### Cell Culture

In European Hospital Georges Pompidou, Dr. Chachques has developed a technique harvesting a sample of the thigh vastus lateralis, through a 5 cm incision under local anesthesia. The skeletal muscle from biopsy is subjected to enzymatic digestion to release satellite cells. The cells are then washed and the enzymatic reaction is stopped by adding one ml of the patient's serum. A benefit of human autologous serum cell culture is that it can be performed without risk of prion, viral or zoonoses contamination.[3] Cells are collected by sedimentation and the supernatant is discarded. Cell cultures are incubated for three weeks at 37 °C in a humidified atmosphere containing 5% $CO_2$.[6] Commonly, after three weeks, more than 200 X $10^6$ cells are routinely obtained.[6] Recommended density of implanted cells is between 50 to 70 million cells per ml. Cellular implantation can be performed by an epicardial or an endovascular delivery approach[6].

### Clinical Trials Using Myoblasts

Menasché's group in Paris began using skeletal myoblasts in cell cardiomioplasty in humans, in 2000.[4] Autologous cultivated skeletal myoblasts have been implanted in postinfartion myocardial scars during coronary artery bypass graft surgery.[3, 6, 8, 12]

As of 2003 over 100 patients had been treated worldwide[3], with different techniques and variety of cell types.[3, 4] Cellular cardiomyoplasty using autologous skeletal myoblasts was performed by the group of Chachques in 18 patients by 2003.[3]

Inclusion criteria for adult patients are: a low ejection fraction, akinesis and non-viable post-infarction scar.[3] In 2002 in Argentina, Trainini *et al.* reported a case of a patient with a diagnosis of ischemic-necrotic myocardiopathy who was treated with an implant of autologous skeletal myoblasts. This implant was the first one of this kind performed in Latin America[5] and results were favorable.

Cellular cardiomyoplasty promises a variety of beneficial effects such as: reduction of size and fibrosis of infarct scars, limitation of postischemic ventricular remodeling, improved of left ventricular wall thickening, and an increase of regional myocardial contractility (these are preliminary results in humans)[6]. Implanted cells orient themselves against cardiac stress preventing thinning and dilatation of the injured region.

## CONCLUSIONS

Trainini *et al.* confirms that no definitive treatment exists and that such therapy is an urgent research priority.[8] Cell therapy has emerged as a strategy for the treatment of many human diseases.[11] Myogenic cell grafting within the myocardium to improve contractile function has emerged as a promising technique for ischemic left ventricular systolic dysfunction.[2, 15] This novel therapy may be a dream, but if successful, it could be a definitive treatment for heart failure.[9] Our group (México-Research Group at Universidad Autónoma de Ciudad Juárez) is currently working on animal model of myocardial infarction. Our goal is to regenerate a myocardial scar with satellite cells. While thus far, success has been elusive, we continue strive for a day when we can provide a definitive therapy for heart failure.


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ARTICLE

# Should routine antenatal screening for HIV be introduced into New Zealand?


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The issue of antenatal HIV screening becoming routine, rather than based on risk assessment, which is currently the case, has become an important discussion point in New Zealand. This article aims to present arguments for and against the adoption of this new screening policy.

Perinatal transmission of the human immunodeficiency virus can occur during multiple stages, this includes the intrauterine (during pregnancy), intrapartum (during labour) and the postpartum (after delivery through breast-feeding) periods.[1, 2] The risk of transmission from mother to baby varies from 15-45%, with factors such as viral load, viral subtype, maternal immune status, presence of maternal sexually transmitted disease (STD), obstetric technique, labour duration as well as they extent of breastfeeding in infancy accounting to various degrees for this variability.[1, 2] Breast-feeding in particular sees to be an important mode of transmission, increasing the risk by approximately 10-20%.[2] This is why mothers with HIV are advised to use other available and effective alternative to breast-feeding.

In 1994 research in the United States showed that giving AZT to HIV infected women and to their infants after birth could reduce the rate of HIV transmission from mother to child from 25% to 8%, with even further reduction after implementation of other preventive measures, such as caesarean delivery and refraining from breast-feeding.[3] With all the prevention strategies in place the risk of perinatal transmission can be reduced to below 2%.[2, 4] Since the advent of such effective interruption of transmission of HIV from mother to baby, the antenatal identification of HIV-infected women has become of great importance in reducing the number of newborns born HIV-positive of seroconverting after birth.

In many countries overseas, universal counseling as well as offering and HIV test to all pregnant women has been instigated. In 1997 the Ministry of Health in New Zealand developed interim guidelines for risk-based HIV testing of pregnant women.[4] This means that women should be asked a set of questions which screen for various risk behaviors and if any risk factors are present or unclear, they should then be offered counseling and voluntary testing. However, it has become apparent that this policy is not being adhered to very well, and therefore reassessment of the screening strategy needs to be done.[5]

There are several reasons why the implementation of the current risk-based screening method is not adequate. Time constrains, lack of skills at counseling as well as the inaccurate assessment of maternal risk are all cited as factors that play a role.[1] Other reasons that also influence the reluctance of health professionals to ask question about risk status are the generally low rates of HIV in the community and the feeling of fear of offending their patients.[4] There is also a certain degree of embarrassment when addressing such issues, both on the side of the health professional and the woman. Moreover, women may feel targeted or singled out when HIV testing is recommended and this has the potential of having a negative impact on the maternity carer/woman relationship. Thus, a proportion of at-risk women are not being tested. Another issue to consider is that some women may not be aware of, or underestimate, their risk and therefore would be missed as well.

Putting in practice a routine screening policy has several advantages, which would go some way to counter the barriers of the current screening program. One such advantages is that it would increase acceptability of HIV screening, as it would remove the stigma of being targeted, especially in the populations, which are already at increased risk, such as specific ethnicities or socio-economic groups.[1, 6] Since pre-test counseling would have to be widely implemented, this would provided a good setting for health professionals to discuss HIV and other sexually transmitted diseases, as well as exploring any personal issues related to sexual health. Educating women and thereby increasing knowledge on a population scale would go a low way to increase awareness and reduce stigmatization of the subject. Moreover, women who are better informed about the risks and transmissibility of HIV are more likely to address risky behaviors since they would be more aware of their consequences. This would be a form of primary prevention in those at risk of infection.

The primary reason for screening of pregnant women, however, is to reduce the incidence of perinatal HIV infection. In the 5-year period from 1999-2003, 13 children were diagnosed with HIV, of whom 5 were born to mothers whose status was not known when they were pregnant.[7] According to the discussion document on HIV screening in pregnancy publish in October 2003 by the National Health Committee, if all infected pregnant women in New Zealand were detected, an additional 4 -18 would be diagnosed with HIV annually, and if intervention to prevent perinatal HIV transmission were taken up by all of these women, it is estimated that on average 1-4 perinatal HIV infections could be prevented each year. It should be noted that these figures are only estimates. Although the main route of HIV transmission in New Zealand is still through men having sex with men, the number of men and women infected by heterosexual spread has increased in recent years.[7] With more women becoming infected, the problem of perinatal HIV transmission may become more marked in the years to come. However, with routine screening, more of these women would be diagnosed early and thus would be able to make informed choices

about the rest of their pregnancy. Apart from having obvious benefits for the well-being of the baby, diagnosing the mother would also enable her to make decisions about her own long-term treatment as well has reviewing her behavior so as to limit the risk to others.

An important point is that routine testing should remain voluntary to maintain a woman's autonomy in the decision making process. Otherwise, compulsory testing may actually drive some women away from prenatal care altogether.[5] Compliance with medical care is likely to be greatest when the woman believes that she has made an informed decision regarding HIV testing, and has a relationship of respect and trust with her health care provider.[8] This raises the issue of adequate counseling before testing is offered. Even if HIV testing becomes one of the routine antenatal blood tests, this should not diminish the importance of giving accurate information and asking specifically for consent.

The addition of routine HIV counseling and screening to antenatal care will have great resource implications on the New Zealand health system. Before a screening program such as this is begun, one has to ascertain that the health care system is capable of supporting all the necessary elements of the screening pathway, including the diagnosis, follow-up and program evaluation and monitoring.[5] This means that a national policy has to be put in place, which will mean equitable treatment of the whole population. Such policy development and implementation would require a considerable amount of funding from the government. Areas that would require particular attention are: staff training, facility improvement, application of monitoring and quality assurance systems. It is important to educate and train staff sensitively and in a culturally-appropriate manner to be able to deliver information in the form of pre- and post-test counseling. This is especially important for the Maori population so that their needs are met adequately as well. Printed material that suitably targets various ethnic groups would be of considerable benefit in improving community awareness and test acceptability.

Since the cost of this new screening strategy would be significant, one has to wonder about its cost effectiveness. An analysis carried out in England showed that in areas of high prevalence, routine antenatal screening was indeed cost-effective, becoming less so in areas of lower prevalence.[9] Therefore, in low prevalence populations such as New Zealand, even with a very high uptake, the absolute impact is bound to be limited.[4] This has been a major argument against implementing the new screening policy, as one needs to ask whether it would be the best expenditure of scare health dollars.

Some also argue that the addition of HIV into routine antenatal screening would further add to the medicalisation of pregnancy and a shift of focus from mother to baby.[4] However, this can be reduced by a good explanation of the risks of HIV infection as well as the benefits of screening and early treatment, for both the mother and the baby. Women will most likely be more willing to participate in screening when they are fully informed. Unfortunately, this process is likely to further add to the time-pressure of consultations. One of the important issues is that women will have to be informed about the possibility of a false-positive result. Under the current protocol of testing, one in every thousand uninfected woman would require retesting a month after the initial screen before they could be reassured that they were not infected.[4] This would result in unnecessary anxiety for affected women, during a time that is frequently challenging already. Another source of possible anxiety is whether results will be kept confidential. Patient confidentiality must be maintained as strictly as possible. However, health care providers also have to be aware of specialists to whom infected patients can be referred for further counseling and management.

There are many arguments for and against the routine HIV screening of pregnant women. The main ones against the adoption of the new screening policy are that it will require a substantial amount of scarce health care resources will further medicalise pregnancy and may cause significant anxiety among women who test false positive. On the other hand, there are also many reasons why the new strategy should be put into practice. There is a slowly increasing number of heterosexually infected individuals in the community and this is bound to have an impact on the number of perinatal infections. A voluntary routine screening program, which tries to normalize testing and remove stigmatization, would thus probably be more likely to pick up a greater proportion of HIV infected pregnant women than one based solely on risk assessment. Such routine screening would also hopefully increase public awareness of the issues and augment the safe sex message. In conclusion, to make a well-informed decision about the prospect of altering antenatal screening policy, the government will have to weigh up the cost and benefits of such a policy change.

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CASE REPORT

# A case of Grave's disease and thymic hyperplasia


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A 43 year-old woman presented with a six week history of weight loss, tremor, eye irritation and diarrhoea. A diagnosis of Grave's disease was made based on positive thyroid antibodies and diffuse uptake of tracer on a thyroid scintiscan [figure 1]. Her past history included branchio-oto-renal (BOR) syndrome and a repaired patent ductus arteriosus aged 7. On clinical examination she had a small diffuse goitre. She was commenced on carbimazole and atenolol. Three months later she complained of dysphagia and dysphonia. Her goitre remained unchanged to clinical examination and was thought unlikely to be causing compressive symptoms.

A contrast-enhanced CT scan of the neck and mediastinum was performed [figure 2]. There was posterior projection of the left and right lobes of the thyroid gland but no clear evidence of oesophageal compression. Incidentally, an anterior mediastinal mass was found, separate from the posterior pole of the thyroid and measured 6x2cm transversely and 3cm in length (Figure 1; **x**). Tumour markers for -fetoprotein, -hCG and CA-125 were negative. She was referred for thoracoscopic biopsy of the mediastinal mass. At surgery, an enlarged thymus gland was identified. Histology of the tissue biopsy revealed prominent lymphoid follicles consistent with thymic hyperplasia.

Despite there being several reported cases of Grave's disease and thymic hyperplasia in the literature[1,2,4], this association is often not recognised. Although the pathophysiology of this association is unknown, two hypotheses have been proposed. One proposes that abnormal T-cell recognition is present, similar to that seen in myasthenia gravis. However, this is not supported by that fact that thymectomy does not result in an improvement in hyperthyroidism.[1] The other hypothesis proposes that there is autoimmune stimulation of thymic hyperplasia similar to that seen in pre-tibial myxoedema and Grave's ophthalmopathy. IgG activity against thymocytes has been identified in a patient with Grave's disease and thymic hyperplasia.[2] In support of this theory, thymus size and density have been observed to regress significantly when thyroid hormones and antibodies return to normal levels after successful treatment of Grave's disease.[3] In addition, thyrotoxicosis itself may also stimulate thymic growth. Thyroid hormones have also been shown to increase thymulin, a thymic nonapeptide essential for T-lymphocyte differentiation and function.[4] However, there were no reports of thymic hyperplasia in other forms of hyperthyroidism.

To our knowledge, no association between BOR syndrome, Grave's disease and thymic hyperplasia has previously been reported. BOR syndrome is an autosomal dominant disorder caused by mutation in the human eye absent (EYA)1 gene. EYA1 is involved in the morphogenesis of organs derived from the pharyngeal regions including the thymus, thyroid and parathyroid glands. Inactivation of EYA1 in experimental animals resulted in hypoplasia of the above organs.[5] It is therefore unlikely that BOR syndrome would result in thymic hyperplasia.

In patients with Grave's disease found to have an anterior mediastinal mass, thymic hyperplasia should be considered. Surgery and biopsy may be avoided if the mass is shown to regress in follow-up CT scans. Where uncertainty exists, thoracoscopic biopsy should be undertaken to determine the nature of the mass. In the context of this patient, BOR syndrome is likely a separate and unrelated disorder.

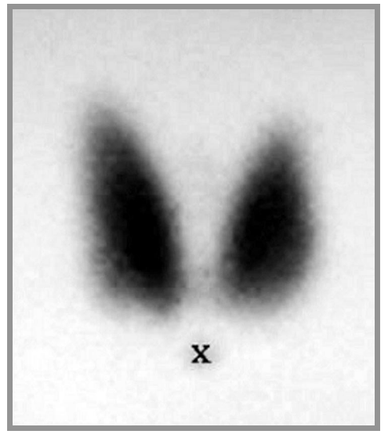


**Figure 1.**
Thyroid scintiscan, indicating hyperthyroidism associated with Graves disease. Note the anterior mediastinum mass (x).