 pregnant women 159 gave birth at term or prematurely, both live and dead fetuses, 50 pregnant women aborted spontaneously or at request.

185 pregnant, puerperium, and abortion have made the correct treatment for syphilis, and 24 aborted and puerperium have not previously received treatment in the maternity hospital.

During pregnancy, these patients were clinically explored (including psychological assessment) and paraclinical by: serological monitoring, ultrasound examination, cytogenetic, anatomopathological examination of the placenta or the product of an abortion performed in the Laboratory of Pathology of the Hospital “Cuza Voda” Obstetrics and Gynecological clinic in Iasi.

The study paid particular attention to patient opinion of disease, determining an optimal communication. agreeing on possible solutions, mobilizing patients to their disease care.

RESULTS AND DISCUSSION
Syphilis in pregnant women remains a significant public health problem in society. Treated unfairly, maternal disease often leaves significant mark in fetus/newborn. Poor prenatal care is a major risk factor in the development of congenital syphilis. In this study we tried investigating and defining characteristics of pregnant women at high risk of having a baby with congenital syphilis. We also witnessed a series of patients who did not receive adequate prenatal monitoring and who presented no data about the development and monitoring of pregnancy and abortion cases in the second trimester.

The average age of the patients from the total study group were 25.64 years, with a range from 14 years to 44 years, with a high proportion of cases aged between 21-25 years (Figure 7).

Observe that despite in general the fact that the incidence of syphilis is declining, cases are seen in rural areas mostly (Figure 8), with low education level, unemployed as indicated by other studies in the country and around the world. Frequency of cases from rural areas is 57.89% and 42.11% in urban areas (Figure 9).
Figure 7. Distribution by age of pregnant women

Figure 8. Structure of the lot according to level of schooling
Figure 9. Distribution by area of origin of patients

There is no primary syphilis cases, and the percentage of women with florid secondary syphilis is 11.96%. If 88.04% of the group reached the stage of latent syphilis (recently, late or no indication) without being detected by family doctors without patients or their sexual partners to notify the presence of clinical signs of primary and secondary stages accordance to population education in this regard.

76% women have carried to term or born prematurely, and in 24% cases pregnancy was terminated spontaneously or on request (Figure 10). Of the 16 cases of spontaneous abortions, 7 patients were already diagnosed with syphilis and were or had entered treatment for syphilis according to the WHO scheme. It should be noted the fact that 2 of the 7 aborted fetuses treated had miscarriages in a dose of Moldamin day or next day. Note that the abortion situation in our group shows that most of pregnancy (68%) have stopped evolving by woman's decision, This decision is not justified by data from medical literature or medical tests, explorations, indicating the urgent need of medical abortion.

From development until birth pregnancies, 80% were term infants and 20% were premature births (Figure 11).
Figure 10. Evolution of pregnancy for patients with syphilis

Figure 11. Distribution of cases by duration of gestation

It should be noted that pregnant women with syphilis showed one or more associated diseases simultaneously. The group study found that there are 24 patients who did not benefit from monitoring.
pregnancy and were the first consultation, they represented 11.48% of the total group of 209 patients. Changes in general clinical examination, which required special attention and further investigation: vegetation warts (genital warts), genital herpes simplex, vaginitis, women with skin manifestations. Changes in laboratory tests that required detailed investigation: anemia, serology discordant serological false positive diagnosis. 45.7% of pregnant women said they had a history of STDs, excluding HIV infection. The study used treponemal tests for confirmation of 180 cases of syphilis diagnosed by performing TPHA (86% of cases) and 29 cases by ELISA (14% of cases).

we proposed and presented arguments for the introduction of TPHA test in routine practice of maternity in Romania:
1) It is a marker that remains positive, usually longer than RPR, after fair treatment performed.
2) 11 cases of pregnant women tested and excluded from the study group showed false positive RPR and interpreted this result as possible in the context of pregnancy.
3) It is known that can be positive RPR and T. pallidum infection outside: elderly (10% of people over 70 years), pregnant, leptospirosis and other infectious diseases,
4) false negative RPR may be due to old or unfit kits (manipulated properly obtained by purchasing at a low price, poor quality)
5) RPR is pozitiveaza later than TPHA (≥ 2 weeks)
6) to 5% of patients with untreated late latent syphilis is negative, while still positive TPHA.

Discrepancy nontreponemal test results between mother and newborn, false positivity or negativity of their tests lead us to recommend completion nontreponemal with treponemal tests.

Even replacing nontreponemal tests with treponemal tests for screening pregnant women is preferable, because detection is possible for both TPHA positive cases of syphilis which are relatively new and the old or previously treated cases. It is better to ascertain the presence
of a positive TPHA serological scar, with subsequent verification of negativity nontreponemal tests and / or absence of IgM by ELISA or FTA-Abs after treatment followed correctly, than to ignore a case of syphilis (new) with nontreponemal tests false negative or old case of syphilis with spontaneous negative result.

In 7 cases, infants were seropositive for syphilis tests nontreponemal, while the same tests were negative mothers.

This could be explained by possible negative spontaneously without treatment, tests nontreponemal in late latent syphilis, while the child may be positive due to new infections of the fetus. Some mothers had a false negativity of RPR perinatal and newborn's HIV test was correct. Another explanation would be false positivity nontreponemal neonatal tests.

Only 25.83% pregnant of serological tests were performed with sexual partners: 16 partners were consistently negative in all serological tests, while women remained positivity, even if antibody titer decreased. The remaining 38 sexual partners showed consistent positivity of serological tests.

Average gestational age at the time of application of treatment was 17.7 ± 3.9 weeks.

The first step in the diagnosis of syphilis is (anamnesis) a detailed history of symptoms and sexual activity, correlated with physical exam. Diagnosis of syphilis is confirmed by serological tests.

Some doctors have advised pregnant patients diagnosed with syphilis in the first trimester of pregnancy to abortion that could compromise the current product design. But it is known that negative serology may take many years, and in some cases may have a lifetime with a scar positiv.

In addition, *T. pallidum* crosses the placenta after gestational age of 16-18 weeks. It is therefore absurd indication of abortion in pregnancies with syphilis detected in the first quarter. Simple treatments under schemes in place ensure the fetus influenced by syphilis is treated.
Ultrasound

Ultrasound was employed as a monitoring tool for diagnosis and for monitoring the 145 pregnancies to birth, who received treatment.

The results showed that ultrasound couldn’t find placentomegaly presence at any of the monitored cases (Figure 12), there were two reported cases of hepato-splenomegaly and two cases, one with ascites & polyhydramnios, the other with Hydrops fetalis. Eco-doppler examinations of fetuses during pregnancy showed no significant changes.

![Ultrasound Image](image)

Figure 12. Measurement of placental thickness

Pathological changes of the placenta

In this study we analyzed histopathologically 23 placentas from mothers with positive serology for syphilis and 17 products of abortion (and placental trophoblast debris).

Of the 23 patients whose placentas were subjected to anatomo-pathological examination, 19 have received fair treatment for syphilis before birth, and 4 pregnant women were treated. 17 placentas from
mothers with positive serology for syphilis and following treatment, showed no macroscopic or microscopic morphological abnormality.

Of the four untreated pregnant, 3 were born at term (one dead fetus) and the 4th was aborted at 22 weeks pregnant. In the latter case, the placenta had dimensions: 9 cm diameter and 2 inches thick and villitis lesions of chronic plasma cell infiltrated intra villous, fibroblast proliferation and hypertrophy villous.

One of the placenta, derived from pregnant and diagnosed with untreated syphilis had increased macroscopic volume and weight, without major objective microscopic changes.

The 5 placentas from women with syphilis treated 2 and 3 of the untreated lesions presented as: chorioangioma-like (vascular congestion villous massive hypertrophy with immature Villi) (Figure 13), edema and vascular lesions (Figure 14), hematoma deciduous basal, acute chronic villitis (Figure 15). Vascular remodeling changes occurring in stillbirths. Old areas of infarction were identified on histopathologic preparations from the placenta. No characteristic features were found.

It should be noted that the parents of two of the dead babies refused autopsy. In the third fetus, which was autopsy, no specific syphilitic changes were found. Histopathology of the product of curettage in 17 cases of pregnant women diagnosed with syphilis and who experienced miscarriage or to request a pregnancy between 6-9 weeks of age did not mention changes that could prove the disease or its causative agent. Eritroblastosis was constant and significantly different. Fetal membranes were found thickened due to edema and vascular damage. The results, combined with our observations on placental eritroblastosis found almost entirely due to the syphilitic stillbirths suggests that anemia is an important factor in fetal death with syphilis congenital. Funicular type necrotizing lesions require diagnostic tissue necrosis with severe acute perivascular inflammation in the umbilical cord. Lack of vascularization of chorio is probably downstream effects caused by a clinically significant vasculopathy and have been described in congenital syphilis. It was not possible to evaluate anatomical pathological proliferative vasculopathy syphilis in pregnancy when the placenta comes from stillborn, because it is difficult to differentiate these.
Figure 13. Histopathological chorangioma

Figure 14. Trunk vilozitar, swelling and vascular congestion

Figure 15. Plasma cells infiltrating chorionic villi, Hofbauer cell hyperplasia - syphilitic placenta without treatment
Discussion of psychological study

More than 50% of doctors believe that pregnant women infected with syphilis should continue the task with the necessary treatment due to the possibility of healing and not submitting congenital syphilis by 16 to 18 weeks of pregnancy. Attitude of pregnant women was significantly influenced by the news (infection with T. pallidum), meaning that made their appearance symptoms of stress, tension, concern for children, concern for concealing the diagnosis (48% have not talked to family about the situation, while 39% husband hide this event). More difficult seems to be working with the medical staff showing that would treat these women with reluctance, superiority and seem to make them feel guilty (42% do not feel comfortable in relationships with health professionals, while 28% are ashamed, embarrassed by professionals, just because they are so diagnosed. The main feelings are facing the shame and guilt, and in addition, self-esteem threat. Their anxiety will increase tensions on the grounds of "always on guard" (No one have to know her husband, family, relatives). Women show confidence in medical and radiotherapy without significant worry about the future status of the newborn.

Treatment of pregnant women with syphilis

Most pregnant women in the study and received treatment during pregnancy were diagnosed with syphilis on the first trimester of pregnancy (57% cases) and only 3% of patients were detected in the third trimester of pregnancy.

Pregnant women with syphilis treatment consisted of administration of crystalline penicillin G in small quantities on pre-treatment itself, IM in 4 doses at 6 hourly intervals, as follows: first dose: 25,000 IU, second dose: 25,000 IU, the third dose: 50,000 IU, a fourth dose: 100,000 IU.

The next day, as the Jarisch-Herxheimer reaction has forced postponement of treatment were followed by administration of Moldamin, by 2.4 million IU / dose, IM deeply at 5 day intervals, each with 3 doses in recent syphilis and 4 respectively doses for late syphilis or received Retarpen, 2,400,000 IU / dose, im deeply at 7 days interval, 2 doses - recently syphilis 3 doses - late syphilis.
In the present study was performed on 24 pregnant cardiotocography and selective during the first 12 hours after intramuscular injection of extremely small dose crystalline penicillin G (25,000 IU or 50,000 IU) before the therapeutic dose of Moldamin / Retarpen. The intention of this study was the evaluation of fetal distress and uterine contractions during injection and for event Jarisch-Herxheimer reaction.

Cardiotocography was made for monitoring purposes during the course of pregnancy and after administration of Moldamin / Retarpen large quantities, according to current treatment for syphilis, serum concentration should reach and maintain a high level to be effective for curing syphilis.

It should be noted that pregnant women at high risk for preterm delivery have received treatment from Moldamin/Retarpen up to 7 days, treatment with progestogen and antispasmodic prophylaxis to prevent installation of uterine contractions.

Cardiotocography not recorded due to significant changes following treatment of pregnant women in third trimester of pregnancy, which indicates that treatment for syphilis is safe for mother and fetus, but with always the possibility of installing a Jarisch-Herxheimer reactions.

A pregnant women, begin treatment at the 33rd week gestational age, treated with 2.4 million IU GP Moldamin, 5 doses at 7 days interval.

If threatened abortion / premature birth, pregnant women was receiving progestogen (Duphaston 2 tablets / day in the first trimester of pregnancy or progesterone , Utrogestan 100 mg x 2-3 / day in the next two trimesters of pregnancy, in varying doses, periods adjusted each) and tocolysis (No-Spa, Scobutil, scopantil etc.).

Treatment of sexual partners was shown along with that of pregnant women with syphilis.

Tracking efficacy quantitative syphilis serology tests is through periodic inspections (at 3 months, 6 months, then annually).
Treatment of the new born with syphilis

Neonates of mothers with syphilis were treated according to the schemes in force by some doctors immediately after birth without asking the child serological test results from blood obtained from fontanelle. Other doctors have expected "confirmation" RPR and TPHA positivity in children, whatever was compared to the mother's RPR titer, which is equivalent to a confirmation of the diagnosis of syphilis. Other physicians preferred serological confirmation of syphilis diagnosis in children to treat: — test FTA-Abs -19S IgM positive or EIA-IgM positive —netreponemici antibody titre (RPR) of the newborn more than four times the mother's antibody status netreponemici.

Treatment of newborns was crystalline penicillin G for 14 days at a dose of 50,000 IU / kg every 12 hours within 7 days of life (because renal function does not allow increasing the dose) and 8-hourly intervals in Following days of life. Prompt treatment of syphilis is necessary to cure infection, prevent complications and transmission to others. Antibiotics are effective treatment at any stage. Exposed spouses must be examined, tested and treated.

Penicillin remains the first line treatment of syphilis. Antibiotics can cure syphilis and prevent complications. Complications may arise in congenital syphilis in the late trimester and may be irreversible, but with the right treatment the disease course is stopped. Parenterally administered penicillin is the treatment of choice for syphilis in all stages. Pregnant women for syphilis infection should be treated properly early in pregnancy. Patients with penicillin allergy reports, including pregnant women with syphilis in any stage, should be desensitized and treated with penicillin.

At 1 year after treatment performed correctly, only a minority of pregnant and confined women studied aborted 12.91% (27 cases) had negative VDRL or RPR, but in all other cases handled 87.09% (182 cases) to noted a decrease in RPR titer and quantitative VDRL.
Screening pregnant women for prophylaxis

Investigations are recommended for pregnant women screening for syphilis, due to fetal infection. Screening is done:

• the pregnant woman's first prenatal visit
• the early third trimester of pregnancy and again at birth for women at high risk of being infectate.

As other studies have shown, antenatal screening results should be reviewed by specialized teams of physicians, multidisciplinary teams have experience in the management of syphilis. This would ensure timely diagnosis with a thorough assessment of mother and fetus, a strategy of rapid and effective treatment, and follow the evolution of both the mother and child.

Study III: prospective study over a period of six years (2005-2010) of children born to mothers diagnosed with syphilis

MATERIALS AND METHODS

Prospective study of children from mothers with syphilis took place between 2005-2010, 2011 year was dedicated for statistics interpretation. In the study group were included 121 newborns suspected of congenital syphilis, coming from mothers with syphilis admitted to the maternity service Neonatology "Cuza Voda". Among them was confirmed serological diagnosis of syphilis with only 8 infants. The County Emergency Clinical Hospital for Children "St. Maria "Iași were followed 55 children of different ages (0-14 years) from all the geographical area of Moldova, diagnosed with early or late congenital syphilis, between 2005-2010.

RESULTS AND DISCUSSION

Of the 121 infants of mothers with syphilis, only 8 cases were serologically confirmed congenital syphilis. Premature babies come from mothers diagnosed with syphilis were 14% (17 cases) of total.

The group sought to maternity 4.96% (6 cases) were premature with confirmed congenital syphilis, representing 3.77% of babies born to mothers with syphilis. The proportion of premature infants between
confirmed congenital syphilis was 75% percent (6 of 8 cases). All 8 children diagnosed with confirmed congenital syphilis were from mothers untreated or incorrectly treated for syphilis. It is noted that prematurity is common in children with confirmed congenital syphilis come from mothers with untreated syphilis. Among newborns of "Cuza Voda" hospital with confirmed congenital syphilis, 75% cases (6 of 8 children) came from rural areas of poor coverage localities in terms of family care, which were referred by family doctors, but the course of gestation was not followed properly, patients were not tested for syphilis or did not receive proper advice and treatment. These facts emerge from the data presented in this thesis I study, which are referred, in detail, the specific features of the case.

APGAR test was used for assessing the health of the child a few minutes after birth. It can have values between 1 and 10, where 10 is the best evaluation. This note is given a relatively small number of children and a baby is perfectly healthy. Notes from 7-10 children are healthy and not need medical attention. Children who have grade below 7 at birth need special care and may even have trouble breathing. Among infants with confirmed congenital syphilis, 62.5% had Apgar score <7 (Figure 16).

![Figure 16. Distribution according to Apgar score of newborns with confirmed diagnosis of congenital syphilis in Cuza Voda Maternity](image-url)
In "St. Maria " Children's Hospital from Iasi were hospitalized, and treated properly serological diagnosis 55 children with congenital syphilis cases, of which only 19 (35% of cases) were symptomatic.

Signs found in these cases, is characterized by frequency: hepatomegaly (6 cases, representing 9.09%) and anemia (4 cases, representing 7.27%), and the rarity of cases: craniotabes nose associated with (1 case), premature nasal septum necrosis, anemia and neonatal respiratory distress (1 case), osteochondritis, congenital scapular-humeral arthritis and elbow Dr TSG talus valgus foot (1 case), pale skin with increased abdominal venous drawing associated with hepatosplenomegaly (1 case). Non-treponemal tests used to diagnose syphilis infection in newborns showed that 25 children had negative RPR 96 RPR positive. Infants undergoing radiological examinations to assess whether or skeletal changes reported in the literature. Hepatomegaly was present in 13.11% of children with congenital syphilis (Figure 17).

Figure 17. Thoraco-abdominal radiography newborn with confirmed syphilis, hepatosplenomegaly
Infants evaluate and follow up
Congenital syphilis is suspected in all infants symptomatic or not, born to syphilis positive mothers, but the diagnosis of congenital syphilis require highlighting treponemelor in secretions or tissues. Any child who may have congenital syphilis should be treated with crystalline penicillin G, according to the WHO scheme.

Plan to track children with congenital syphilis
All children serological active(or the serological active mothers at birth) should be followed clinically and serologically (nontreponemal tests) for 3 months to test or until negativarea titer decreased 4 times. If the child was not infected (ie positive tests were due to passive transfer of maternal IgG) antibody titers netreponemici should decrease by age 3 months and tests must be negative by the age of 6 months.

The same result will be achieved and whether the child was infected, but properly treated immediately after birth. Serological response after treatment in children treated after the neonatal period may be slower. If titers are stable or increase after the age of 6-12 months children should be evaluated, including CSF and treated with a course of 14 days of penicillin G parenterally.

Treponema passively transferred maternal antibodies may be present in a child until the age of 15 months. A reactive treponemal test after age 18 months is still a diagnostic sign for congenital syphilis.

III. DISCUSSION
There is an increased incidence in sexually active young people especially in rural areas because it has a proper sex education due to excessive sexual permissiveness, extraordinary ease of contracting sexual relations and lack of health education.

It is noted that 73% of patients have a poor economic level, get no education and therefore requires the existence of socio-economic measures for raising the cultural and health education, sanitation and daily life, combating risk sexual practices.

The number of women who give birth each year in Maternity "Cuza Voda" has not changed scored more than 10 years, but this study
shows that, in Iasi county area of pregnancy and congenital syphilis are strictly related to socially disadvantaged.

Maternal risk profile it has increased the young woman who has not received adequate prenatal monitoring and no knowledge about personal health and hygiene rules.

A great fault of these cases the primary health system, that the family doctor because most patients who had positive serology were young without sex education elementary and unattended with a load of gestation advanced. Many of the characteristics of the disease have been described for over 100 years.

Affordable costs of tests used to detect syphilis were introduced in antenatal screening programs in order to control disease congenital syphilis.

Moreover, one can say that these programs were responsible for the decrease to near elimination of congenital syphilis in many countries and it is believed that this disease in the past, even if it continues to persist in poor third world countries.

Congenital syphilis is mainly a consequence of lack of antenatal surveillance and control of sexually transmitted infections and can be easily prevented if infected mothers are identified and treated properly during pregnancy.

The devaluation of marriage and the notion of family, extra-marital relations and the existence of multiple partners are factors favoring the disease. Investigating people on marital status is observed a high percentage of infection to the unmarried and concubinage. There is an increased incidence in women who did not work (unemployed, housewives, etc..).

A percentage of 13.4% of women have sexual partners workers who stay for a long time away from family (long-haul drivers, oilmen marine and trade representatives in remote locations or even abroad).

All pregnant women who gave birth to a child with confirmed congenital syphilis has not belonged to other ethnic groups than Romanian.
Pregnant women from other ethnic groups (Gipsy, Hungarian, ..etc.) were subjected to appropriate treatment during pregnancy giving birth to children without congenital syphilis.

If syphilis, whatever the stage early pregnancy), treatment is correct and timely it will be effective.

In the last four years (2008-2011) were not diagnosed cases of congenital syphilis in Iasi.

Sex partners of syphilis patients called to be tested serologically responded small percentage (25.83%). From the 54 partners of pregnant women with positive serology who have chosen to present the serological results demonstrated: 29.63% 70.37% were RPR negative and positive RPR.

VDRL and RPR tests can have false positive results in various conditions and, therefore, must be confirmed by treponemal tests: TPHA, FTA-ABS, MHA-TP. They remain positive throughout life and therefore cannot be used to monitor disease evolution.

FTA-ABS test was introduced for the diagnosis of congenital syphilis. This test is based on the principle that IgM does not cross the placenta and therefore their presence in blood of infants is a response to an active syphilis infection and not a transfer as a positive for IgG crossing the placenta.

IV. CONCLUSIONS

1. Syphilis disease with polymorphic clinical picture, with unpredictable evolution and dismal prognosis in cases undiagnosed and untreated in time, had a considerable rate of 0.4% among pregnant women admitted to maternity "Cuza Voda" in the Dermatological Clinic of Iasi between the periods 2005-2010.

2. The data provided by the Department of Public Health Science, shows about one quarter of women in Romania who were diagnosed with syphilis are pregnant.

3. The incidence of congenital syphilis in the county fell sharply to 59.2%000 Iasi births in 2006 to 38.6 %000 births in 2007, being then zero in recent years (2008-2011). This is due to intensive work, the team
of epidemiologists, physicians, dermatologists, obstetricians and family doctors (Figura 18).

Figure 18. Comparison of cases suspected / confirmed congenital syphilis between 2003-2011, the county of Iasi, recorded by the Department of Public Health

4. Much of the blame for the increasing number of cases of congenital syphilis have had family doctors who have followed women with positive serology during pregnancy and have not found a way to convince mothers to be treated properly. All children were diagnosed with congenital syphilis were from mothers who were not treated for syphilis during pregnancy.

5. For a more accurate epidemiological investigations and for the proper treatment to all sexual partners diagnosed while pregnant should assist doctors a body to Department of Public Health Science, to carry out what the doctor prescribed, the interest of the patient for a healthy life and society.

6. Sex education has an important role in preventing syphilis.
7. All pregnant women with syphilis should be referred by family doctors, should have a uniform distribution in each area of the county of Iasi, no hiatus in meeting the needs of patients in a geographical area or administrative.

8. In Iasi, pregnant women with syphilis came more frequently in rural areas, perhaps by combining the effects of epidemiology, the incidence is influenced by many factors, most important are: the degree of culture, hygiene, the economic basis of individual, changing sexual behavior, immune status of the contact, the amount of inoculum, extending behavioral manifestations of social pathology.

9. Breast with the risk profile it has grown young woman, who did not receive adequate prenatal monitoring without basic sex education, which has no personal knowledge about health and hygiene rules.

10. Pregnant women with syphilis in this study came mainly from the category of population with secondary education (46.88%) and only 2.87% have graduated college.

11. Syphilis most commonly affected age group 21-25 years (40.19% of 209 cases) in women studied.

12. Analyzing occupation pregnant women with syphilis there is an increased incidence in those who did not work (unemployed, housewives, etc.).

13. Following our research shows that attitude of pregnant women was significantly influenced by the news (infection with Treponema pallidum), in the sense that there appeared symptoms of stress, tension, concern for children, concern for family and hiding diagnosis society.

14. Woman's attitude is changing, since the diagnosis of syphilis stay. The main feelings are facing the shame and guilt and diminishing self-esteem. Anxiety increases as a result of state pressure.

15. The clinical presentation varies from one flare to another, but treatment must be properly set up, according to WHO scheme without too much variability from one patient to another.

16. Clinical forms of syphilis in pregnant women are often seen today purely serological or minimum mucocutaneous lesions, often go unnoticed.
17. With enough certainty IgG and IgM determination can appreciate the type of recent or late infection, but clinical form of the disease a clinician sets.

18. We believe that should be mandatory testing of pregnant women in maternity while the RPR and TPHA to avoid diagnostic mistakes. In uncertain cases, a test or FTA-Abs EIA for determination of IgM antibodies to *Treponema pallidum* can be extremely useful. TPHA technique should be routinely included in the arsenal of techniques for diagnosis of syphilis in the maternity ward, because the accuracy of results is evident, whether the standard conditions.

19. As early treatment of pregnant women detected positive syphilitic serology may prevent onset congenital syphilis.

20. In the study could not identify only 6 cases (9.84% of all children with congenital syphilis) have been found to be touching bone specific congenital syphilis. Radiology has provided one of the best diagnostic methods for syphilis fetal and newborn.

21. Hepatomegaly was present in 8 cases (12.7% of children with congenital syphilis), very small percentage from the literature (51%).

22. Given that more and more parents misunderstand to exercise parenting, fair treatment while refusing sexual partners, it is imperative to reestablish service for health (dissolved after 1989) to activate by the Departments County Public Health and can carry out medical act on the parents, the child's interest.

23. All pregnant women will make a serological screening test for syphilis at least twice during pregnancy: first trimester, as early as possible after the 28th week of pregnancy.

24. Tracking patients over time requires regular checks to establish the state of cure of syphilis and for monitoring pregnancy / fetus and the child after birth.
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