SOUTHWESTERN NEWS

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UT SOUTHWESTERN RESEARCHERS DISCOVER BETTER TESTS TO DETECT CONGENITAL SYPHILIS IN NEWBORNS

DALLAS – June 6, 2002 – A UT Southwestern Medical Center at Dallas research team has developed two blood tests that quickly and reliably diagnose congenital syphilis in newborns.

"This is the first study to document the presence of the syphilis spirochete (bacteria) in the cerebrospinal fluid of infected infants. Thus we are the first to accurately assess diagnostic evaluations of infants for the possibility of central nervous system invasion," said Dr. Pablo Sanchez, professor of pediatrics and senior author of the study appearing in today's issue of *The New England Journal of Medicine*.

Sanchez said the two blood tests detect either neonatal antibodies to the syphilis bacterium or the DNA of the syphilis organism itself as predictors of central-nervous-system (CNS) infection. Results from the two tests correlated with the detection of the organism in the infants' cerebrospinal fluid, and, therefore, the tests could serve as predictors of CNS infection.

This work produced the first valid data to select an effective, cost-efficient neonatal treatment regimen for congenital syphilis.

A pregnant woman with syphilis has about a 60 percent to 80 percent chance of infecting her fetus. Infants born to mothers with syphilis are traditionally hospitalized for multiple daily injections of penicillin over a 10-day period because physical exams and conventional laboratory tests are unable to detect all cases. The most accurate lab test until now required a three-month incubation period.

The UT Southwestern study showed that two tests – immunoglobin M (IgM) immunoblotting and polymerase chain reaction (PCR) – detected all cases of central-nervous-system infection in the group of 148 infants studied. The babies were born to syphilis-infected mothers during the 1989-1999 study period.

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Earlier research at UT Southwestern had suggested that congenital syphilis might stimulate a detectable reaction by the newborn's immune system, despite its immature development, said Dr. Michael Norgard, chairman of microbiology and a co-author of the study.

"We believed we could evaluate this by searching for the presence in neonatal blood of the infant's IgM antibodies," Norgard said. The study confirmed the theory.

The researchers also successfully modified the PCR test – a technique commonly used by forensic scientists to reveal DNA or RNA molecular sequences – to detect the DNA of the syphilis organism in the blood.

"The diagnostic gap had been further aggravated by the belief and clinical experience indicating that up to 50 percent of infants with congenital syphilis are born without any telltale clinical signs or symptoms and otherwise appear to be healthy babies," Norgard said. "The detection of neonatal IgM antibodies seems to be the best single surrogate marker for substantiating infection of the infant."

The blotting test, similar to an AIDS diagnostic tool, is a molecular technique for detecting IgM antibodies in the serum of infected infants.

"I believe that this work, spanning more than a decade, will stand alone as the most thorough description of the diagnosis of a rare but potentially devastating infection in newborns," said Dr. George Wendel Jr., a professor of obstetrics and gynecology who worked on the study.

The study focused primarily on 76 of the 148 examined infants, most at 1 day of age but ranging up to 3 months old. Among the 76 infants, those whose mothers had not been treated with antibiotics while pregnant, 17 were found to have central nervous system invasion by *Treponema pallidum*, the bacterium that causes syphilis, Sanchez said. While traditional physical exams, spinal taps, arm- and leg-bone X-rays, and blood-cell counts identified up to 16 of the 17 babies with infected nervous systems, the IgM immunoblotting and PCR tests were required to detect all 17 cases, he reported.

Sanchez said the findings support newly revised syphilis treatment guidelines issued by the Centers for Disease Control and Prevention and the American Academy of Pediatrics.

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"Previously, using a fail-safe approach, the CDC had recommended a blanket 10-day regimen of two to three daily penicillin doses for every baby born to a mother with syphilis," he said. "But often all that is needed is one dose for infants with no invasion of the central nervous system. Our study shows us the tools that help to identify both the infants who need the 10-day treatment and those who can be treated effectively with one dose of long-acting penicillin."

Other researchers on the study included lead author Dr. Ian Michelow, a pediatric infectious diseases research fellow, and Fiker Zeray, a senior registered nurse in pediatrics.

The study was supported by the CDC and the National Institute of Allergy and Infectious Diseases.