

## The contribution of laboratory investigations in diagnosis of congenital infections

SIMONA NEAMȚU<sup>1)</sup>, G. GĂMAN<sup>1)</sup>, LILIANA STANCA<sup>2)</sup>, IULIANA BUZATU<sup>3)</sup>,  
 LORENA DIJMĂRESCU<sup>4)</sup>, MAGDALENA MANOLEA<sup>4)</sup>

<sup>1)</sup>Department of Hematology

<sup>2)</sup>Department of Legal Medicine

University of Medicine and Pharmacy of Craiova

<sup>3)</sup>Resident physician, Clinical Laboratory,  
 "Filantropia" Municipal Hospital, Craiova

<sup>4)</sup>Department of Gynecology,  
 University of Medicine and Pharmacy of Craiova

### Abstract

Congenital diseases are an important indicator of the degree of development of primary health care, because primary prevention is paramount in diagnosing and diminishing the number of those types of cases. Syphilis is a sexually transmitted chronic infectious disease and with an evolution, often unpredictable. Primary prevention aims to prevent infection of the fetus, while secondary prevention aims for a reduction in the severity of sequels already installed.

**Keywords:** congenital diseases, prevention.

### Introduction

Infectious diseases in pregnancy are capable of damaging the product of conception, leading to premature termination of pregnancy, the death of the fetus *in utero*, or neonatal.

Multiple and varied changes that occur in congenital disorders require a thorough paraclinical study, with a major role in diagnosis.

Because of the existence of similarities between some antigens of infectious agents and host tissue components, can occur complications through auto-immune mechanisms in the context of the immune response to aggression.

### Materials and Methods

Laboratory research has been conducted on a sample of 114 patients hospitalized in "Filantropia" Municipal Hospital and in the Hospital for Infectious Diseases, Craiova, of which five were diagnosed with congenital syphilis.

We collected these biological products for laboratory investigations: blood, (bronchial, oropharyngeal, eye drops, ear, vaginal, urethral) secretions, urine, cerebrospinal fluid, feces, vesicular scraper, pus.

Laboratory investigations consisted immunoassay, virological, hematological, biochemical, bacteriological and imaging.

Laboratory tests included:

- Nonspecific tests highlighting the changes caused by the etiologic agent on the body: blood tests, biochemical, bacteriological and imaging;

- Specific tests that we pursued to identify the microorganism that caused the infectious disease: immunological tests and exams by molecular techniques.

### Results and Discussion

The results of laboratory investigations have had an essential role in the diagnosis of congenital diseases (Tables 1–3 and Figures 1–3).

**Table 1 – Laboratory investigations performed in a newborn diagnosed with severe multiorgan congenital syphilis, with unfavorable evolution**

Paraclinical investigations	Results
	Hemoglobin 6.11 g%
	WBC 13 400/mm <sup>3</sup>
	Platelets 90 000/mm <sup>3</sup>
	<i>Leukocyte formula:</i>
	Metamyelocytes 1%
<i>Complete blood count</i>	Nonsegmented granulocytes 3%
	Segmented granulocytes 38%
	Eosinophil granulocytes 1%
	Lymphocytes 45%
	Monocytes 12%
	Erythroblast oxyphils, polychromatophils, basophilia 51%
<i>VDRL</i>	positive
<i>Bleeding time</i>	12 min.
<i>Coagulation time</i>	20 min.
<i>Necropsy protocol</i>	The bloody fronto-parieto-occipital bosa and disseminated the fronto-parieto-temporo-occipital meningo-periosteal hematoma and cerebral edema stasis,

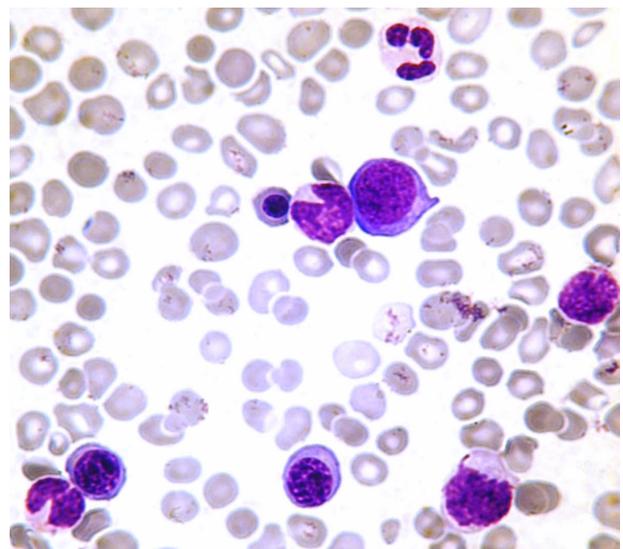
Paraclinical investigations	Results
	stasis and meningo-cerebral edema, thymus hypotrophy, pulmonary hemorrhage, hepato-splenomegaly with ascites sero-citrine approximate 100 mL, kidney with fetal lobulate and stasis, stasis generalized visceral; micropetesia purpuric rash on the face, trunk, abdomen and limbs root.

**Table 2 – The laboratory results obtained in a newborn diagnosed with symptomatic congenital syphilis, with unfavorable evolution**

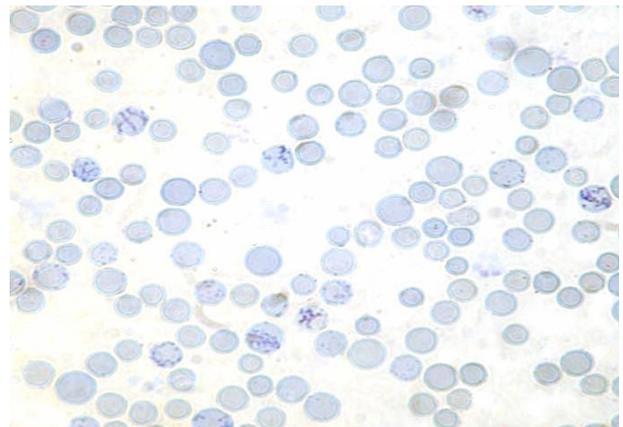
Paraclinical investigations	Results
Complete blood count	Hemoglobin 13.5 g%
	WBC 9500/mm <sup>3</sup>
	Platelets 160 000/mm <sup>3</sup>
	<i>Leukocyte formula:</i>
	Metamyelocytes 1%
	Nonsegmented granulocytes 4%
	Segmented granulocytes 37%
	Eosinophilic granulocytes 2%
	Lymphocytes 48%
	Monocytes 8%
Erythroblast oxyphils, polychromatophils 10%	
Erythroid anisocytosis with macrocytosis	
Skeletal radiography	We discovered two small areas of bone lysis in the center of the center humerus and femur diaphysis, periostitis suspect on the upper – left humeral epiphysis: possible early congenital syphilis.
Quantitative RPR Carbon	Positive - titer 1/32
TPHA	Positive - titer 1/80
Necropsy protocol	Skull: The bloody right parieto-temporal bosa, stasis and meningo-cerebral edema,
	Lungs: Condensed outbreaks hemorrhage subpleural micro-outbreaks, predominantly in the left lung, pleural microabcess on the left lung.
	Cord: atrial septal defect with a diameter of 0.8 cm; arterial channel present.
	Hepatosplenomegaly: F: 18×18×4 cm; S: 8×4×2.5 cm, gallbladder elongated, relaxed.
	Stomach: bleeding micro-outbreaks near the great curvature.
	Bilateral adrenal hemorrhage and fetal kidney lobulate stasis.
	Generalized visceral stasis, jaundice, intense generalized to the skin, mucous and serous membranes.
	Petechiae and vesicles released.
	Flictena bare – haluce left.

**Table 3 – Laboratory results obtained in a newborn diagnosed with congenital syphilis**

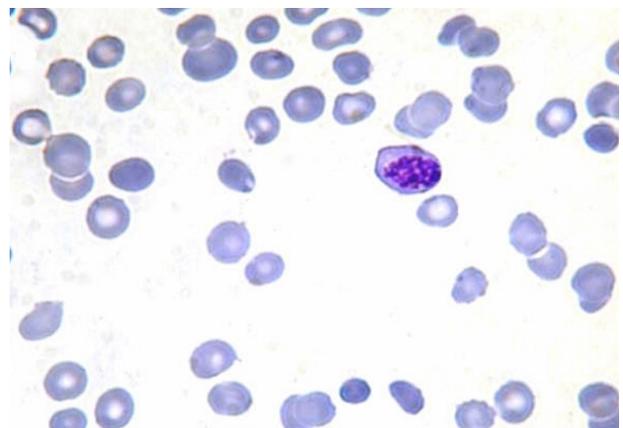
Paraclinical investigations	Results
Complete blood count	Hemoglobin 16.5 g%
	WBC 9800/mm <sup>3</sup>
	Platelets 504 000/mm <sup>3</sup>
Total bilirubin	1.76 mg%
Direct bilirubin	0.51 mg%
Quantitative VDRL	Dilutions: 1/1 1/2 1/4 1/8 1/16 1/32 ++ ++ + +/- - -



**Figure 1 – Blood smears collected from a newborn diagnosed with severe multiorgan congenital syphilis, with unfavorable evolution (MGG staining). We noticed the presence of erythroblast oxyphils, polychromatophils, basophilia and metamyelocytes on peripheral blood smears, we found thrombocytopenia poikilocytosis anisocytosis and red blood cells.**



**Figure 2 – Smear of blood collected from a patient diagnosed with symptomatic congenital syphilis (Brilliant Cresyl Blue staining). We found increased number of reticulocytes in peripheral blood smears.**



**Figure 3 – Stained blood smear M.G.G. collected from a child diagnosed with congenital syphilis. I noticed this erythroblast, poikilocytosis anisocytosis and red blood cells.**

It was demonstrated that aggression (including infection) that addresses to the maternal–fetal system are intercepted at the chorio-decidual interface level, which will express the release of proinflammatory cytokines, the process could lead or not to the onset of labor.

The most effective way to prevent congenital syphilis is to identify and treat syphilis in pregnant women, as early in pregnancy. Therefore, during pregnancy is important for pregnant women to be examined serologically for syphilis at least twice: as early in the first quarter and after the 28<sup>th</sup> week of pregnancy [1].

Recent research has allowed the development of criteria for defining congenital syphilis:

- Confirmed congenital syphilis: by showing *Treponema pallidum* in lesions, placenta, umbilical cord or other tissue taken from newborn babies;
- Presumptive congenital syphilis: any newborn whose mother had syphilis during pregnancy treated unfairly or untreated, any newborn with a reactive serologic test for syphilis, premature birth and intrauterine fetal death due to syphilis.

Recent studies emphasize the correlation between clinical signs and laboratory diagnosis of syphilis:

- Primary seronegative syphilis appears in a tough base erosion, net margins are well defined, usually single, painless (sancru hard) at the site of inoculation, after about three weeks after contamination, followed by regional lymphadenopathy is the non-inflammatory and serology negative; *Treponema pallidum* in lesions stand out or to lymph nodes or ultramicroscopical affected by direct immunofluorescence.

- Primary seropositive syphilis: the same clinical manifestations as in primary seronegative syphilis adding positive serology.

- In secondary syphilis, systemic damage occurs (polymorphic generalized rash on the trunk, palmar–plantar regions, the genital region, mucosa; uninflammatory polyadenopathy, ocular manifestations: uveitis, iritis, scleritis, retinitis, papilla, optic neuritis), alopecia “clearings”, meningitis, cranial nerve palsy, hepatosplenomegaly, glomerulonephritis, periostitis, positive serology.

In tertiary syphilis, the following forms were highlighted:

- Benign tertiary syphilis (bone disease, cutaneous and visceral, with the exception of the nervous system and heart);
- Neurosyphilis: meningovascular, parenchymatous, asymptomatic CRL abnormalities are described [2];
- Cardiovascular: aortic insufficiency, angina pectoris, aortic, aortic aneurysm, aortic stenosis hostile, positive serology.

In latent syphilis – it was confirmed the positivity of both non-*Treponema* and *Treponema* tests and the absence of clinical manifestations of syphilis; it represents a period of time in which the patients with *Treponema pallidum* did not presented manifestations of the disease.

It turned out that the transmission of syphilis from mother to fetus is from the 9<sup>th</sup> week of gestation [3].

Reduced immune response until four months of the scarcity of biochemical substances cause minimal alterations in the first trimester of life.

It was observed that syphilis transmission during delivery is exceptional.

From the study, we found that children born to mothers with untreated primary or secondary syphilis had congenital infection.

Clinical research shows that syphilis can cause fetal death, premature birth, congenital syphilis or neonatal death [4].

Following the analysis of clinical and laboratory data it was concluded that early congenital syphilis can present itself as serious, common form with mucocutaneous lesions in apparently healthy child or a form easily serological, which may develop into a late congenital syphilis.

Numerous studies have shown the diversity of clinical signs in early congenital syphilis.

The most common symptoms that we met in early congenital syphilis were:

- Mucocutaneous: coryza, sifilide erythematopapular rash, warts, pemphigus palmar–plantar;
- Osteo-articular: periostitis, osteochondritis;
- Visceral: hepato-splenomegaly, hepatitis, adenopathy, pneumonia, myocarditis, orchitis, nephropathy [5].

A study showed that late congenital syphilis occurs after the first two years of life and clinical manifestations include the following:

- Dental: damage to the upper central incisor and molars of six years;
- Eye: uveitis, interstitial keratitis;
- Sequelae of periostitis: bosc front tibia in the “scimitar”, affecting the clavicle;
- Sequels of osteochondritis: otic capsule damage to cochlear degeneration and deafness;
- Sequels of rhinitis: nose “to” lower jaw, ogival palate;
- Sequels of CNS damage: mental retardation, hydrocephalus, seizures, cranial nerve palsy, optic nerve atrophy [6].

In this paper, we showed that two of the clinical forms congenital syphilis are:

- The extremely serious form incompatible with life, leading to death, it occurs when pregnant women shows the primary or secondary syphilis is untreated and macerated fetus with vesicular skin lesions, increased abdominal volume and hepatosplenomegaly.

- The severe form of congenital syphilis in the appearance dressed early sepsis, which is manifested by: malaise, seizures, pallor, subicterus birth, mucocutaneous and visceral hemorrhages, anasarca, hepatosplenomegaly, with fatal outcome [7].

Besides the two clinical forms of congenital syphilis there is a common form of low or even absent symptoms, the disease manifested itself after the first week of life or later.

## ☐ Conclusions

To prevent congenital syphilis serologic screening for syphilis is recommended at least twice during

pregnancy, how soon after conception and after 28 weeks. Depending on the time and confirmed fetal damage during pregnancy, have taken the decision to discontinue treatment or therapy of pregnancy. The severity of consequences caused by infectious agents justifies the action of primary prevention measures, combined with the need to find and apply an algorithm for early diagnosis.

### References

- [1] BACALBASA GD, HUDITA, *Fundamental reactions of maternal-fetal functional system. Implications for reproductive pathology*, Obstetrics and Gynecology, 2003, LI:137–139.
- [2] BLIDARU I, CIANGA C, ZLEI M, STOICA L, STRAT A, CARASEVICI E, *Immunological aspects in preterm labor*, Obstetrics and Gynecology, 2002, LII:243–248.
- [3] BLIDARU I, CIANGA C, ZLEI M, , *Role of plasma from pregnant immunomodulator on the immune-mediated natural killer cells (NK)*, "Carol Davila" University Press, Bucharest, 2003, LI:63–68.
- [4] HAFED BM, BILIKOVA E, KOVACICOVA G, KOPRNOVA J, SVETLANSKY I, CHOVANCOVA D, HUTTOVA M, KRČMERY V, *Prognostic factor for 246 neonates with infections*, Clin Infect Dis, 2003, 36(9):1203–1205.
- [5] SEDGE S, SILOS I, *Immunology – ongoing*, University Medical Publishing House, Craiova, 2002, 224–240.
- [6] STAMATIEN F, *Modern methods for assessing fetal distress*, "Carol Davila" University Press, Bucharest, 2003.
- [7] VLADAREANU R, VEDUTA A, *Pregnant women at high-risk approach in GP practice*, InfoMedica, 2003, 10:42–47.

### Corresponding author

Simona Neamțu, Assistant, MD, PhD, Department of Hematology, University of Medicine and Pharmacy of Craiova, Clinical Laboratory, "Filantropia" Municipal Hospital, 3 Constantin Brâncuși Street, 200136 Craiova, Romania; Phone +40745–574 308, e-mail: simona\_0712@yahoo.com

Received: November 20<sup>th</sup>, 2010

Accepted: December 20<sup>th</sup>, 2010