The challenge of globalization and change to research

In such an environment, globalization and the enormous acceleration of social, economic, and political transformation process demands a different kind of research. While in the past the natural sciences including biology, primarily had a descriptive character, today they are becoming more and more synthetic and complex. For example, because of great increases in knowledge about molecular bases of pathogenesis and the course of illnesses, there are potential new improved therapeutic approaches. More attention will be devoted to individual diagnosis and personalized treatment, that is, treatments tailored to individuals, or a group of individuals with a similar clinical picture and a similar genetic background.

It is common knowledge that without the uncertainty of the new, nothing new is possible. Research means recognizing challenges and taking responsibility for the new.

However, it must be acknowledged that many errors will be made if we are to make progress. Therefore, we need a culture of tolerance for error, in which the error is seen as a constitutive part of acting.

While medicine is international, legal regulations are not. We can react in different ways to the challenges that these international differences pose to education in each country. Science must transcend parochial national laws. Innovation arises through creative and intensive processes in dealing with scientific problems. These processes are extremely complex and require intensive cooperation between many different disciplines in the natural sciences. These teams, their optimum composition, their necessary degrees of freedom, and their support should be the focus of every leader. Knowledge should be able to flow across borders through international partnerships and coordination at the global level. The International Academy of Perinatal Medicine and World Association of Perinatal Medicine are paradigms of this effort.

Europe: an effective response

Scientists in Europe have made a plea to the European Commission to support the European Research Council (ERC). This organization is governed by science itself and operates solely on the basis of scientific excellence and creativity. To date, the Commission has set up a committee consisting of 22 outstanding scientists with the task of developing the necessary rules for the ERC and its operation. In addition, some countries are already preparing themselves and their scientists for new variants of competition. At the beginning of last year, France founded an independent research financing organization, the Agence Nationale de la Recherche (ANR), with a starting capital of 350 million euros. At the end of June 2005, the federal and state governments of Germany launched the Excellence Initiative, which intends to infuse an additional 380 million euros into research each year. The aim is to bring German Universities on a par with other countries in research endeavors. Five years ago, in Barcelona, European leaders agreed to boost the level of research funding to 3% of GDP, with two-thirds of that coming from the private sector.

It has been estimated that the European Union produces almost one-third of the world’s scientific knowledge. The EU has acknowledged expertise in medical
research and environmental sciences and leads the world in many areas of chemistry, physics, pharmaceuticals, aerospace, telecommunications and transport. We need a coherent approach to build a Europe of knowledge whose main engines are research and innovation. This shows that the public spending on research represents not a cost, but an important investment in Europe's future.

An aging population: problem or solution?

As birth and death rates fall in Europe, the aging of our population is a trend that has long been recognized. According to demographic predictions, by 2050, the number of young people will drop by 20%. And by 2050, the number of people over 65 will make up 20% of our population. Elderly people are becoming an increasingly important group in society, and not just in statistical terms but as voters, consumers and opinion-makers. It is clear that no country in Europe will escape these demographic changes. However, older workers should not be considered part of Europe's problem but rather as part of the solution. Ivo Slaus has proposed the Italian word “Svecchiamento” – or “younging” – to encapsulate the positive sense of active-aging. What is very clear is that in a modern knowledge society, senior citizens must be increasingly viewed as an asset, and not as a burden. Perinatal medicine is a good example how we progress on the shoulders of our predecessors.

In the area of research more should be done to value and recognize the contribution of retired scientists. As well as continuing to use their intellect and knowledge, they can play various “ambassadorial” roles, and act as mentors for younger individuals. One excellent example is the annual meeting of Nobel Prize Winners in Lindau, where distinguished scientists “of a certain age” interact and debate key political and scientific topics with young researchers setting out in their careers.

Challenges for perinatal research

General health problems influence perinatal research. The proportion of couples diagnosed as infertile across Europe could double in the next decade, from about one in seven today, to one in three by 2015. A set of factors influence fertility across Europe. First, growing numbers of women now delay trying to start a family until their mid or late 30s. Second, there is a steep increase in the spread of sexually transmitted infection. Chlamydia in recent years has left many young women with blocked fallopian tubes, many of them unaware of the damage or the difficulties ahead when they try to conceive. Third, obesity is becoming more common, and obese women are more likely to experience abnormal ovulation and other reproductive problems. Fourth, sperm counts appear to be declining, although the evidence is less clear than for the other three factors.

Although Europe's case may be extreme, almost every industrialized nation is producing too few babies to satisfy the demographers. For example, for every woman who has a child at age 40, there are five or six who have failed.

A major goal of perinatal research is the prevention, early detection and treatment of malformations and genetic diseases. Statistics from developed countries show that mortality due to malformation has decreased substantially. It is clear that the potential health burden of congenital disorders can be reduced by implementing basic reproductive health approaches, including family planning, adequate diet, prevention and management of maternal infections.

However, perinatal medicine is at a stage when we can usually only recognize clinical syndromes rather than distinct disease entities caused by specific pathological mechanisms. This is true for five common obstetric complications: premature labor/delivery, premature rupture of membranes, small for gestational age, congenital anomalies and pre-eclampsia. The challenge is to apply the techniques of developmental biology to perinatal research, in order to prevent and treat these disorders by defining the pathophysiological mechanisms at the molecular and cellular levels. Only then could we hope to develop effective screening programs for the chronic intrauterine diseases that usually manifest themselves clinically in the third trimester or after birth, too late in their natural history to optimize perinatal outcome.

Comprehensive screening programs, eventually based on non-invasive alternatives to the invasive tests we have today, are required to identify mothers and fetuses destined to develop pre-eclampsia, premature labor, placental abruption, premature rupture of membranes and fetal growth restriction. They should be identified early enough to allow intervention to prevent not only the clinical manifestation of disease but the resulting long-term handicap.

Traditionally, the major focus of perinatologists in genetic screening and diagnosis has been the detection of chromosomal abnormalities. In the past decade, major breakthroughs in molecular biological technologies have enhanced understanding of the molecular basis of monogenic genetic diseases as well as many non-fatal or chronic diseases. This allows the possibility of precise prenatal diagnosis of these conditions. At the same time, the elucidation of the genetic basis of many chronic diseases or multifactorial diseases has challenged perinatologists with regard to the ethics of prenatal screening and diagnosis of these conditions.

It appears that the most reliable and precise method of diagnosis and screening of a mutation or deletion is by molecular tests. In the next decade, it is likely that there will be an exponential increase in the number of
diseases and mutations that can be detected or diagnosed during pregnancy, not only using samples obtained by invasive tests such as amniocentesis and chorionic villus sampling, but also non-invasively by examining the cell-free DNA in the maternal plasma. A major obstacle at present is the high cost. However, as for any technology, this is unlikely for the future. Technologies develop so fast that our problem will no longer be what we can test for, but rather what we should test for.

Cerebral palsy (CP) is the commonest cause of severe physical disability in children in Western countries. The main etiological factors were found to be perinatal in two-thirds of the children and prenatal in about one in five. The underlying causes of CP have been difficult to identify, but recent advances in neuroimaging have shed some light on the timing of the brain lesion, if not always on the cause of damage. Central nervous system (CNS) malformations occur during the first and second trimester, while white-matter lesions occur predominantly between the 24th and 34th week of gestation, followed by basal-ganglia and gray-matter lesions from the 34th week and onwards. From neuroimaging findings, it has been suggested that no fewer than 75% of the lesions causing CP are derived before the third trimester, some of them of prenatal and some of perinatal origin.

During the last 20 years, real-time ultrasound has facilitated in vivo observation of human fetal movements, and behavioral patterns in utero can be assessed as a one-to-one match between manifestation of an individual activity and corresponding CNS function. However, to date no generalized antenatal screening system for fetal CNS function has been developed and validated. With the advent of 3D/4D sonography new improved and promising possibilities for studying the fetal brain function are possible.

Familial cerebral palsy was uncommon, and it accounted for 1.6% of all cerebral palsy cases. However, for parents who had had one affected child, the risk of recurrence in another child was considerably increased, as documented by a recent paper from Sweden.

The remarkably high familial risks are difficult to explain without some contribution of heritable factors. The lack of discordant pairs may suggest that heritable factors are disorder type-specific. Affected concordant sibling pairs should be subjected to molecular studies aiming at identifying the susceptibility gene. Obviously, we will need help from molecular geneticists in future research endeavors.

Conclusion

In conclusion, globalization and change are an undeniable reality. The future of perinatal research will require new approaches to perennial problems. If this challenge is confronted, the potential has never been greater to improve the quality of care for the mothers, fetal patients, and children we serve.

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