allots separate categories to these forms of anxiety disorder—that is generalised anxiety disorder (300.02) and panic disorder (300.01). Furthermore, it recognises two distinct forms of agoraphobia—agoraphobia with panic attacks (300.21) and agoraphobia without panic attacks (300.22). Extensive definitions of all these categories are given. Panic attacks are defined as discrete episodes of apprehension or fear accompanied by at least four (from a list of 11) symptoms of somatised anxiety such as dyspnoea, palpitations, chest pain, and faintness. Panic disorder is defined by the occurrence of at least three panic attacks in three weeks in the absence of a life threatening situation or the coexistence of other psychiatric disorder.

Does this delineation of a separate form of anxiety disorder matter? The answer must be yes, for the existence of panic disorder is confirmed by clinical observation and it is becoming clearer that the correct choice of treatment depends on the form of anxiety. Though most psychiatrists accept that both biogenic and psychogenic factors contribute to the development of depressive disorders, there is a general unwillingness to acknowledge a biogenic origin for anxiety. The term “endogenous anxiety” has not yet crossed to the British side of the Atlantic, yet evidence accumulates for considering panic disorder to be biogenic or endogenous. In 1959 West and Dally³ observed that a form of neurotic disorder characterised by panic attacks and phobic symptoms responded to treatment with monoamine oxidase inhibitors and, since these drugs were conventionally regarded as antidepressants, they called the disorder “atypical depression.” Shortly afterwards an American worker made a similar observation and showed that an anxiety syndrome characterised by sudden onset, panic attacks, palpitations, and foreboding of death responded to a tricyclic antidepressant drug.⁴ A recent paper has summarised the evidence for response of panic disorder to either monoamine oxidase inhibitors or tricyclic antidepressants.⁵

Sheehan *et al* introduced the term endogenous anxiety for a disorder which is marked by spontaneous panic attacks, multiple autonomic symptoms, and overwhelming fear⁶; they pointed out that this disorder has sailed through medical history under many aliases, including effort syndrome, cardiac neurosis, separation anxiety, and the hyperdynamic beta-adrenergic circulatory state. They drew attention to the chronic course of this disorder before its effective treatment with antidepressant drugs was recognised. It is now time for this fact to be underlined. Patients suffering from this condition often present at accident and emergency departments, whence they may be referred to cardiac clinics and other medical departments: time and expense may be wasted on diagnostic procedures, and the patient, becoming increasingly demoralised by the unexplained attacks, develops ever more firmly entrenched hypochondriacal beliefs. If the patient is referred for psychiatric treatment psychotherapeutic methods, including behaviour therapy and cognitive techniques, will be ineffective until the panic attacks stop. Panic anxiety rapidly leads to secondary avoidance responses and the familiar neurotic disorder of agoraphobia develops.⁷ If antidepressant drug therapy is to be effective it must be prescribed early in the course of the disorder; entrenched phobias cannot be expected to respond to drugs and will require psychotherapy.

There are no firm grounds for preferring one type of antidepressant drug to another in the treatment of panic disorders, though two recent studies have shown that a monoamine oxidase inhibitor is more effective than a tricyclic drug in relieving anxiety accompanying neurotic depression.^{8,9} Patients suffering from panic disorder are very sensitive to the

side effects of these drugs and often stop treatment unless the dose is initially low and increased gradually over two or three weeks.

The increasing evidence that there is a biogenic form of anxiety disorder characterised by spontaneous panic attacks raises interesting questions and new directions for future research. The biological substrate of the disorder is likely to be similar to that of the biogenic form of depression since both respond to the same treatment. In turn this raises the question of whether panic disorder is atypical depression; certainly symptoms of both disorders may occur together but either may exist alone, and this points to a dimensional rather than a categorical classification and returns us to a view, recently abandoned, that at least some forms of anxiety state should be classified as affective disorder.¹⁰ A recent review has also suggested the need for new thoughts on classification.¹¹

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¹ American Psychiatric Association. *Diagnostic and statistical manual of mental disorders*. 3rd ed. Washington DC: American Psychiatric Association, 1980.

² World Health Organisation. *Mental disorders: glossary and guide to their classification in accordance with the ninth revision of the international classification of diseases*. Geneva: WHO, 1978.

³ West ED, Dally PJ. Effects of iproniazid in depressive syndrome. *Br Med J* 1959;ii:1491-4.

⁴ Klein DF. Delineation of two drug-responsive anxiety syndromes. *Psychopharmacologia* 1964;5:397-408.

⁵ Grunhaus L, Gloger S, Weissstut E. Panic attacks: a review of treatments and pathogenesis. *J Nerv Ment Dis* 1981;169:608-13.

⁶ Sheehan DV, Ballenger J, Jacobsen G. Treatment of endogenous anxiety with phobic, hysterical and hypochondriacal symptoms. *Arch Gen Psychiatry* 1980;37:51-9.

⁷ Mendel JGC, Klein DF. Anxiety attacks with subsequent agoraphobia. *Compr Psychiatry* 1969;10:190-5.

⁸ Ravaris CL, Robinson DS, Ives JO, Nies A, Bartlett D. Phenelzine and amitriptyline in the treatment of depression. A comparison of present and past studies. *Arch Gen Psychiatry* 1980;37:1075-80.

⁹ Rowan PR, Paykel ES, Parker RR. Phenelzine and amitriptyline: effects on symptoms of neurotic depression. *Br J Psychiatry* 1982;140:475-83.

¹⁰ Lewis AJ. Psychological medicine. In: Bodley Scott R, ed. *Price's textbook of the practice of medicine*. 10th ed. Oxford: Oxford University Press, 1966.

¹¹ Matuzas W, Glass RM. Treatment of agoraphobia and panic attacks. *Arch Gen Psychiat* 1983;40:220-2.

Infection and defences in neonates

Sepsis neonatorum—bacterial infection in the first month of life—affects up to 10 babies per 1000 births. Septicaemia accounts for up to half these cases, and about one in five babies with this develop meningitis; infection may also involve bones, joints, kidneys, or lungs. Preterm babies are especially vulnerable, but those born at term are not spared.

The clinical features of neonatal septicaemia range from a fulminating, early onset type presenting in the first 24 hours of life with peripheral circulatory failure and respiratory distress to a more indolent form manifesting later with non-specific signs such as an unstable body temperature, lethargy, jaundice, apnoeic attacks, and abdominal distension. Sclerema—a diffuse, non-oedematous, tallow like hardening of the sub-

cutaneous tissues—is an ominous sign associated with a mortality approaching 100%.

Early onset infection is generally acquired by the fetus from the maternal birth canal just before or during delivery, whereas septicaemia presenting later is more likely to be a nosocomial disease acquired, for example, from intensive care apparatus or the hands of attendants. The pattern of causative organisms varies widely from country to country. In North America group B streptococci and *Escherichia coli* are responsible for more than half of all cases of neonatal septicaemia. In Britain, though *E coli* probably tops the list, group B streptococci appear to be much less common. Other bacteria causing neonatal septicaemia include *Staphylococcus epidermidis* and *aureus*, *Klebsiella-Enterobacter* species, *Pseudomonas aeruginosa*, *Listeria monocytogenes*, and group D streptococci.

The mortality in septicaemia ranges from 20% to 70% or even more, the higher end of the range being associated with fulminating early onset group B streptococcal infection and with meningitis. Neurodevelopmental sequelae are seen in about 20% of survivors of septicaemia, and the outlook after meningitis is even worse—despite new antibiotics and improvements in intensive care. The gravity of neonatal septicaemia is partly explained by impairment of host defence mechanisms in the newborn, including reduced plasma opsonic activity,¹ defects in the number and function of granulocytes,² and deficient cell mediated immunity.³

Can anything be done to bolster these host defences? The transfusion of whole blood and plasma has been used successfully to treat neonatal septicaemia, and it is difficult to ignore accounts of the survival of babies with sclerema after exchange transfusions.⁴ These treatments are effective partly because of the donor blood having opsonic activity⁵ or sufficient opsonic antibody against the infecting organism.⁶ What is not clear is the relative importance of other potentially beneficial effects of simple or exchange transfusion such as an increase in plasma volume, blood pressure, and tissue perfusion; improvement in oxygen transport when adult haemoglobin replaces the fetal type; improved haemostasis; removal and dilution of bacteria and toxins; and an increase in the number of mature circulating granulocytes. Until such information is forthcoming we can only speculate about whether simple or exchange transfusion is better, the choice of donor, how fresh the blood need be, the ideal storage conditions before use, and the role of plasma. All these considerations are important because in a busy clinical service the paediatrician may have to settle for whatever product is immediately available if it improves the outlook, rather than the "ideal" product in terms of its humoral and cellular qualities.

Defects in neutrophil chemotaxis,⁷ phagocytosis,¹ and intracellular killing⁸ have each been described in newborn babies. Furthermore, in neonatal sepsis the marrow stores of neutrophils are rapidly mobilised and only slowly replenished, eventually exhausting the marrow and causing neutropenia.² Against this background, the idea of giving transfusions of mature granulocytes to babies with septicaemia is attractive, and the subject has been reviewed recently by Christensen and his colleagues from Salt Lake City.² Two reports on the successful use of this treatment in neonatal septicaemia are especially important because they concern contrasting series of babies. Those treated by Laurenti *et al*⁹ in Rome were nearly all suffering from infections with highly antibiotic resistant *klebsiella* or *pseudomonas*; the onset was towards the end of the first week and lasted several days. These infants received between two and 15 transfusions, each 20 ml/kg body weight, of a packed cell suspension containing $0.5-1.0 \times 10^9$

white blood cells obtained by continuous flow filtration leukapheresis. The mortality was only 10% compared with 72% in a similar group of neonates with septicaemia not treated by granulocyte transfusions.

In contrast, Christensen *et al*¹⁰ treated babies who were suffering from early onset fulminating septicaemia with neutropenia and exhausted marrow reserves confirmed by marrow aspiration. They used a similar concentration of granulocytes in each transfusion, but the transfusion was repeated only if neutropenia persisted; no more than two transfusions were ever required. None of the seven transfused babies died, whereas eight out of nine similar babies with septicaemia who were not transfused succumbed. Side effects, such as graft versus host reactions, were not observed in either series. More controlled studies are needed, but granulocyte transfusions may well improve the outlook for babies with fulminating early onset sepsis and those with a more indolent infection caused by antibiotic resistant organisms.

Improving host defences might also be one way of preventing neonatal bacterial sepsis. A vaccine prepared from capsular polysaccharide of type III group B streptococci is immunogenic in adults.¹¹ We may look forward to active immunisation of antibody deficient mothers and the passive acquisition of type specific antibody by the fetus. It might even be possible to prevent bacteria acquired by the mother colonising the epithelial surfaces of the newborn. Cox¹² recently reported that in studies on mice, maternal to newborn colonisation with group B streptococci was reduced by the topical application to the newborn of lipoteichoic acid—a substance known to interfere with adherence of group B streptococci to epithelial surfaces.

The problem of sepsis neonatorum will not be solved simply by introducing new antibiotics or by innovations in cardiorespiratory support of ill babies. However, the idea of improving host defences will make important new demands on laboratory services at the interface of microbiology, haematology, and immunology.

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¹ Miller ME. Phagocytosis in the newborn infant: Humoral and cellular factors. *J Pediatr* 1969;**74**:255-9.

² Christensen RD, Anstall HB, Rothstein G. Review: deficiencies in the neutrophil system of newborn infants, and the use of leukocyte transfusions in the treatment of neonatal sepsis. *Journal of Clinical Apheresis* 1982;**1**:33-41.

³ Chandra RK. Serum thymic hormone activity and cell-mediated immunity in healthy neonates, preterm infants, and small-for-gestational age infants. *Pediatrics* 1981;**67**:407-11.

⁴ Vain NE, Mazlumian JR, Swarner W, Cha CC. Role of exchange transfusion in the treatment of severe septicaemia. *Pediatrics* 1980;**66**:693-7.

⁵ Pelet B. Exchange transfusion in newborn infants: effects on granulocyte function. *Arch Dis Child* 1979;**54**:687-90.

⁶ Shigeoka AO, Hall RT, Hill HR. Blood transfusion in group-B streptococcal sepsis. *Lancet* 1978;**i**:636-8.

⁷ Miller ME. Chemotactic function in the human neonate. Humoral and cellular aspects. *Pediatr Res* 1971;**5**:487-92.

⁸ Wright WC Jr, Ank BJ, Herbert J, Stiehm ER. Decreased bactericidal activity of leukocytes of stressed newborn infants. *Pediatrics* 1975;**56**:579-84.

⁹ Laurenti F, Ferro R, Isacchi G, *et al*. Polymorphonuclear leukocyte transfusion for the treatment of sepsis in the newborn infant. *J Pediatr* 1981;**98**:118-23.

¹⁰ Christensen RD, Rothstein G, Anstall HB, Bybee B. Granulocyte transfusions in neonates with bacterial infection, neutropenia, and depletion of mature marrow neutrophils. *Pediatrics* 1982;**70**:1-6.

¹¹ Baker CJ, Edwards MS, Kasper DL. Immunogenicity of polysaccharides from type III group B streptococcus. *J Clin Invest* 1978;**61**:1107-10.

¹² Cox F. Prevention of group B streptococcal (GBS) colonisation in newborn mice with topically applied lipoteichoic acid (LTA). *Pediatr Res* 1982;**16**:238A.