Perinatal listeriosis

Perinatal listeriosis was first reported by Burn in 1933 and is now estimated to affect one in 20 000 births.¹ About a quarter of the 424 reports from England, Wales, and Scotland in 1983 to 1985 were in children less than 1 month old, and half of these were neonatal infections (Communicable Disease Surveillance Centre, unpublished data).

Listeria monocytogenes is a short, Gram positive, non-spore, motile rod whose isolation is enhanced at 4°C. It is a facultative anaerobe, and there are four antigenic serotypes, of which types 1 and 4 are the main ones causing infection in man.² The epidemiology of listeria infections has remained obscure: although the organism infects many different animals and has been cultured from soil and faeces, infection in man does not result primarily from direct contact with infected animals.³ Neonatal infection may be caused by cross infection,⁴ and outbreaks often occur in clusters⁵ or epidemics.⁶⁻¹⁰ *L. monocytogenes* may be a normal resident of the intestinal tract with potentially pathogenic properties, which would explain why antibodies to listeria are common in healthy people.² Rectal carriage by pregnant women was 10 times higher during an epidemic in New Zealand.⁹ In Israel the symptomless carriage of *L. monocytogenes* in the genital tract was associated with a history of recurrent abortion,¹¹ but this was not confirmed in Britain¹² or the United States.¹³

Listeric infection of the fetus during pregnancy is often associated with a non-specific, flu like, pyrexial illness in the mother.^{14,15} Decidual microabscesses and characteristic foci of purulent villitis within the placenta have led some to believe that fetal infection is caused by the bloodborne transplacental passage of organisms from the mother^{10,16}; severe chorioamnionitis is, however, in keeping with an ascending pathway of infection.^{6,17} Fetal infection in early pregnancy results in abortion, and the extensive maceration seen at delivery, so soon after the maternal symptoms, suggests that the maternal bacteraemia may result from rather than be the cause of the fetal infection.² Fetal infection later in pregnancy causes stillbirth¹⁵ or preterm labour associated with meconium stained liquor and an infected baby.⁶⁻¹⁰

Congenital listeria infection presents soon after birth as pneumonia and septicaemia, and *L. monocytogenes* was isolated from the vagina of 37% of mothers of such infants.¹ The high mortality of 35-55% reflects associated prematurity.¹⁶⁻¹⁸ Microabscesses and granulomas containing the organism are found throughout the body at necropsy¹⁸—particularly in the lungs, liver, and spleen—giving rise to the term granulomatosis infantiseptica.¹⁶ A high rate of disability among survivors has been reported,¹⁹ but this does not always occur.^{6,9} Neonatal infection, acquired during delivery from the mother's genital tract¹⁴ or later by cross infection,¹⁴ presents as septicaemia and meningitis several days or even weeks after an uneventful birth.^{7,8,19} A granulomatous macrocytic inflammation of the meninges may lead to microabscesses in the brain, but this form of neonatal listeriosis has a lower mortality,^{7,9} and survivors are unlikely to have neurological sequelae.^{9,19}

Treatment of suspected neonatal infection usually begins before firm bacteriological confirmation. The combination of ampicillin or penicillin with gentamicin or kanamycin is more effective against listeria than other agents alone or in combination.^{8,20} Listeric septicaemia in the mother during

pregnancy has been successfully treated with ampicillin, and such treatment prevented perinatal listeriosis.^{10,21} Success in managing this condition depends not so much on considering the diagnosis¹⁰ but more on the degree of fetal or neonatal infection at the time of presentation.¹⁵

JOHN A D SPENCER

Senior Lecturer and Consultant,
Royal Postgraduate Medical School Institute
of Obstetrics and Gynaecology,
Queen Charlotte's Maternity Hospital,
London W6 0XG

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Make way for the new genetics

Although recombinant DNA technology may not be easy to understand, the new genetics is important for clinical practice.¹ Much better information can be given to potential parents worried about genetic disease, while genetic diseases are increasingly preventable and may eventually be treatable.

The potential is vast and there are so many diseases that are mainly genetic in origin that one in 50 children suffers death or chronic disability from these. Premature coronary artery disease, cancer, and other common diseases also have an important genetic component and are candidates for renewed genetic exploration. For example, recent DNA studies with rare familial Alzheimer's presenile dementia² and manic depressive psychosis³ have introduced a new genetic and biochemical approach to common psychiatric problems. At the present rate all genetic disorders will probably be mapped to their chromosomal location by the year 2000,⁴ and most important genes will eventually be sequenced and their products identified.

As the potential of the new genetics increases it is not clear who will look after the interests of the families and undertake the explanation and counselling that must precede tests designed to probe the most intimate and socially sensitive genetic secrets. Who will insure that informed consent is obtained, arrange the family studies, keep the confidential records, and store the banks of DNA spanning whole families and several generations? This is a dangerous topic for amateurs, and if they have received no genetic training doctors may have difficulty recognising genetic risk. Litigation by older women who have produced infants with Down's syndrome showed that family doctors, obstetricians, and paediatricians in particular have an obligation to warn people when they have a high genetic risk and to arrange genetic tests.

Who then will take up the challenge of the new genetics and link laboratory work to good family medicine? The size of the task means that clinical geneticists cannot cope alone. Young found that most general practitioners were aware of this,⁵ and my experience on training committees shows that some paediatric and obstetric trainees are already seeking clinical genetic training. But who will teach medical undergraduates and postgraduates and insure that what they are taught is relevant to clinical needs?

A survey of British medical schools in spring 1986 showed that some of the next generation of medical graduates may not be well prepared (unpublished data). Two medical schools reported that there was no separate preclinical teaching of genetics, and 13 reported that there was no separate clinical genetics. We have little evidence on the relevance of the teaching given by non-medical geneticists in anatomy, biochemistry, pathology, or other courses. Similarly, the General Medical Council noted 10 years ago that ad hoc clinical teaching in genetics is variable and difficult to verify.⁶

The survey of medical schools showed, however, that university departments of medical or human genetics linked with genetic clinics in the National Health Service provide a good environment for this teaching (Royal College of Physicians, unpublished data). Schools with departments of human or medical genetics did more undergraduate teaching of genetics than schools without such departments—an average of 23.5 preclinical hours and 8.1 clinical hours compared with 14.4 and 1.8 hours. Those with departments also included more scheduled visits by students to genetic clinics, where genetic counselling techniques may be observed. The departments' associations with NHS consultant clinical geneticists and regional genetic centres are valuable as they encourage clinically relevant teaching and research.

Unfortunately such combined genetic centres are few and have limited resources. Similarly, although specialist training in clinical genetics is well established, the number of clinical geneticists falls far short of the minimum required⁷: there are only seven senior registrar training posts in the

NHS and about 30 consultants in the whole of Britain. Plans to increase this to about 60 consultants were conceived before the dawn of the new genetics—yet one clinical geneticist for each million of population will be hard pressed indeed.

Because genetics has important implications for all specialties priority should be given to education in medical genetics for all grades of health care professionals.⁸ This is best achieved by developing NHS regional genetic centres associated with universities that will provide specialised laboratory and clinical genetic services and also coordinate genetic education of non-doctors. Fortunately the Department of Health and Social Security is well informed about medical genetics and has already contributed to evaluating new techniques. Unfortunately it has other claims on its resources and is hampered by the current central policy of non-intervention in the affairs of dilatory NHS regions. In these circumstances the DHSS and the NHS regions require unambiguous evidence of need from consumers before major developments can be approved. Ironically, patients with genetic diseases may be the least able to express their needs, and the pleas of individuals at risk of relatively rare genetic diseases will go largely unheard. If consumers want genetic services a coordinated approach from an association of all the genetic organisations is essential, and this should include factual data on the benefits of the new genetics for their members. We could not ignore such an appeal because genetic disorders are responsible for much preventable anxiety, handicap, and premature death.

RODNEY HARRIS

Professor of Medical Genetics,
University of Manchester,
St Mary's Hospital,
Manchester M13 0JH

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Correction

Use and abuse of allopurinol

An error occurred in this leading article by Professor J Stewart Cameron and Dr H Anne Simmonds (13 June, p 1504). The formula used to calculate clearance was incorrect and—for men—should have read:

$$\text{Creatinine clearance (ml/min)} = \frac{(140 - \text{age in years}) \times \text{weight in kilograms} \times 1.23}{\text{serum creatinine concentration in } \mu\text{mol/l}}$$

For women the value should be reduced by 15%.