Editorial

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The fascination with the mystery of new life in utero dates from very early times. For example, Hippocrates made many astute original observations about pregnancy. However, the beginning of real understanding of fetal physiology and development processes is a relatively recent accomplishment. The development of ultrasound and its application to medical diagnosis has been a milestone in fetal medicine. New surgical techniques and the development of biological markers for early detection of fetal abnormalities have also contributed to significant advances in the area. These developments in research and technology have made it possible to detect congenital defects at very early stages of gestation. These powerful diagnostic tools, coupled with significant advances in surgical techniques, have given rise to a relatively new concept in medicine; the fetus as a patient. This new area of medicine seeks to provide effective intrauterine treatment which may uniquely prevent or ameliorate otherwise irreversible fetal defects in various congenital disorders. The fetus, therefore, becomes the central entity in terms of active therapy. In a sense, such treatment can be considered to be preventive medicine, since successful intrauterine therapy may prevent

the devastating consequences of congenital defects in postnatal life.

Antenatal diagnosis of a defective fetus presents three options to a physician. The first is not to intervene until birth, and hope to alleviate the problem postnatally. The second option is to terminate the pregnancy. The third option, which avoids the moral and psychological conflicts presented by the first two, is to intervene with some form of fetal therapy. Clearly, the third option is an attractive one but is far from universally accepted by the medical community. Given the relatively primitive level of our current knowledge, even the strongest proponents of fetal therapy would agree that many, perhaps most, congenital defects cannot be treated successfully in utero. However, there remains a significant number of fetal anomalies in which the results of treatment can be significantly improved by in utero intervention. Even in the case of favorable prognosis for treatment, there are many physicians who still insist on either of the first two options rather than risk a venture into the somewhat less familiar area of fetal medicine. This scepticism is a common phenomenon when a radically new approach appears. Physicians have the well-being of their patients as their

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foremost consideration. Our current poor state of knowledge of fetal physiology and pathology and the rather mixed results in some attempts of intrauterine intervention have caused many

clinicians to adopt a cautious course. A better understanding of all aspects of fetal life and further development in treatment techniques is bound to change these attitudes. A strong driving force in favor of development of fetal medicine is the simple fact that as more and more fetal anomalies are detected as a result of rapid advances in diagnostic techniques, the demand for the third option (fetal treatment) will grow.

Intrauterine treatment has broad implications in terms of legal and moral problems, some of which have yet to be resolved. In all cases where in utero surgical treatment is contemplated, it must be justifiable on the basis of biological feasibility and bioethical acceptability. As in any procedure, the guiding criterion has to be that the contemplated treatment significantly enhances the possibility of a more positive outcome over that of some other course of action.

Another very important aspect of fetal therapy, particularly when surgical techniques are used, is the fact that two patients are involved, the fetus and the mother. It is obvious that any surgical procedure entails some risk. In the case of the materno-fetal unit, a healthy mother is placed in a position of risk in order to alleviate the problems of the other patient – her unborn child. Thus, it is vital that such procedures be carried out only after a consensus has been agreed to by a group of highly qualified professionals and then only with the informed consent of the mother and father of the fetus. The mother should never be forced to agree to intrauterine surgery. This unique situation is entirely

different from postnatal treatment involving a single patient who will bear the risks of the proposed treatment, but will also reap its benefits. Unfortunately, there are already initial signs that some members of the legal and medical professions are interested in testing the possibilities that a mother might be forced into an unwanted surgical intervention in order to protect the rights of the fetus. If this view prevails, a court of law would be able to force the mother to involuntarily undergo a potentially hazardous procedure to benefit her unborn child. It is of paramount importance that such legal intrusions into what are largely medical and personal decisions should be actively resisted.

In spite of these problems, significant strides in fetal therapy have been made already.

At this stage of our knowledge, some fetal deficiencies may be alleviated effectively by antenatal administration of various drugs to the pregnant mother or by direct injection into the amniotic fluid. Treatment of genetic diseases by such novel techniques as stem cell reconstitution or genetic manipulation are very interesting concepts, but are still at an early experimental level. In utero corrections of anatomic malformations, which interfere with fetal development, is an active area of basic and clinical research. In most cases, these new procedures necessitate the development of new surgical expertise.

The first efforts in fetal therapy were the fetal intraperitoneal transfusions to treat Rh incompatibility causing erythroblastosis fe-talis. The pioneer in the area was Liley who published the first description of his procedures in 1963. It would not be an overstatement to call him the father of fetal surgery. Dr. Liley was to have been an editor of this journal; unfortunately, his premature death

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in 1983 deprived us and the whole field of his creativity and wise counsel. This issue contains a reprint of Liley's article from the Australian and New Zealand Journal of Psychiatry, in which he argues that the fetus is not only a patient but is also endowed with a definite behavioral pattern.

Fetal surgery declined when the frequency and seriousness of erythroblastosis fetalis was reduced dramatically by preventive measures. Moreover, the lack of reliable antenatal diagnostic techniques of lethal or serious congenital anomalies left fetal surgery without a diagnostic foundation. As early as 1966 Adamson and 1968 Jackson, the pioneers of fetal surgery, were predicting that fetal surgery would have a place in the future for treatment of hydrocephalus, diaphragmatic hernia and fetal neoplasms. These visionaries also predicted accurately that this type of intervention would have to be predicated upon the possibility of making an accurate diagnosis and a clear understanding of the fetal pathophysiology for each of the lesions for which therapy is contemplated. Louw suggested in 1974 that the list could possibly be extended to other lesions such as spina bi-fida and esophageal or intestinal atresias. He felt that the pediatric surgeon should 'not stop at neonatal nor fetal anomalies, but maybe start tampering with the embryo: -removing a gene here and implanting one there,... forever striving to improve the quality of life...'.

Recent developments in fetal surgery have followed the earlier predictions. Thus, serious attempts have been made to treat fetal hydrocephalus by implantable ventriculo-amniotic intrauterine shunts. Hydrocephalus frequently results in brain damage and various neurological complications, which may be a prelude to severe mental retardation.

Although initial treatment attempts have had mixed outcomes, better techniques, better shunts and better patient selection will make intrauterine therapy a viable choice for a significant number of cases of fetal hydrocephalus. Attempts to treat fetal obstructive uropathy (which leads to progressive renal dysfunction and death) by intrauterine catheterization of the bladder or the kidneys have had variable success. It appears that at least some of the failures were caused by inappropriate patient selection, since many of the treated fetuses with obstructive uropathy already had severely damaged kidneys and expired either from respiratory or renal failure. It is highly encouraging that the clinical investigators in their early attempts have been scrupulously honest in reporting of the results, even when these were not particularly attractive. This attitude allows others to learn from their experiences and permits a careful assessment of future developments. Currently, serious consideration is being given to the possibility of in utero surgical intervention for such anomalies as diaphragmatic hernia and spina bifida.

The most attractive aspect of fetal surgery is that the recovery of the patient is aided by a number of unique factors which are not present in postnatal life. Among these are the fetomaternal immune surveillance system, regeneration and redifferentiation potential, high vascularity of fetal tissue, and rapid healing promoted by fetal growth factors.

Fetal treatment is not a new concept, but it has only recently gained considerable momentum. In July 1982, twenty-nine international experts on fetal medicine met in California. Among other things, it was decided to establish a registry of fetal treatment at the University of Manitoba to monitor the various experimental treatment protocols. The statistics gathered by the registry will

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allow an assessment of the benefits and liabilities of fetal therapy. The second meeting of the fetal therapy group held in Aspen in 1983 was much larger and resulted in the formation of the Society of Fetal Medicine and Surgery. An important accomplishment of the first meeting in California was to establish a set of general and specific criteria for fetal treatment, whose purpose was to maximize the likelihood of successful outcome of the therapy. At the same time, a consensus was reached that an institution undertaking fetal surgery should meet certain

standards. It must have a high-risk obstetric unit and a level 3 (high technology) intensive care nursery. Moreover, since fetal treatment involves two patients, it requires a well-organized team effort with ready access to various specialists. Among these are: an obstetrician experienced in intrauterine fetal blood transfusion and surgery, a pediatric neurosurgeon, a pediatric surgeon with expertise in the treatment of preterm neonates, level II sonographer experienced in the diagnosis of fetal anomalies, a geneticist, an obstetric/neonatal anesthesiologist, and a neonatologist. Support from mental health staff and access to bioethical consultation should also be available. In fact, the hope of progression of fetal treatment from an experimental to a routine approach depends very much on a team approach and cooperation among these experts. There are several well-established fetal program centers in the United States and Canada. There are also several well-known European centers such as King's College in London (UK), the University of Bologna (Italy), Zagreb (Yugoslavia) and Bonn (FRG). One of the first centers was in Auckland (New Zealand) and there is one in Sydney (Australia), in Israel and in Chile. The number of centers and the level of interest in fetal medicine are growing rapidly. However, just over one hundred cases of various congenital defects, particularly hydronephrosis and hydrocephalus (sonographically diagnosed and treated in utero) have been entered into the international registry of fetal treatment in Manitoba. In general, the outcome of intrauterine treatment of obstructive uropathies showed high mortality and low morbidity, in contrast to the treatment of fetal hydrocephalus, where mortality was low but morbidity was relatively high.

It is important to stress here that these data are derived from first attempts of fetal treatment and therefore should not overshadow the scope and potential of fetal therapy. Some of the early attempts of intrauterine intervention such as repeated taps of dilated kidneys or lateral cerebral ventricles, were not based on sound assessments of fetal physiology and usually gave poor results. In general, some of the problems associated with intrauterine treatment of hydrocephalus and obstructive uropathy are very similar to those observed with fetal transfusions 3 years after the technique was introduced. The parallels are striking. A major problem was then, and still is, patient selection. The early transfusions were carried out in severely affected babies, late in their course of development. In fact, many of them died because the intervention had been inadequate. Similarly, many patients with obstructive uropathy have been treated after the kidneys were severely damaged and beyond salvage. Consequently, the mortality in neonates was very high because of respiratory failure. In utero treatment of fetuses with severely damaged brain parenchyma and decreased cortical mantle associated with multiple malformations and hydrocephalus has also resulted in a poor outcome in some cases reported.

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One important reason for the early failures has been the fact that various procedures have been attempted without the benefit of adequate testing in a relevant animal model. The need for such testing cannot be overemphasized. It seems self-evident that development of surgical techniques requires some trial-and-error, but a great deal of uncertainty can be removed if a substantial part of such development is performed on animals. Moreover, necessary data on the pathophysiology of congenital defects can be obtained with less legal and moral restraints in animal models. Considering what we now know about fetal treatment, success could be maximized by carrying out the procedures on carefully selected patients, performing the treatment at an optimal time in fetal development, improvement of techniques (especially shunting techniques) and application

of optimal toco-lytic agents to prevent premature labor. It is also important that these procedures be carried out in a coordinated effort by a team of specialists. We believe that additional research will help to resolve many of these problems in the near future and will make fetal surgery a truly important, perhaps first-choice method of treating some congenital anatomic defects.

Successful fetal therapy is an emerging field of medicine that requires the coordinated efforts of various specialists with a wide range of expertise in clinical medicine and basic sciences.

Currently, scientists who are concerned with the implication of fetal therapy tend to publish their work in various speciality journals. It has, therefore, become increasingly apparent that it would be advan-

tageous for proper advancement of this field to have an international journal of fetal therapy, which would provide a central forum for rapid exchange of information in the format of case reports and scientific papers in basic and clinical research. It will gather within its covers a wide range of topics related to fetal problems. We hope that this journal will help to foster better communication among all those who have a common interest in fetal therapy, but who came from diverse professional backgrounds.

With the help of all the contributors the principal objectives of the journal will be a quick exchange of information and the development of new strategies for fetal treatment as well as the promotion of this newly emerging field of medicine.

In the first issue we have chosen to emphasize the past and to try to 'take a peek at the future'.

Articles such as Liley's 'The fetus as a personality' underline the fact that although this is the first issue of a new journal, the field of fetal medicine is over 20 years old. Common threads which run through most of the papers are that effective therapy is absolutely dependent upon accurate diagnosis and upon accurate assessment of prognosis. Furthermore, sound fetal therapy can only be based on a solid foundation of understanding of fetal physiology and pathology.

Future issues will contain both clinical and experimental reports. It is an exciting time because it is virtually certain that the most important discoveries in fetal medicine are still in the future. We sincerely hope that this journal will make a contribution to this field's bright tomorrow.