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Reduction of the Risk of Vertically Transmitted HIV by Cesarean Section

ABSTRACT & COMMENTARY

Synopsis: *Elective cesarean section reduces the risk of transmission of HIV-1 from mother to child independently of the effects of treatment with zidovudine.*

Source: The International Perinatal HIV Group. The mode of delivery and the risk of vertical transmission of human immunodeficiency virus type 1: A meta-analysis of 15 prospective cohort studies. *N Engl J Med* 1999;340:977-987.

Data from 15 prospective cohort studies involving hiv-infected mothers were subjected to meta-analysis. A uniform definition of "elective" cesarean section was used (i.e., one that was performed before the onset of labor or rupture of the membranes). The data were adjusted for receipt of retroviral therapy, maternal stage of disease, and birth weight. The likelihood of vertical transmission of HIV-1 was reduced approximately 50% with elective cesarean section as compared to other modes of delivery (vaginal, nonelective cesarean section). The likelihood was reduced by approximately 87% with elective cesarean section and receipt of retroviral therapy during the prenatal, intrapartum, and neonatal periods as compared to other modes of delivery and the absence of therapy. Among mother-child pairs receiving appropriate antiretroviral therapy, the rates of vertical transmission were 2.0% among 196 mothers who underwent elective cesarean section and 7.3% among the 1255 mothers with other modes of delivery.

COMMENT BY WARREN ANDIMAN, MD, FAAP

It has been known for at least several decades that some viral pathogens pass most frequently from mother to infant, not in utero, but at the time of delivery. These microorganisms share particular characteristics: they are found in blood in very high titer or

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INSIDE

they are shed in large numbers in the female genital tract. Hence, as the baby passes through the birth canal, virus particles enter the infant's body by way of the mucous membranes of the mouth, nose, or conjunctiva or through small tears in the skin. In addition, blood may be "transfused" from mother to baby during labor contractions. Obstetricians and pediatricians have learned that vertical transmission of herpes simplex virus can be interrupted, in most cases, if women actively shedding virus deliver by cesarean section within four hours of rupture of the membranes. Mother-to-child transmission of hepatitis B can be controlled if babies born to surface antigen-positive mothers receive hepatitis B hyperimmune globulin at birth, followed by serial vaccinations with bioengineered recombinant hepatitis B surface antigen. HIV shares a number of biologic characteristics with both herpes simplex and hepatitis B. Thus, it is not surprising that cesarean section has been entertained as one among several methods that might be used to avert mother-to-child transmission of the virus.

The report by the International Perinatal HIV Group, a consortium of five European and 10 North American prospective cohort study groups, pooled individual patient data on 8533 mother-child pairs and showed that elective cesarean section significantly reduced the risk of vertical transmission of HIV, independent of the already proven benefits of treatment of mother and infant with zidovudine. The two major advantages of this study over previous attempts to show a salutary effect of cesarean section were the large sample size and the application of uniform definitions that clarified the differences between elective and nonelective cesarean section.

The findings of this study are likely to affect obstetrical practice in the United States, at least for the time being. By combining antiretroviral therapy of mother and child with elective cesarean section, the risk of vertical transmission of HIV can be reduced approximately nine- to tenfold, to 2%, a long sought-after goal. Nevertheless, the durability of the study's results may be limited. The study failed to take into account a number of critical co-variates, either because they were not collected uniformly by all participants or because the study ended before current pharmacologic interventions could be adequately evaluated. For example, data on viral load were not included in the analysis, and it is not inconceivable that viral load may greatly influence the risk of vertical transmission. Furthermore, most mother-child pairs included in the analysis by the International Perinatal HIV group received monotherapy or dual antiretroviral therapy. It will be critical to learn if receipt of highly active poly-antiretroviral therapy by childbearing women, a practice that has become commonplace only in the past two years, reduces vertical transmission more dramatically than previous regimens. Such a finding may eliminate or significantly abrogate the need for cesarean section.

In the meantime, women's health care providers must use the data now available to weigh the risks of surgical morbidity against the benefits of cesarean section. Unfortunately, the benefits of cesarean section may not apply to countries in the undeveloped world, the site of the great majority of incident cases of perinatal HIV infection. In such settings, gestational age cannot be assessed accurately; hence, an increased frequency of preterm births could be expected following elective cesarean section. Also, the hazards associated with surgical procedures of any kind may outweigh the benefits. Alternative solutions, both medical and surgical, to the high prevalence of pediatric AIDS in less-developed countries remain elusive. (*Dr. Andiman is Professor of Pediatrics and Director of the Pediatric HIV/AIDS Program at the Yale-New Haven Children's Hospital and the Yale University School of Medicine.*) ❖

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A Cure for the Common Cold?

ABSTRACT & COMMENTARY

Synopsis: *Studies of tremacamra, which competes with the cellular receptor for the virus, used prophylactically in humans with experimental rhinovirus infections showed efficacy in diminishing the incidence and severity of the common cold. While promising, the clinical usefulness of this strategy requires further study.*

Source: Turner RB, et al. Efficacy of tremacamra, a soluble intercellular adhesion molecule 1, for experimental rhinovirus infection. A randomized clinical trial. *JAMA* 1999; 281:1797-1804.

In randomized, double-blind, placebo-controlled trials conducted in humans, experimental rhinovirus type 39 inoculation was tested with preinoculation or postinoculation administration of tremacamra or placebo. Tremacamra was associated with decreased incidence of clinical colds (44% ± 11% vs 67% ± 9%), improved total symptom scores (9.6 ± 2.9 vs 17.6 ± 2.7), and decreased nasal mucus weight (14.5 ± 9.4 vs 32.9 ± 8.8 g) ($P < 0.001$ for all comparisons). Tremacamra was not associated with any adverse effects or evidence of absorption through the nasal mucosa and did not interfere with development of neutralizing antibody to rhinovirus.

COMMENT BY HAL B. JENSON, MD, FAAP

We continue to search for the cure for the most common human infection, the common cold. Strategies that have been attempted include antivirals, which show some promise when used prophylactically but not once symptoms develop, and symptomatic treatments such as antihistamines, decongestants, and anti-inflammatory agents, all of which have limited efficacy and on only some but not all of the typical cold symptoms.

Of the 101 types of rhinoviruses, which account for 70% of upper respiratory tract infections, 90 types use intercellular adhesion molecule 1 (ICAM-1) as the cellular receptor for cell entry. This is the basis for this particular strategy to attempt to prevent or treat rhinovirus infections by intranasal administration of the soluble extracellular portion of the ICAM-1 molecule to compete with virion binding.

This study included both preinoculation and postinoculation administration, but both were actually prophylactic since clinical symptoms had not yet appeared. Thus, this strategy is not curative, but rather preventive. Tremacamra has been studied with one rhinovirus type 39, which appears to be particularly susceptible to the effects of tremacamra. The effects on the other rhinoviruses remain to be proved. Soluble tremacamra is cleared rapidly from the nasal mucosa. In these studies, two formulations were used—one solution and the other a mannitol-based powder with carboxymethylcellulose to retard clearance of the drug from the nasal cavity. Unfortunately, the carboxymethylcellulose was associated with nasal irritation. It is enticing that a strategy such as this actually shows efficacy, but we remain a long way from being able to use this clinically. ❖

Preimplantation Genetic Diagnosis Ensured Normal Babies in Two Parents with Sickle Cell Trait

ABSTRACT & COMMENTARY

Synopsis: *Using in vitro fertilization and preimplantation genetic diagnosis, a couple, both of whom had sickle cell trait, delivered normal twins. This technique may offer parents at risk for having infants with severe genetic diseases a chance to have unaffected offspring.*

Source: Xu KP, et al. First unaffected pregnancy using preimplantation genetic diagnosis. *JAMA* 1999;281: 1701-1706.

Xu and colleagues at the cornell medical College in New York report on their work with a couple, both of whom were carriers for a sickle cell gene (Hb AS). Each pregnancy of this couple had a one in four chance of resulting in a child with sickle cell anemia (Hb SS). The mother had had two previous pregnancies interrupted after sickle cell anemia was diagnosed by DNA analysis. The couple was offered the option of undergoing in vitro fertilization (IVF) and prenatal genetic diagnosis (PEG) in order to ensure an unaffected baby. A first IVF was not successful. In a second attempt, IVF resulted in seven embryos that were subjected to PEG by taking a single cell from the embryos and analyzing the DNA using polymerase chain reaction and analysis for the presence of sickle cell and normal hemoglobin genes. Of the embryos tested, four were normal (Hb AA) and two had sickle cell trait (Hb AS). Three of the normal embryos were transferred to the uterus on day four after oocyte retrieval and later ultrasonography revealed a twin pregnancy. Pregnancy was uneventful. Amniocentesis showed

that both fetuses had normal hemoglobin genes, and healthy twins with normal hemoglobin genotype were delivered at 39 weeks.

Xu et al conclude that their work indicates that IVF and PEG offer an alternative for couples at risk for having a child with a severe genetic defect who wish to avoid the presently available method of prenatal diagnosis by chorionic biopsy at 8-12 weeks of pregnancy followed by termination of pregnancies in which the fetus is affected.

COMMENT BY HOWARD A. PEARSON, MD, FAAP

The availability of prenatal diagnosis for a number of serious genetic diseases has made it possible to diagnose an affected infant as early as 8-12 weeks of gestation by analyzing fetal DNA obtained by chorionic villus biopsy. Availability of this technique has resulted in marked reductions in births of infants with genetic diseases such as thalassemia major and Tay-Sachs disease in the United States and elsewhere. Implicit in this procedure is the assumption that the parents will usually opt to terminate an affected pregnancy shortly after diagnosis, in the first trimester.

The report by Xu et al describes an alternative. IVF has become a fairly standard, albeit technically difficult and expensive, technique over the past decade. Xu et al combined IVF with PEG in order to ensure the birth of a normal infant to a couple at risk for sickle cell anemia. It is of some interest that this couple had previously had two standard prenatal diagnoses with termination of affected pregnancies. I have a little trouble with the rationale and justification of this kind of scientific tour de force. I completely understand parents who do not accept abortion on religious and moral grounds. Such individuals also usually believe that life begins at conception and that a multicell embryo is a "person." In this procedure, the embryos that have sickle cell anemia (and in the present report those with sickle cell trait) would presumably be destroyed and this should pose the same kind of ethical dilemma for individuals who object to any abortion for any reason.

IVF is a difficult, often unsuccessful, and expensive procedure but is widely performed throughout the world. PEG is still in the research stage and is available in relatively few centers. Whether IVF and PEG can be completely justified for carrier couples who "desire to have a healthy child but wish to avoid the difficult decision of whether to abort an affected child" is a debatable issue. Because of the expense and difficulty, I doubt that there will be many of these procedures performed except on an investigational basis in the foreseeable future. ❖

Brief Reports

The Disappearance of Reye's Syndrome

Sources: Belay ED, et al. Reye's syndrome in the United States from 1981 through 1997. *N Engl J Med* 1999; 340:1377-1382; Monto AS. The disappearance of Reye's syndrome—A public health triumph. *N Engl J Med* 1999; 340:1423-1424.

Reye's syndrome is an acute illness characterized clinically by encephalopathy and hepatic dysfunction and hepatomegaly, resulting from fatty infiltration, often occurring in association with influenza or varicella. Sporadic cases of what is now called Reye's syndrome were probably seen previously in the United States, but it was not until after Reye's report from Australia in 1963[1] that increasingly larger numbers of cases were recognized in the United States in the 1970s, with as many as 400-600 cases per year. It was also recognized early that Reye's syndrome occurred in the wake of infection—respiratory infections, especially influenza[2] and varicella—in almost all cases. However, the disease was somewhat difficult to diagnose. The gold standard for diagnosis, namely, the finding of specific mitochondrial changes in liver biopsy specimens, was infrequently performed, so the diagnosis was usually based on clinical and historical criteria.

It was not until 1980 that an association between Reye's syndrome and the use of aspirin during children's respiratory infections and varicella was first formally suggested by Starko et al.[3] This paper, published in *Pediatrics*, was followed by larger studies that strongly supported a causal association.[4] However, the association was rather reluctantly accepted by the public and medical profession because aspirin, a drug that was in wide use for many years, was considered safe and also because there appeared to be no relation between the amount of aspirin taken by a patient and the subsequent development of Reye's syndrome. In 1982, the surgeon general issued an advisory concerning the use of salicylates and Reye's syndrome.[5] Beginning in 1980, the numbers of cases of Reye's syndrome began to fall sharply. This was due to the heightened public and professional awareness of possible dangers as well as an increasing use of acetaminophen as an antipyretic in the United States. In 1986, the FDA mandated labeling of salicylate-containing medications.

In 1980, 550 cases of Reye's syndrome were reported; between 1985 and 1986, fewer than 100 cases were reported annually; from 1987 through 1993 there were no more

than 36 cases per year; and from 1994 through 1997, no more than two cases were reported annually. Thus, Reye's syndrome has virtually disappeared from the United States. There is now a generation of physicians who have never seen or treated children with Reye's syndrome.

There are at least two important points to be emphasized concerning Reye's syndrome. First, because it is unusual today, children presenting with symptoms that mimic Reye's syndrome are more likely to have certain inherited rare inborn errors of metabolism that may result in encephalopathy and hyperammonemia. Differentiating these from Reye's syndrome may require a liver biopsy.[6] However, despite its current rarity, Reye's syndrome must remain in the differential diagnosis of children with acute encephalopathy and hepatic dysfunction. A history of a preceding illness and the use of medications—especially salicylates—must be carefully explored. Second, U.S. children may ingest salicylates, either inadvertently or as treatment for conditions such as juvenile rheumatoid arthritis and Kawasaki's disease. As many as 5% of children who developed Reye's syndrome in the past were receiving chronic aspirin therapy. Children who must receive salicylate therapy should receive influenza and varicella immunizations. —**hap**

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Pain Control After Outpatient Surgery in Children

Source: Kokinsky E, et al. Postoperative comfort in paediatric outpatient surgery. *Paediatr Anaesth* 1999;9:243-251.

One-day, outpatient surgery is becoming increasingly common for a variety of surgical conditions. Children are usually observed in a one-day-care surgical unit until they have recovered from the immediate effects of anesthesia and are stable. They are then sent home with medications to control discomfort. Kokinsky and associates evaluated postoperative conditions in hospital and after going home in 200 children who had one-day outpatient surgical procedures using questionnaires and telephone interviews. Depending upon the patient's age, pain was assessed by behavior observation or a fates rating schedule. Anesthetic methods, events of nausea and vomiting, and use of analgesics were also recorded. Seventy percent of the children had received regional anesthesia that was often supplemented by intravenous sedation. Immediate postoperative analgesia was judged to be satisfactory in 75% of children. However, when the effects of intra-operatively administered analgesics wore off at home, nearly half of the children complained of pain rated higher than mild. The increased pain was especially pronounced after regional anesthesia. Twenty-eight percent of children experienced nausea and vomiting, and this was higher in children who received fentanyl.

This study indicates that immediate postoperative comfort obtained by prophylactic analgesia needs to be followed by continuing effective analgesia for the first days after surgery. The pediatrician should be certain that the surgeon or anesthesiologist is cognizant of the need to prescribe appropriate pain medications, and that the family understands the schedule for administering these medications. It goes without saying that they should be certain that the prescriptions can be filled in time for indicated administration. —**hap**

Vaccination for *Haemophilus Influenzae* Type b is not Associated with a Risk of Diabetes Mellitus

Source: Karvonen M, et al. Association between type 1 diabetes and *Haemophilus influenzae* type b vaccination: Birth cohort study. *BMJ* 1999;318:1169-1172.

Because most children receive various vaccines on many occasions during their first five years of life, it is not at all surprising that a variety of conditions and events may occur in proximity to a childhood immunization. A question in most of these cases of vaccination-disease associations is whether the vaccine actually was

causally related to the condition or was only coincidental. There have been a number of linkages of childhood immunizations and specific diseases that have led to public concern (recently an alleged relationship between hepatitis B immunizations and multiple sclerosis prompted a moratorium on HpB immunizations in France). Damage to the pancreatic beta cells leading to type 1 diabetes is believed to be caused by environmental factors including infections and possibly immunizations.

In 1988, the vaccine for *H. influenzae* type b was given to virtually all children born in Finland as part of a nation efficacy trial. The design of the trial was that children born between 1985 and 1987 who were born on odd-numbered days received the conjugate Hib vaccine at 3, 4, and 6 months of age followed by a booster at 14-18 months of age. Children born on even-numbered days were a control group and received Hib vaccine at 24 months of age only. Of interest is the fact that Finland has the highest incidence of type 1 diabetes mellitus in children younger than 14 years of age in the world, and its incidence has been increasing by 2-3% per year since the 1940s. Classen and Classen described an apparent accelerated increase in the incidence of type 1 diabetes in children after the national program for Hib immunization began in 1988 and have speculated that there may be a causal association.[1,2] However, because of the near universality of immunizations in infancy and childhood and the relative rarity of diabetes, an enormous database of appropriate data is necessary to generate statistically convincing conclusions.

Karvonen and associates from the Diabetes and Genetic Epidemiological Unit of the National Public Health Institute in Helsinki compared the cumulative incidence and risk of type 1 diabetes in three cohorts of Finnish children: those born 24 months before the start of the national Hib immunization program was begun; those in the 1988 trial cohort who received Hib vaccine at 3 months of age followed by a later booster; and the control cohort from the trial who were vaccinated at 24 months only. The data were obtained from a nationwide hospital discharge registry. There were no differences between the incidence of type 1 diabetes in the three groups. Karvonen et al conclude that it is unlikely that *H. influenzae* type b vaccination or its timing causes type 1 diabetes mellitus in children. It is hoped that similar rigorous analysis will be used to establish or disprove causal relationships between beneficial procedures such as childhood immunizations and rare pediatric conditions. In fact, a recent article showed no association between autism and MMR immunizations.[3]—**hap**

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Special Report

Long-Term Prognosis of Women with Birth Defects

By Margaretta Seashore, MD, FAAP

Persons born with birth defects are known to be at high risk for death during the perinatal period and infancy. Much less is known about their later survival, reproduction, and risk of recurrence of birth defects in their offspring. Skjaerven and associates reported on survival and reproductive outcome in a large, national cohort of all women with birth defects identified in a population-based registry of all births in Norway between 1967 and 1997. They compared survival, frequency of childbearing, and frequency of birth defects in offspring in women who had birth defects to outcomes in 451,214 women without birth defects.[1] This is an extension of a similar study reported by them in 1994, in which they looked at recurrence of birth defects in children born to women whose first child had a birth defect.[2] Their current interesting data are also discussed in an accompanying editorial by Jean Golding.[3] They collected information on 459,433 live or stillborn female infants delivered between 1967 and 1982 in Norway. These women were between 15-30 years of age when the data on their survival and childbearing and frequency of birth defects in their offspring were collected. A total of 8192 women with birth defects was identified.

Skjaerven et al present and analyze data about a broad variety of birth defects, including neural tube abnormalities, other CNS defects, musculoskeletal, limb (club foot was considered separately), kidney, genitalia, esophagus, anus, abdominal wall, eye, cardiac, and vascular defects. Also included were cleft lip; cleft palate; defects in skin, hair, and nails; defects in ear, face, and neck; multiple anomalies; and Down's syndrome. Abnormalities were classified according to ICD-8. The frequency of birth defects in the Norwegian population studied (1.8%) was not significantly different from the approximately 2% incidence of birth defects reported in various surveys around the world.

Survival between the normal and abnormal cohorts of women differed dramatically. The overall survival rate for female infants born during the interval studied was 97.4%. However, the survival rate among infants and children with birth defects was significantly lower. Babies with birth defects were 6.5 times more likely to be stillborn than those without defects. The relative risk of death in the first year of life for subjects with birth defects was 14.8, and in the second year of life, 12.0. Even as far out as the tenth to fourteenth year of life, the relative risk for death was 4.6.

Overall, a total of 62% of the women between the ages of 28 and 30 years had borne children. In every age group, however, there was a lower rate of childbearing among the women with birth defects as compared to those without. The overall ratio of childbearing among surviving affected women compared to those without birth defects was 0.7. Whether a woman with a birth defect gave birth to a child was related to the severity of the birth defect, but even among women with treated birth defects such as club foot, the rate was lower.

Offspring of women affected with a birth defect were more likely themselves to have a birth defect. A total of 1101 women with birth defects gave birth to children, and 3.8% of these children had an identifiable birth defect. This frequency was compared to a 2.4% frequency of birth defects in the offspring of the unaffected women. The offspring of the affected women were much more likely to have the same defect as their mothers than expected by chance. Particular defects that recurred more frequently than others included: cleft palate, cleft lip, club foot, and limb defects. For affected women who gave birth to a child with a dissimilar defect, the relative risk compared to women without birth defects was 1.0, suggesting that a woman with a birth defect is no more likely to have a child with a different birth defect than any other women in the general population. In addition, none of the women with multiple defects gave birth to a child with any defects.

These observations raise a number of interesting questions and provide data to guide counseling of women who are affected with certain birth defects. It has been known since the seminal observations by Carter and Evans in 1982 that certain birth defects recur in multiple generations in families.[4] Both individual family studies and population-based studies have corroborated these observations. Certain defects, especially cleft lip and palate, congenital heart defects, and club foot, are classic examples. The multiple generations involved, the similarities among affected relatives, and the decrease in risk to relatives with increasing genetic distance from the proband have all suggested that genetic factors are involved. However, in most situations, the recurrence risks are low and do not reach anything like those of the single gene disorders. The data presented here do not change those conclusions.

The striking new insights described in the study by Skjaerven et al have to do with survival, childbearing rates, and specific recurrence of birth defects. Decreased survival among infants and children with birth defects is not surprising, but the high rates of stillbirth and death in the first two years of life are important for physicians caring for affected women and children to know. Decreased childbearing among women with severe birth defects, especially with intellectual disability and inability to live independently, should not be surprising. It is not clear how much of this decrease might involve social factors and how much may reflect decreased fertility or fetal survival. More data will be needed to sort this out.

Several observations of recurrence risk are of note. Recurrence in offspring was more characteristic of some defects than of others, as has been observed by others. When affected women had a child with a birth defect, it was much more likely to be similar to the one the mother had; indeed, the risk of having a child with other birth defects was not different from the risk in the general population. One of the most helpful observations is that there was no increase in the risk of anomalies in children born to women with multiple anomalies. This parallels the observations made in VACTERYL syndrome association.

There are certain obvious limitations to this kind of study. First, ascertainment of birth defects was confined to the first five days of life. Later identification of conditions, such as congenital heart disease, could change the conclusions about some birth defects. There is no indication that Skjaerven et al went back to examine mothers when a child with a birth defect was identified. Of course, a study using a registry limits that approach. Changes in survival with improved medical care over time could affect their data on survival. Much has changed in the medical and surgical management of congenital malformations since 1967. It is also unclear how the use of prenatal diagnosis may have altered their data in later years. Of course, this study points to a need for further knowledge. We need further understanding of the role of genes in developmental abnormalities. Environmental components may also play a role. It will be useful to identify the reasons for decreased childbearing among these women. More data are needed to determine whether the same outcomes occur for boys and men.

These data have implications for pediatric practice as well as for obstetric practice. For pediatricians, the data point to the importance of anticipatory guidance. The relatively high mortality rate for children (or at least

girls) with birth defects in the first few years of life dictates high vigilance on the part of the pediatrician. The more severe the defect, the higher the risk. Optimal medical management will often require a multidisciplinary approach, involving children's surgeons, clinical geneticists, services for children with special health care needs, and a variety of organ-based specialists. The anticipatory guidance may also need to address the possible reasons for decreased childbearing among these women. To the extent that misinformation or a negative effect on social development is involved, pediatric and genetic counseling can help.

Skjaerven et al have expanded our knowledge of the effect of birth defects on the lives of girls and women. Pediatricians, clinical geneticists, and obstetricians and other primary care providers can use this information to enhance their care of children and families who face the effect of birth defects. (*Dr. Seashore is Professor of Pediatrics and Human Genetics at the Yale University School of Medicine.*) ❖

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CME Questions

1. Tremacara, a soluble adhesion intercellular molecule:

a. has been shown to be effective in infections caused by a majority of the 101 rhinoviruses that produce upper respiratory disease in humans.
b. appears to be systemically absorbed through the cells of the respiratory epithelium.
c. appears to act prophylactically against cold symptoms when administered either experimentally pre- or postinoculation of RSV type 39.
d. appears to interfere with the immune response to RSV infection.

2. True statements about the long-term survival and reproductive prognosis of women who were born with congenital birth defects include all of the following *except*:

a. Their mortality during gestation, infancy, and childhood is greater than control women born without birth defects.
b. They are more likely to deliver infants with birth defects similar to their own than expected by chance.
c. Congenital defects that occur in offspring of women with severe defects are also likely to be severe.
d. Their rate of childbearing is the same as that of control women born without birth defects.

3. Cesarean section of pregnancies in which the mother has HIV/AIDS:

a. is effective in reducing the rate of vertical transmission when the cesarean section is done after the rupture of membranes.
b. has no additive protective effect if zidovudine is given prenatally to the mother and postnatally to the infant.
c. is strongly indicated in underdeveloped countries with high prevalence of HIV/AIDS.
d. has an unassessed effect when the mother is receiving poly-antiviral therapy.

4. True statements concerning type I diabetes in children include all of the following *except*:

a. Its incidence in Finland is the highest in the world.
b. Environmental factors, including infections, have been suggested as a possible etiology.
c. An association with immunization with Hib vaccine has been proven.
d. A causal association with immunizations is difficult to establish.

5. Reye's syndrome:

a. can be easily differentiated from inherited metabolic disorders with encephalopathy and hepatic dysfunction on the basis of clinical features.
b. is less common today in the United States than inherited disorders of metabolism characterized by encephalopathy and hepatic dysfunction.
c. can be related to the dose of salicylate that a child has received.
d. does not occur in children receiving chronic aspirin therapy for rheumatoid arthritis.

6. True statements about early diagnosis of sickle cell disease include all of the following *except*:

a. A diagnosis can be made at 8-10 weeks of gestational age by analysis of fetal DNA obtained by chorionic villus biopsy.
b. A diagnosis can be made within days of conception by preimplantation genetic diagnosis.
c. The combination of IVF and preimplantation genetic diagnosis is widely available for general use for couples at genetic risk.
d. IVF and PEG are experimental at the present time.

In Future Issues:

Bruising in Normal Infants

Brain Function in Adolescents Who Were Born Premature