Perinatal Outreach Program of Southwestern Ontario

Partner

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Parvovirus B19 Infection in Pregnancy

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PARVOVIRUS B19 infection, also known as 'slapped cheek disease', fifth disease or erythema infectiosum, is common in young children. Fortunately, most adults show evidence of having had the infection as a child, and are therefore, immune. In adults that develop infection, the symptoms are usually self-limited and do not require treatment. However, pregnant women that develop infection risk vertical transmission rates to the fetus that may be as high as 33%. Fetal infection can result in serious complications, including hydrops fetalis and resultant fetal death. Although these complications are rare, it is important to diagnose maternal parvovirus infection and monitor for fetal complications.

Pathophysiology of Parvovirus Infection

Parvovirus B19 is a virus named from the Latin *Parvum*, meaning small. It is the smallest DNA-containing virus that infects mammalian cells. B19 is a type of the virus that can only replicate itself in human red blood cells and erythrocyte precursor cells. In 1975, Cossart *et al*.[1] discovered the virus by identifying an anomalous result in blood sample #19 on panel B of an electrophoresis gel while screening serum samples for hepatitis B. Using electron microscopy of sample B 19, he found particles similar to other known parvoviruses. It was not until 1980 that it was reported in association with a clinically significant febrile illness[2], and in 1981, transient aplastic crisis was described in sickle cell anemia patients[3]. Later, the virus was recognized as the causative agent of erythema infectiosum. In 1984, it was recognized that intrauterine infection could result in hydrops fetalis[4,5].

B19 infection is most commonly seen in children aged 4 to 11. Outbreaks usually occur in the spring form March to May, but isolated cases can occur at any time throughout the year. About 50% of adult women are immune due to prior infection[6]. Therefore, the incidence in pregnancy is low. The risk of seroconversion of a sero-negative person is dependent upon the exposure risk. If exposed to a household or close contact, the seroconversion rate is 50%. If exposed to a school or casual contact the seroconversion rate is 20-30%[7,8].

(Cont'd)

What's Inside…

B19 is transmitted through inhaled particles, hand-to-mouth contact, direct contact with contaminated blood and through transplacental transmission. In 1990, the Public Health Laboratory Service Working Party on Fifth Disease in the United Kingdom estimated a fetal transmission rate of 33%.

Parvovirus B19 targets the blood group P antigen that is found on human erythroid progenitor cells and erythroblasts in the final stages of red blood cell production, resulting in a transient arrest of erythropoesis[9]. The blood group P antigen is also found on megakaryocytes, endothelial cells and fetal liver and myocardial cells. These cells are involved in the complex of symptoms that characterize the infection.

Diagnosis of Parvovirus B19 Infection

Viral infection produces a viremia 4 to 14 days post-exposure, during which the patient is highly contagious. Viremia produces symptoms of fever, headache, generalized malaise, gastrointestinal upset, sore throat and/or cough. The rash appears 16 to 18 days post-exposure. In general, the patient is not contagious after the first day of rash. The classic rash has a “slapped cheek” fiery red appearance, with a relative pallor surrounding. The characteristic maculopapular rash then spreads to the trunk and extremities where it fades to a fine reticular appearance. The exanthem is typically transient, but may persist or recur for weeks. More atypical appearances include pustular or glove-and-stocking rashes, or erythema multiforme.

While children generally experience the typical constellation of symptoms and a self-limited resolution, adults are more commonly asymptomatic. Fifty to 80% of non-pregnant adults experience symptoms. In contrast, 70% of pregnant adults remain asymptomatic [8,10,11]. Adults can experience viremia, although rash is far less common than in children. Symmetric polyarthralgias of the small joints of the hands, wrists and ankles occur in 50-80% of symptomatic adults[12]. Arthralgia is often associated with joint stiffness and swelling. It is more common in women and generally lasts 1 to 3 weeks, but may persist or recur for months or even years. In the chronic case, or the absence of rash, it is commonly mistaken for rheumatoid arthritis.

Transient aplastic crisis is an important complication that is due to an abrupt arrest of erythropoeisis. It is precipitated by infection in patients with underlying hematologic or immune disorders, such as sickle cell anemia, thalassemia, iron-deficiency anemia, transplant patients or immunodeficiencies. It is usually fatal, unless diagnosed early and treated appropriately. Other less common clinical manifestations of infection include myocarditis, vasculitis and central nervous system disorders, such as encephalitis, meningitis or neuropathies.

Laboratory features are usually clinically insignificant in healthy individuals. They may include hemolytic anemia with absence of reticulocytes, lymphopenia, neutropenia, thrombocytopenia or hepatocellular enzyme rise. Patients are occasionally pancytopenic. There may be transiently positive antinuclear antibodies, rheumatoid factor, anti-double-stranded DNA or anti-phospholipid antibodies, making the distinction between the symptoms of systemic lupus and B19 infection difficult [13,14].

Patients exposed to the virus, or those experiencing symptoms consistent with infection, should have serology performed. IgM antibodies appear within 10-21 days of inoculation and last 2-10 months[7]. IgG antibodies appear 2 weeks after inoculation. Positive IgG and negative IgM indicate past infection and immunity. Both antibodies negative indicate susceptibility to infection. Exposure should be avoided, or if already exposed, the patient should be retested in 2-3 weeks. Positive IgM, but negative IgG indicate a very recent infection, likely within 1 week, or a falsely positive IgM. Both antibodies positive indicate a recent infection within 6 months. There is no method of direct viral culture due to the transient nature of the viremia.

Diagnosis of Intrauterine Infection

Hydrops fetalis is the most significant consequence of intrauterine infection. It

occurs in approximately 2.9% of maternal infections contracted prior to 20 weeks[15]. B19 infection may account for 10-15% of cases of non-immune hydrops[16]. Hydrops is thought to be secondary to aplastic anemia causing high output congestive heart failure, myocarditis, direct hepatotoxicity or combinations thereof. It is detected by ultrasound showing generalized skin edema, ascites and effusions. Other ultrasonographic manifestations of B19 infection include placentomegaly, polyhydramnios and doppler studies consistent with anemia.

Serology may not be useful if infection is suspected after hydrops fetalis is diagnosed. Maternal IgM may not be detectable and development of fetal IgM is gestational age dependent. Amniocentesis or cordocentesis can be performed for amniotic fluid and fetal blood respectively to assess antibody status, as well as to measure fetal hemoglobin in cases of hydrops. Viremia is cleared slower from amniotic fluid and fetal blood. Therefore, the method of choice for detection of intrauterine infection is PCR amplification of viral DNA via amnio or cordocentesis[17].

Outcomes of Parvovirus B19 Infection in Pregnancy

Fetal death can occur at any gestational age. The overall death rate in infected fetuses has been reported from 2 to 9%, but is more common with maternal infection occurring in the second trimester[17]. Fetal death has been reported from 1 to 11 weeks following maternal infection. Death is more common in hydropic fetuses. Rodis *et al*. reported 46% fetal death with hydrops[18]. B19 infection has not been proven to carry a risk of congenital anomaly above that of the general population.

The natural history of fetal hydrops in B19 infections is variable. There are few prospective studies on outcomes of hydrops due to this cause. There are reports of spontaneous resolution and, in general, outcomes appear to be better than in other causes of non-immune hydrops.

Persistence of B19 infection after birth may result in chronic anemia, hepatitis, thrombocytopenia or myocarditis[16,19]. There are case reports of permanent neurological sequelae resulting from childhood infection. However, follow-up studies of neonates fail to detect any association with developmental abnormalities[20].

Management of Parvovirus B19 in Pregnancy

Prevention of exposure is ideal, but difficult, in susceptible pregnant individuals. The period of contagion is prior to the onset of symptoms. Exclusion of susceptible high risk pregnant women, teachers and child-care workers for example, is controversial and not currently recommended as routine policy by the American College of Obstetrician-Gynecologists. A vaccine is currently being developed, however it may be some time before it is potentially approved for use in pregnancy.

Patients with symptoms or history of exposure should have serology to determine antibody status. Confirmed maternal infection is usually self-limited with no treatment required. The patient should be counseled regarding the fetal risks of infection during pregnancy. Plasmapheresis or intravenous immunoglobulin administration has been described in cases of severe anemia in immunocompromised patients[21]. At this time, there is no evidence that it would prophylactically improve fetal outcomes.

Patients with confirmed maternal infection should be referred to an obstetrician. Serial ultrasounds should be performed weekly for 8 to 10 weeks. If hydrops develops at or near term, consideration should be made for delivery. If hydrops develops in late first or early second trimester, when directed fetal therapy is impractical, management should be expectant or pregnancy termination could be considered.

Fetal hydrops developing in the late second or early third trimester should be managed in an appropriate centre with intensive fetal monitoring, serial ultrasounds and fetal percutaneous umbilical blood sampling (PUBS) with possible intrauterine transfusion. In the case of mild fetal anemia proven by cordocentesis, mild fetal hydrops or resolving hydrops, management may be expectant[17]. An observational study by Fairley *et al*.[22],

compared expectant management to intrauterine transfusion (IUT). After controlling for gestational age and severity of anemia, a 7.1-fold reduction in fetal death was shown. Although there have been no randomized controlled trials of expectant management versus IUT, it appears reasonable to offer IUT in cases of fetal anemia. A single transfusion is often sufficient due to the transient nature of the red blood cell aplasia[17]. Patients must be aware of the 1-2% loss rate of the procedure and of the potential for spontaneous recovery without treatment.

Although rare in pregnancy, parvovirus B19 infection requires a high index of suspicion. Susceptible patients with a history of exposure or symptoms should be investigated, counseled and managed appropriately depending on gestational age. Confirmed maternal infection necessitates serial ultrasound monitoring for fetal complications. Fetal hydrops should be managed in a referral centre and anemia evaluated by PUBS. Consideration should be given to intrauterine transfusion. Overall, 90% of affected pregnancies have successful outcomes.

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NEONATAL - PAEDIATRIC EXTENDED ROLE TRANSPORT TEAM - LONDON, ONTARIO

NICU - ST. JOSEPH'S HEALTH CARE
PCCU - CHILDREN'S HOSPITAL OF WESTERN ONTARIO

TO REQUEST THE TRANSPORT TEAM
PLEASE CALL

TOLL-FREE:	**1-866-367-8044**
LOCAL:	**685-8044**

FOR YOUR INFORMATION

As of December 1, 2003, the Neonatal-Paediatric Extended Role Transport Team, London, Ontario will be implementing a new transport recorder system. The purpose of the system is to:

- simplify the process for patient transport
- document all transport calls
- improve overall response time
- and to identify clinical training opportunities.

This change essentially means that stakeholders will be "recorded" at all times in the system. New toll-free and local phone numbers are to be used for **all** neonatal/paediatric transport-related calls. There will also be a phone menu to navigate. As soon as the dial tone is heard, the call is being recorded. Then a series of "beeps" will be heard to indicate the call is being recorded.

All initial calls are to be directed to the Transport Supervising Physician or his/her delegate. Even if the unit is closed at the time of the call, the call will still be handled by this attending physician/delegate, who will then be available to provide medical advice for ongoing stabilization. This attending physician/delegate will then activate the transport team and will assist in locating an appropriate bed through CritiCall. The phone number options are as follows:

Toll-Free: 1-866-367-8044

Local: 685-8044 or,

- St Joseph's Health Care:
  - 646-6000 ext. 58044

- London Health Sciences Centre
  - 685-8500 ext. 58044

Both the SJHC and the LHSC numbers are interchangeable. When a call is placed it is not necessary to wait until the menu access has finished cycling if you know the menu option number you wish to use.

Intregrated Prenatal Screening in Southwestern Ontario: What you Need to Know

The Medical Genetics Program of Southwestern Ontario – London Health Sciences Centre

Many of you may recall the introduction of the Maternal Serum Screen (MSS Triple Screen) about 10 years ago. As of April 2003, you may also have noticed that this screen was expanded to include a fourth biochemical marker (Quadruple Screen). The vast majority of prenatal diagnosis centres in Ontario have now established Integrated Prenatal Screening (IPS). We are pleased to announce that resources are now in place to offer this program to Southwestern Ontario.

Prenatal Screening Options in Ontario

Currently there are three prenatal screening options available to women in Ontario:

1) First trimester screening (nuchal translucency ultrasound plus 1st trimester biochemical markers – PAPP-A and free beta hCG),
2) Second trimester screening (maternal serum screen with four biochemical markers plus anatomical ultrasound at 18-19 weeks),
3) Combined first and second trimester screening (integrated prenatal screening).

What is Integrated Prenatal Screening?

IPS is a three-step process involving first and second trimester screening. In the first trimester, between 11 weeks, 0 days to 13 weeks, 6 days, women will receive a dating ultrasound with nuchal translucency measurement, plus maternal serum PAPP-A measurement. In the second trimester, ideally at 15-16 weeks, women will receive the maternal serum triple marker screen (AFP, uE3 and hCG). These results will be combined to provide risk figures for Down syndrome, trisomy 18 and open spina bifida. *A detailed anatomical ultrasound at 18-19 weeks is still recommended in addition to IPS.

Why change our prenatal screening protocol?

MSS has an uptake of only 30% in Southwestern Ontario. Both providers and patients have been unsatisfied with MSS. That dissatisfaction relates directly to the HIGH INITIAL SCREEN POSITIVE RATE. MSS triple screen has an initial screen positive rate of 10%. In April 2003, we introduced the MSS quadruple marker screen, which lowered that rate to approximately 7.5%. While this was an improvement, patients and providers alike still remained cautious about proceeding with MSS.

Women generally seek reassurance from prenatal screening, but a woman whose initial screen is positive does not get reassurance – she's told that her pregnancy is at increased risk. This can create undue panic and anxiety, even when the patient has been appropriately counselled prior to having the test. The patient who receives an initial screen positive result is upset, often needs to schedule an urgent visit with the primary health care provider, may have to travel up to 3 hours out of town for genetic counselling, and may choose to have an amniocentesis. Amniocentesis is associated with a 1/200 risk of miscarriage, so over time, chromosomally normal pregnancies are lost because of positive MSS results. We therefore recognize the need to reduce this initial screen positive rate and the number of resulting amniocenteses.

In addition, the MSS triple screen has a Down syndrome detection rate of 70%, and the MSS quadruple screen only served to increase this detection rate to 75%. Although this is a significant improvement over screening based upon age alone (30-40%), MSS PROVIDES A SUBOPTIMAL DETECTION RATE when compared to the integrated approach.

Fortunately, we now have a newer and better option for prenatal diagnosis that we feel will better meet the needs of our patient population, and we have accumulated enough evidence and experience to implement this throughout our region.

When using a Down syndrome risk cut-off of 1/200, **IPS is estimated to have an Initial Screen Positive Rate of just 3%.** This is a dramatic improvement upon our previous screening options, and will result in decreased anxiety, fewer urgent appointments, fewer patients traveling out of town for genetic counselling, and fewer amniocenteses, resulting in fewer unnecessary pregnancy losses. IPS is predicted also to have a **Down syndrome detection rate of 90%**.

What is Nuchal Translucency?

Nuchal translucency (NT) is a measurement of the collection of fluid behind the fetal neck. This measurement normally increases with gestational age, and therefore must be interpreted in the context of the fetal crown rump length. An increased size of NT in the first trimester is associated with an increased risk of: 1) chromosome aneuploidy, 2) congenital cardiac anomalies, 3) other congenital anomalies, and 4) specific syndromes.

Why is NT so important?

NT is the most critical factor in the IPS program, and is heavily weighted in the Down syndrome risk calculation. It is also a difficult measurement to obtain, and its accuracy depends upon the skill and education of the operator, as well as the radiologist interpreting the measurement and dictating the report. Therefore, clinical use of this measurement can only be accepted from accredited ultrasound units and must be made by an accredited sonographer or radiologist. Training (theoretical course, logbook of NT images and practical assessment), monitoring and auditing of accredited centres are coordinated through the Fetal Medicine Foundation (www.fetalmedicine.com). Information about training can also be obtained at (416) 586-4800 ext. 2489. Email: Dpettai@mtsinai.ca.

How will IPS change my practice?

By implementing the IPS program, prenatal health care providers will need to see patients earlier in the first trimester, to provide education about the screening options available to them. This program will also require arranging a first trimester dating ultrasound with NT measurement for every patient, regardless of the certainty of LMP. However, while IPS will mean more early appointments for prenatal care, the lower initial screen positive rate will result in fewer urgent "return-to-clinic" appointments to discuss abnormal results and fewer referrals for genetic counselling. In the long run, this will reduce the workload for the referring health care provider and staff. Furthermore, providing a dating ultrasound for every woman who chooses prenatal screening means fewer calls from the MSS lab for urgent dating ultrasounds to verify screen positives. In addition, fewer women will need to repeat a detailed 18-week ultrasound that was scheduled too early, and fewer women will have ultrasound abnormalities identified after 20 weeks, when prenatal testing and termination options may be limited for those patients considering such options.

Potential Challenges with IPS

We recognize that implementing a new prenatal screening program will present many challenges initially. However, we feel that the benefits to the patient greatly outweigh these challenges, and we can no longer withhold this service from our population. We have outlined some of the challenges that we anticipate:

1) IPS is a 2-stage, 3-step process, rather than the 1-step MSS

- A dating ultrasound with NT measurement must be performed prior to, or in conjunction with the first trimester blood test. The patient must then retain the second portion of the requisition and have a second blood test drawn in the second trimester. While the patient does not need to meet with the health care provider

for this second blood test, the patient takes on the responsibility of having this blood drawn at the appropriate time.

2) LIMITED NT ULTRASOUND SPOTS

- During our implementation period, not all women will have access to an accredited centre to have an NT measurement. These women should still have a dating ultrasound, as the first trimester blood sample is time-sensitive. In addition, this will help non-accredited centres to obtain practice measurements en route to becoming accredited.
- Women who do not receive an NT measurement from an accredited centre cannot have the NT weighted in the final risk calculation. However, in these cases we will provide a 5-marker serum screen: 1st trimester PAPP-A and 2nd trimester AFP, uE3, hCG, DIA (MSS quadruple screen). This test is not as sensitive or accurate as the IPS, but is improved over MSS quadruple screen alone, as its initial screen positive rate is 5% and its detection rate is approximately 85%.

3) PATIENT DROP-OUT

- With our current protocol for risk calculation, if a patient has not had the 2nd trimester bloodwork, we will be unable to generate a risk assessment for the patient.
- Education of the patient prior to proceeding IPS is crucial to ensure their understanding of the 3-step process.

4) PATIENTS PRESENTING AFTER 14 WEEKS:

- will not be eligible for IPS, and will receive the MSS quadruple screen at 16 weeks.
- Ultrasound to confirm gestational age is still required, but a valid NT measurement will not be possible.
- This will have a lower detection rate (75%) and higher screen positive rate (7.5%) than IPS.

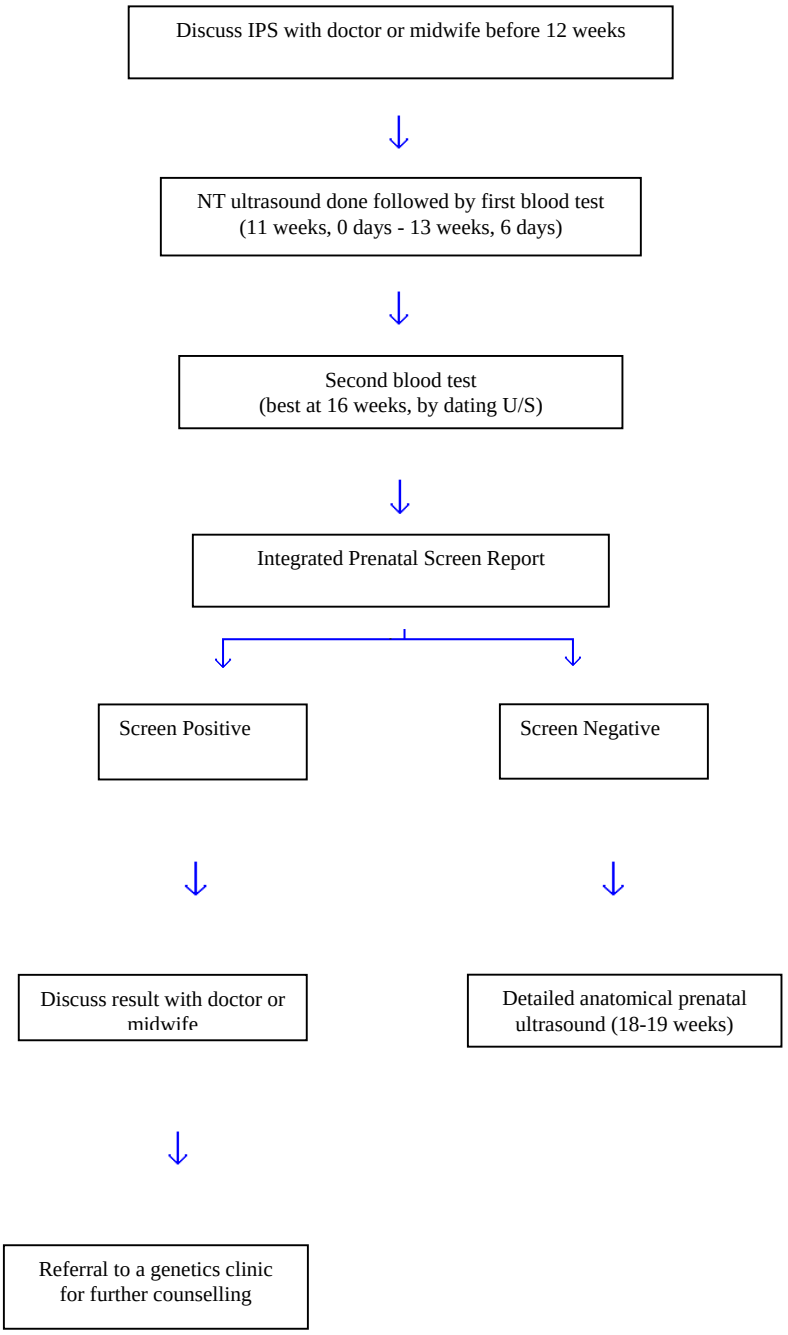
5) VERY LARGE NT MEASUREMENTS:

- NT measurements > or = 3.5mm will appear on the ultrasound report to the health care provider.
- In this situation, we suggest a referral for genetic counselling, to discuss amniocentesis and fetal echocardiogram.

I'M READY TO OFFER IPS TO MY PATIENTS. WHAT DO I DO?

IPS has been available as of 1 December 2003, and information packages were mailed in November 2003. These packages included a flowchart outlining the protocol for ordering IPS, as well as a supply of IPS patient brochures and requisitions. If you have not yet received your package, or need to order more brochures or requisitions, **please contact the Genetics Clinic at (519) 685-8140 or fax (519) 685-8214**. Please also contact us if you have any questions or would like to arrange an in-service for your clinic or call group.

IPS Flow Diagram



Questions?

Medical Genetics Program of Southwestern Ontario

London Phone 519-685-8140
Fax 519-685-8214
Windsor Phone 519-258-2146 Extension 1220
Fax 519 258-8431

For your information:

Changes in the Division of Neonatal-Perinatal Medicine, UWO

Dr. Jill Boulton, Medical Director of NICU at St. Joseph's Health Care London, and city-wide Director of Newborn Nurseries, has recently been appointed as Senior Medical Director, Women's and Children's Clinical Business Unit, LHSC. While Dr. Boulton will continue her roles as a staff neonatologist in the NICU, and as the Neonatal Co-Director of the Regional Perinatal Outreach Program of Southwestern Ontario, her current position as Director of Nurseries will now be filled by Dr. Henry Roukema.

Dr. Henry Roukema has been appointed as Medical Director of NICU at St. Joseph's Health Care London, and city-wide Director of Newborn Nurseries, assuming the role previously held by Dr. Jill Boulton. Dr. Roukema is currently a member of the Division of Neonatal-Perinatal Medicine and also Program Chair of the Postgraduate Education Program. For the time being, Dr. Roukema will continue his position as Director of Postgraduate Education. Dr. Roukema is also familiar with the Perinatal Outreach Program and may be filling in for Dr. Boulton from time to time.

You asked us:

Question:
Is it acceptable practice for gel packs to be used to warm the heel of infants requiring a blood draw?

Answer:
No, the use of gel packs on infants is not recommended. Severe burns have been reported with their use on infants. To promote vasodilation for the purpose of blood sampling, it is recommended that a warm washcloth be applied for several minutes prior to sampling.

Question:
What is the acceptable range of oxygen saturation for infants receiving oxygen supplementation?

Answer:
The acceptable oxygen saturation for infants receiving 0_2 is 88-95%. One must always remember that high levels of oxygen can be toxic and can lead to oxidative stress in the infant.

Upcoming Events:

Mark Your Calendar!

ALARM Course
London: February 27-28, 2004
Toronto: November 28-29, 2004
(in conjunction with ON CME)
For more information, contact the SOGC
1-800-561-2416 / www.sogc.org

Maternal Newborn Nurse Education Course
London:
Mondays: Mar 22 – May 10, 2004*
St. Joseph's Health Care, London
(*excluding April 12, 2004)*

Contact:
Gwen Peterek
Perinatal Outreach Program
Phone: (519) 646-6100 ext 65901
Fax: (519) 646-6172
Gwen.peterek@sjhc.london.on.ca

Southwestern Ontario Perinatal Partnership
Wednesday, March 24, 2004
Location: Lamplighter Inn, London

Contact: Perinatal Outreach Office
(519) 646-6100, ext. 65859

Fetal Health Surveillance Workshop
April 15, 2004
Location: Groves Memorial Hospital, Fergus

Contact: Judi Grozelle, Staff Development
(519) 843-2010

"Nurses Moving Forward: Evidence Based Practice in Action"
A one-day Nursing conference sponsored by the Regional Perinatal Outreach Program in collaboration with LHSC and SJHC
Friday, April 23, 2004
Location: Lamplighter Inn, London

Contact: Perinatal Outreach Office
(519) 646-6100, ext. 65859

NRP instructor course
Wednesday, April 28, 2004
Location: Education Centre, Rm 35
373 Hill Street, London

Contact: Perinatal Outreach Office
(519) 646-6100, ext. 65859

Maternal Newborn Nurse Education Course
Palmerston:
Thursdays: Apr 29 – Jun 10, 2004
Palmerston District Memorial Hospital

Contact: Kim Williamson
North Wellington Healthcare Corp.
Phone: (519) 343-2030 x 4264

Regional Nurse Manager's Meeting
(for entire region)
Thursday (eve), Friday, May 6/7, 2004
Location: Arden Park Hotel, Stratford

Contact: Perinatal Outreach Office
(519) 646-6100, ext. 65859

Neonatal-Paediatric Transport Conference – Southwestern & Northern Ontario Regions
Friday, May 28, 2004
Location:LHSC, Westminster Campus
800 Commissioner's Rd. E., London

Contact:
Kris Kristjanson, Transport Coordinator
PCCU & Paediatric Critical Care & Transport, LHSC
(519) 685-8500 x 57380
kris.kristjanson@lhsc.on.ca

18th Annual Regional Perinatal Outreach Conference
Wednesday, September 22, 2004
Location: Lamplighter Inn, London
Topics: TBA

Contact: Perinatal Outreach Office
(519) 646-6100, ext. 65859

Acute care of the at risk newborn (ACoRN)
Watch for upcoming details of the launch of the NEW ACoRN Program in the southwest region.

This newsletter is a publication of the Perinatal Outreach Program of Southwestern Ontario.

Letters, queries and comments may be addressed to:

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To have your name included on our mailing list, please contact the above, or
E-mail: gwen.peterek@sjhc.london.on.ca
www.sjhc.london.on.ca/sjh/profess/periout/periout.htm