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The SOGC has strongly suggested that umbilical cord blood gas analysis should become a routine procedure following every delivery. The policy was based on the assumption that a normal cord artery pH value would be a powerful factor in defence of any lawsuit that might allege obstetrical negligence as a cause of any subsequent problems with the baby. This is undoubtedly true. However, a couple of articles in the recent literature demonstrate some of the surprises we may get if we do routine umbilical blood gases. They also reinforce what Dr. Jim Low in Kingston has been telling us for many years about the unreliable predictive value of extremely low cord artery pH values. Today's third article introduces a good measure of doubt into another of our widely accepted guidelines concerning risk factors for development of early onset neonatal group B strep septicaemia.

Follow-up of children born with an umbilical arterial blood pH < 7.

Nagel HTC, Vandenbussche FPHA, Oepkes D, Jennekens-Schinkel A, Laan LAEM, Gravenhorst JB.
(Am J Obstet Gynecol 1995;173:1758-64).

Routine cord blood gases were collected from 1,614 deliveries at Leiden University Hospital. Of these, there were 30 arterial pH values < 7.0 (1.9%). Nine of the babies were preterm (only 1 < 32 weeks), one was post-term, and one had intra-uterine growth restriction. Interestingly, in 10 of the 30, there was no suspicion of fetal distress with normal vaginal deliveries. Seven of the babies never required admission to the neonatal intensive care unit (NICU).

Two of the 30 babies died during the neonatal period. Follow-up neurological examinations were performed at one to three years of age on all 28 surviving babies, and the Denver Developmental Screening Test (DDST) was administered to 25 of the 28. Three children experienced "an episode of mild hypertonia" and one displayed a mild motor developmental delay. This latter baby had no evidence of fetal distress and was not admitted to NICU. There were no abnormal DDST scores!

There can be no doubt that these low pH values represent significant acidosis at the time of birth. It is no surprise that this predicted a very high rate of short-term neonatal morbidity. What surprised me was that 25 percent required no special immediate care and at least 80 percent (likely > 90%) appeared to have no long-term sequelae. Obviously, not only the degree, but probably more importantly the cause and the duration of the acidosis are the crucial prognostic factors. Other studies have shown that the poor outcomes usually occur in those babies who leave the nursery with obvious neurological damage. As for the others, it appears that we should not be pessimistic to the parents simply because of the extreme acidosis that we uncover by measuring routine cord blood gases.

Influence of acid-base status at birth and Apgar scores on survival in 500-1000-g infants.

Gaudier FL, Goldenberg RL, Nelson KG, Peralta-Carcelen M, Dubard MB, Hauth JC.
(Obstet Gynecol 1996;87:175-80).

This study examined the effect of low Apgar score (≤ 3 at 1 minute or ≤ 6 at 5 minutes) and abnormal cord artery blood gases (pH < 7.05; $pCO_2 \geq 69$ mmHg; bicarbonate ≤ 14 mEq/L) on neonatal mortality rates. Data from 1,073 infants with birth weight 500–1,000 grams were analysed using multiple logistic regression analyses controlling for gestational age, birth weight, mode of delivery, glucocorticoid use, and other potentially confounding factors. Blood gas values were available for 658 of these babies.

Almost half of these very low birth weight infants had low Apgar scores at one and/or five minutes. Approximately five percent of these babies had one or more abnormal blood gas parameter (4.7% had pH < 7.05).

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Odds ratios (OR±95% confidence intervals) were calculated for neonatal death according to the various abnormal findings. None of the blood gas abnormalities had a significant effect on the rate of neonatal death. However, a low Apgar score at either one minute (OR 2.67; 1.95–3.64) or five minutes (OR 2.76; 2.02–3.77) was associated significantly with neonatal mortality.

There may be little value to these studies other than to emphasize the poor predictive performance of abnormal blood gases, particularly in the longer term. Although the second study showed better results with Apgar scores, this applies only to this large population and does not pertain to the use of Apgar scores in any individual case. Others have demonstrated conclusively that the Apgar score is a good discriminative index to determine which babies require resuscitation and how the baby responds to resuscitation but it is a poor predictive index of longer term outcome. All of this underscores our lack of a measurement tool that will provide some sort of reliable predictive index of outcome. Research trials of obstetrical interventions are seriously hampered by the lack of such a tool.

Intrapartum factors in early onset group B streptococcal sepsis in term neonates: a case-controlled study.

McLaren RA, Chauhan SP, Gross TL.
(Am J Obstet Gynecol 1996;174:1934-40).

This is a retrospective study of 21 women delivering term babies that became septic with group B streptococcus (GBS) compared to 63 controls who were also GBS positive but had normal babies who were not infected. The controls were matched for race, age, parity, and gestational age.

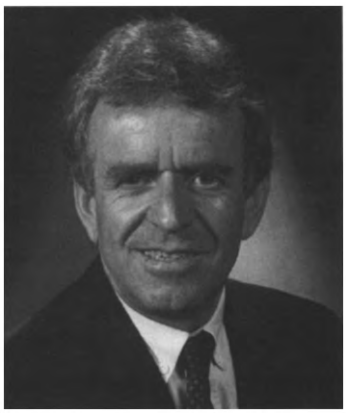
Although not a particularly well designed or discussed paper, the results do bring out some interesting points. Not surprisingly, the babies who became infected had mothers with longer duration of ruptured membranes, longer labours, and more vaginal examinations. However, surprisingly, only two of the 21 mothers had one of the accepted risk factors for neonatal GBS sepsis (ruptured membranes > 18 hours, intrapartum temperature > 38°C or previous history of neonatal GBS sepsis). One of these was treated, unsuccessfully, with chemoprophylaxis.

These data question both the validity of the risk factors for GBS at term and the efficacy of chemoprophylaxis. It is not clear why this population of patients from Illinois is so different from the original population, also from Illinois, that was studied by Boyer to arrive at the risk factors. The overall incidence of GBS sepsis was about two per thousand, which is quite high considering that this includes only infants at term and ignores the much higher risk preterm infants. Certainly this rate is no lower than historical controls from the era before chemoprophylaxis was instituted.

The very low prevalence of risk factors in the women with septic babies is disappointing. The authors suggest that decreasing the limit for ruptured membranes from 18 to 10 hours would increase the positive predictive rate to about 50 percent. However, if antibiotic treatment optimally should be commenced at least four hours prior to delivery to be effective, this would mean starting treatment at six hours and would result in a large proportion of labouring women receiving antibiotic therapy.

It is clear that we have very little reliable data on which to base recommendations regarding prophylaxis of neonatal GBS sepsis. Yet that has not hampered a malignant proliferation of "guidelines." The SOGC, CPS, ACOG, AAP, CDC, and likely the XQCYJ have all made recommendations. Local hospitals have got in on the act as well. In our institution, we have a customized policy that will result in treatment of approximately 40 percent of all labouring women. One wonders when GBS will become super-resistant and how many iatrogenic cases of non-GBS neonatal sepsis have occurred. There has recently been a concern in our nursery about a possible increase in the rate of neonatal sepsis. This has been attributed to health care "restructuring" (?"destructuring") and other unknown factors, but one has to wonder how much of the problem may be due to our abuse of antibiotics.

This is a problem that is eminently amenable to clinical research. There is a variety of useful and clear questions that could be posed with definitive primary and secondary outcome measures. The incidence of the disease is such that a large trial would be necessary, but the manoeuvres would be no more interventive than current therapy so a trial would be acceptable to patients and physicians. In our current state of ignorance, there could be no valid ethical concerns. Canada would be an ideal setting for such a study. Hopefully, one of our enthusiastic clinical trial groups will take up the challenge.



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The management of patients with trophoblastic disease is one of the great success stories of oncology. Different means have been used to gain this end. In the first instance, the development of a tumour marker (hCG) allowed logical treatment. Secondly, we gained understanding of the disease through the study of its genetics. Finally, there was early realization that this uncommon disease should be managed in specialized units.

A number of advantages accrued from the referral of patients to sub-specialists in centres of excellence. Most importantly, patient survival was better in such units. In addition, most new information concerning trophoblastic disease came from special centres. One such centre is the New England Trophoblastic Disease Center in Boston; the other is in London at the Charing Cross Hospital. The same authors' names, from the same locales keep recurring in the literature of gestational trophoblastic disease, namely Goldstein of Boston and Bagshawe from London. One of the ironic results of the centres' success in standardizing management is that fewer patients are referred to them. It would appear that the New England centre is seeing one-half the number of patients that they saw in earlier decades.

The changing clinical presentation of complete molar pregnancy.

Soto-Wright V, Bernstein M, Goldstein DP, Berkowitz RS. (Obstet Gynecol 1995;86:775-9).

Twenty years ago, hydatidiform moles were only diagnosed in symptomatic patients. Most (97%) of the patients were diagnosed after they complained of abnormal vaginal bleeding. On occasion, severe hyperemesis gravidarum or pre-eclampsia in early pregnancy were the presenting complaints. Physical examination would often show that the uterus was enlarged and that the ovaries contained theca lutein cysts.

Present-day diagnosis of hydatidiform mole depends on the availability of sensitive radio-immunoassays for hCG and pelvic ultrasound. The authors of this paper examine the influence of these techniques on the presentation and the natural history of molar disease. The 74 study patients with hydatidiform mole who were managed between 1988 and 1993 were compared with 306 control patients who were seen between 1965 and 1975.

At present, diagnosis is usually made through use of pelvic ultrasound. The investigation is normally prompted by first trimester bleeding (84% of patients). Patients are less likely to have other classical complaints; nine percent of the patients are asymptomatic.

Diagnosis of molar disease is now made at an earlier stage of pregnancy; the average gestational age at evacuation is now 12 weeks as compared to 16 weeks in former decades. Nevertheless, there are physical limitations to the early ultrasound diagnosis of hydatidiform moles. Ultrasound diagnosis cannot be made until vesicles form. In the first trimester, the villi are too small to produce vesicles so that ultrasound diagnosis cannot be made at that time.

The downside of the diagnostic advances is that they have not resulted in a decrease in the incidence of persistent trophoblastic disease. Persistent disease developed in 23 percent of current patients compared to 19 percent of the controls. Although disappointing, this is an understandable outcome; early diagnosis does not change the nature of the disease.

Epidemiology and aetiology of trophoblastic disease.

Chung TKH, Cheung TH, Lam SK, Chang AMZ. (Curr Obstet Gynaecol 1995;5:2-5).

A gestational trophoblastic tumour contains excessive numbers of male chromosomes. Male chromosomes are important in the development of the trophoblast; the excess male chromosomes cause a proliferation of the trophoblast.

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Hydatidiform moles may be classified into complete and partial moles. Complete moles contain 46 chromosomes; all are paternal in origin.They are either the result of the doubling of a haploid sperm (a single set of chromosomes contains 23 chromosomes [the haploid number]) or by the fertilization of an anuclear egg by two sperm. Partial moles are usually triploid (69 chromosomes). They are the result of fertilization of a maternal egg by two sperm.

Complete moles have diffuse hydropic swelling of the chorionic villi and diffuse trophoblastic hyperplasia. There is no fetal tissue. Partial moles are a mixture of normal chorionic villi and hydropic villi with focal trophoblastic hyperplasia. In addition, their maternal chromosomes cause them to contain fetal tissue.

It is difficult to determine the epidemiology and aetiology of trophoblastic disease because of the lack of precise definition of the disease and because of the variance of the populations which are described. Many authors have mistakenly extrapolated their experience with hospital-based populations to the general population.

The factors which lead to the development of a hydatidiform mole are unknown. There is more chance for molar disease with increased maternal age, Asian race, history of trophoblastic disease, and a blood group A woman with a group O consort. There is no proof that nutritional (lack of carotene) or environmental (smoking, alcohol, oral contraceptives) factors are important.

Clinical managment of trophoblastic disease in the United Kingdom.

Newlands ES.
(Curr Obstet Gynaecol 1995;5:19-24).

The term gestational trophoblastic disease (GTD) is used when patients have persistently raised human chorionic gonadotrophin. In most instances the condition follows a molar pregnancy. Nevertheless, it is important to remember that GTD can follow other types of pregnancy (full term, stillbirth, abortion or ectopic). Unfortunately, this latter group of patients may present with advanced gestational trophoblastic disease. The usual presentation at the time of diagnosis is abnormal bleeding.

After evacuation of a complete mole, weekly hCG measurements must be taken until the measurements are normal for three weeks. If this occurs within eight weeks, monthly measurements are undertaken until hCG is undetected for six months. If the hCG takes more than eight weeks to return to normal, follow-up is for two years. If a patient with a partial mole has normal hCG in eight weeks, measurement of monthly hCG levels can be discontinued after three months.

Persistent disease is diagnosed if the hCG levels plateau for three or more consecutive weeks or if they re-elevate. The chance of developing persistent trophoblastic disease is approximately 15 percent after complete mole and 0.5 percent after partial mole.

Patients may be categorized into low (62%), medium (22%), and high (16%) risk groups on the basis of their age, antecedent pregnancy, interval between antecedent pregnancy and chemotherapy, hCG, ABO blood groups, number of metastases, site of metastases, size of the tumour, and whether the patient received previous chemotherapy.

The indications for chemotherapy are as follows:

1. Abnormal hCG levels—rising or >20,000 IU/L more than four weeks post-evacuation
2. Histology—evidence of a choriocarcinoma
3. Radiology—evidence of metastases.

Low risk patients are treated with methotrexate and folinic acid. This regime is well tolerated: the main side effect is stomatitis, and there is no hair loss. Treatment with other drugs is required in 20 percent of low risk patients because of methotrexate resistance.

Medium and high risk patients may be treated with a combination of etoposide, methotrexate, actinomycin, vincristine, and cyclophosphamide. If resistance to the latter forms of chemotherapy develops, there is a place for salvage surgery. Computerized tomography and MRI scans are used to localize foci of resistant disease which are then surgically removed.

Current managment of molar pregnancy

Berkowitz RS, Goldstein DP.
(Curr Probl in Obstet Gynecol and Fert 1995;3:69-92).

A careful study of the products of conception has suggested that incidence of partial mole is 1:695 pregnancies and complete mole is 1:1,945 pregnancies.

The distinction between complete and partial moles was only made in the late 1970s. All studies of molar pregnancy up to that time included a small number of patients with partial mole. The numbers were small because most partial moles were included in the spontaneous abortion group.

Pelvic ultrasound is a sensitive technique for the diagnosis of complete mole. Partial moles may be diagnosed because the placenta is found to be excessively large or because cystic spaces are found within the placenta.

The diagnosis of a complete mole is suggested if the hCG level is over 100,000 mIU/ml. The diagnostic suspicion is raised if in addition there is vaginal bleeding and uterine enlargement. Only six percent of partial moles have levels of hCG >100,000 hCG IU/ml.

The chance of persistent gestational trophoblastic tumour with complete moles is between eight and 30 percent. The chance with a partial mole is closer to two percent. There is some suggestion that partial moles which have a diploid DNA content are more likely to lead to persistent disease.