the blood than any other antibiotic. Both sulphonamides and trimethoprim also cross the blood-brain barrier well, and co-trimoxazole has been used successfully in various forms of meningitis, though mainly in countries other than Britain. At the other end of the scale, in no circumstances do aminoglycosides such as streptomycin and gentamicin attain adequate concentrations in the CSF after parenteral injection, and intrathecal doses are imperative.

Intrathecal injections of antibiotics are usually given by the lumbar route, but even this may not be adequate. Cerebrospinal fluid is formed in the choroid plexuses and passes from the ventricles to the meninges. It is not to be expected that substances introduced into the subarachnoid space will flow in the opposite direction: so that if the inflammatory process should affect the ventricles as well it may be untouched by intrathecal medication. Lorber and his colleagues[1] pointed out that ventriculitis is a common complication of spina bifida and other congenital abnormalities of the central nervous system (and even more so if a ventricular shunt has been established), and according to Salmon[2] ventriculitis often occurs in infants with meningitis in the absence of congenital lesions. These authors and others have treated the condition successfully by direct intraventricular injection of antibiotics.

A recent report on the treatment of enterobacterial meningitis by Kaiser and McGee[3] of the Vanderbilt University School of Medicine, Nashville, Tennessee, is of interest. Of their five patients treated with intraventricular injections, three had a *Klebsiella* and one each *Escherichia coli* and *Pseudomonas stutzeri* infection; three were recovering from surgery, one from trauma, and one had immune deficiency. All had positive blood cultures, thus requiring parenteral treatment, but all also had positive cultures from ventricular as well as lumbar fluid. They were therefore treated with either gentamicin or tobramycin by both parenteral and ventricular routes, and the infection was eliminated in all of them, four recovering and one dying of surgical causes with sterile meninges. The main interest of the report is its elaborate study of the distribution of these antibiotics after administration by different routes. After parenteral injection alone the level in cerebrospinal fluid from any site was always less than 1 μg/ml. To follow the effects of local injections means were devised requiring the establishment of subcutaneous reservoirs for obtaining serial specimens of fluid from different sites; as many as ten assays were performed in 24 hours on fluid from a single site. After lumbar injection of either 5 or 10 mg of either gentamicin or tobramycin the lumbar fluid contained up to 80 μg/ml, this concentration falling slowly with a half-life of six hours. Meanwhile the concentration in the cisternal fluid rose slowly to a peak of about 14 μg/ml at 12 hours, suggesting that intrathecal diffusion is even slower than many may have thought. In the graph illustrating these findings the ventricular concentration is shown flat near the base line. After intraventricular injection of 5 mg the concentration there was 40 μg/ml; this fell and the lumbar concentration rose until equilibration between them at about 20 μg/ml was reached in two hours, both then falling slowly together and still being at 5 μg/ml after 24 hours. These results are as would be expected and point to the intraventricular route as achieving the best distribution, as well as presumably being a necessity if the ventricles are implicated in the infection.

Ventricular puncture is fairly simple and safe in skilled hands. If the fontanelle is open the needle can be inserted through it; if not preliminary trephining is required, and this had to be performed in all these patients. Kaiser and McGee recognized nevertheless that treatment by this route is not to be undertaken lightly and defined indications for it. If the causative organism is and remains sensitive to chloramphenicol this drug should be given in large parenteral doses; they describe another patient with a *Klebsiella* infection in whom this treatment eventually succeeded despite extension of the infection to the ventricles. If an aminoglycoside is indicated, and if treatment with it by parenteral and lumbar routes fails, the intraventricular route should be considered—possibly even at an earlier stage.

[1] Lorber, J, Kalhan, S C, and Malgrefte, B, *Archives of Disease in Childhood*, 1970, **45**, 178.
[2] Salmon, J H, *American Journal of Diseases of Children*, 1972, **124**, 35.
[3] Kaiser, A B, and McGee, Z A, *New England Journal of Medicine*, 1975, **293**, 1215.

Caesarean section and respiratory distress syndrome

Perinatal mortality is higher when babies are born by caesarean section. The second report of the British Perinatal Mortality Survey,[1] using a standard mortality ratio of 100, found that when section was done before the woman was in labour the SMR was 275 and when done during labour it was 181. At that time the nationwide incidence of caesarean section was 2·7% of all births; but there is evidence now that it is rising[2] to about 5%. With nearly 36 000 caesarean sections being performed annually in England and Wales, with an increased perinatal mortality rate, and a maternal mortality of about 1 per 1000, it is imperative to know whether it is the operation which contributes to these deaths and, if so, by how much; or alternatively whether it is the disorder for which the operation is done which is the killer.

That question arises because of an article originally written in 1970 and now published again. Reis *et al*[3] have claimed that by taking care with the arrangements for and technique of caesarean section they have almost eliminated the respiratory distress syndrome among babies over 34 weeks of gestation. They emphasised the need for two senior doctors to be present at the operation, one of whom would give his attention to the baby; and they argued that the baby should be delivered fairly quickly. Hence their induction of anaesthesia is by thiopentone; no time is taken in draping the abdomen with sterile towels; the fetal head is delivered through the incision, where its nose, mouth, and pharynx are cleared by suction; ergometrine is given; and the uterus then pushes the body of the baby out of the incision. This has the effect of squeezing the fetal chest, just as in normal labour, and fluid can be seen to be forced from the nose and mouth. The article says nothing of whether the cord is clamped early or late or whether the baby is held below the level of the placenta to obtain some transfusion of blood.

Almost certainly these authors are mistaken in believing that it was operative technique which made their results enviable—11 perinatal deaths in 200 sections. Whenever a condition is not understood there is a tendency to make non-specific technical alterations in management and to think that successes are due to them. But it was not till Gluck *et al* in 1971[4] showed the value of the amniotic levels of lecithin and sphingomyelin in predicting fetal lung maturity that the mechanism of the respiratory distress syndrome became clearer.[5] It is precisely at 35 weeks of gestation that

pulmonary maturity is attained, and more depends on this than anything else. So it is the time of delivery that matters, because that is what determines lung functional development —a view borne out by Gabert *et al*,[6] who showed that caesarean section was not associated with respiratory distress when the lecithin-sphingomyelin ratio offered a good prognosis. Although Usher *et al*[7] thought that caesarean section was associated with the distress syndrome, they too found it to be virtually eliminated if the length of gestation was 37-38 weeks. Similarly the second perinatal mortality survey[1] found that probably the respiratory distress syndrome could not be firmly associated with caesarean section but was mainly associated with pre-eclampsia, placenta praevia, other antepartum haemorrhages, and some elective sections. In all these cases "iatrogenic immaturity could be a factor."

[1] Butler, N R, and Alberman, E D, *Perinatal Problems. Second Report of the 1958 British Perinatal Mortality Survey*. Edinburgh, Livingstone, 1969.
[2] Department of Health and Social Security, *Report on Confidential Enquiries into Maternal Deaths in England and Wales 1970-1972*. London, HMSO, 1975.
[3] Reis, R A, Gerbie, A B, and Gerbie, M V, *Surgery, Gynecology and Obstetrics*, 1970, **130**, 124.
[4] Gluck, L, *et al*, *American Journal of Obstetrics and Gynecology*, 1971, **109**, 440.
[5] Gluck, L, and Kulovich, M V, *Year Book of Obstetrics and Gynaecology 1972*, ed J P Greenhill, p 256. Chicago, Year Book Medical Publishers, 1972.
[6] Gabert, H A, Bryson, M J, and Stenchever, M A, *American Journal of Obstetrics and Gynecology*, 1973, **116**, 366.
[7] Usher, R H, Allen, A C, and McLean, F H, *American Journal of Obstetrics and Gynecology*, 1971, **111**, 826.

Idiopathic oedema of women

The stage is set for misunderstanding, confusion, and mistrust when the true nature of an illness is unrecognised, especially if its symptoms are discounted because the signs vanish as soon as the patient is investigated at rest in hospital. Soon nobody is sure whether the complaint has caused neurosis or neurosis the complaint. Idiopathic oedema of women[1 2] (also known as cyclical or periodic oedema) is a good case in point, a syndrome which can be relied upon to cause resentment and frustration to patient and doctor alike.

As its name implies, this oedema cannot be attributed to heart failure, renal or hepatic disease, hypoproteinaemia, or lymphatic or venous obstruction; to sodium-retaining medicines such as phenylbutazone, carbenoxolone, or oestrogens; or to hypotensive agents. Attacks may be intermittent, or swelling may wax and wane dramatically yet never disappear completely. Early symptoms may mimic premenstrual tension, but the fluctuations become capricious, apart from a tendency for oedema to appear or increase during warm weather, on prolonged standing, and before the menstrual period. Most patients present in their 30s or early 40s; none before the menarche and none after the menopause, though once established the syndrome may continue after the menopause.

Differentiation from the premenstrual tension syndrome is not generally difficult, for in that syndrome weight gain is small and the many subjective symptoms correlate poorly with it. If a diurnal weight gain exceeding 1·4 kg is used arbitrarily to define the extent of fluid retention[3] a moderately homogeneous syndrome emerges,[4] which, however, seems only to be the tip of an iceberg of unexplained oedema in women. All the daily gain is not lost at night, and the extracellular fluid volume increases stepwise, until at last diuresis ensues and body weight subsides to normal. During attacks the face and hands are puffy on waking; as the day progresses gravity collects the fluid in the legs. Very rarely the patient becomes orthopnoeic and dyspnoeic on exertion because of pulmonary oedema. Attacks often seem to coincide with stress and strain, but which comes first is far from clear. Studies in Canada have exposed an alarming degree of disturbance associated with this relapsing syndrome, as shown by a divorce rate 30 times the national average.[5]

An abnormally large leak of plasma fluid from the circulation in an upright posture is the essential abnormality; when the patient is standing, packed cell volume quickly rises and plasma volume falls.[4] The cause of the presumed capillary abnormality is tantalisingly obscure. Unlike normal women, whose plasma volume falls less on standing during the follicular than during the luteal phase of the menstrual cycle,[6] the abnormality of tissue microcirculation in these women is independent of the menstrual cycle.[7] Contrary to earlier suggestions, renal sodium retention correlates well with the fall in plasma volume and is appropriate to the size of the reduction. Likewise the increased plasma renin and aldosterone concentrations in more florid cases are appropriate compensatory changes, and though they may escape abnormally slowly from the action of mineralocorticoid hormones most of these patients succeed in resetting their response.[4]

More than one mechanism mediates the retention of salt and water[8–11] which begins within minutes of tilting these patients into an upright position—a rapidity of onset too great to be explained in terms of increased renin and aldosterone. The fact that the urinary sodium:potassium ratio does not alter also denies a distal tubule mechanism.[4] Glomerular filtration falls by 5 to 10%, but this fall is insufficient to account for the change in urine composition and volume. Increased proximal tubular reabsorption of salt and water provides the only satisfactory explanation for the diminished sodium excretion, though its mediation here is not fully understood. Reduced urinary volume is partly attributable to antidiuretic hormone (ADH) secretion, because even during a forced diuresis (which suppresses ADH secretion) urinary osmolality often increases when these individuals stand.[4] Further, they become able to excrete a water load normally when in an upright position if ADH secretion is inhibited by ethanol.[9] In a small subgroup of patients standing is associated only with water retention; these appear to be the mildest cases of the syndrome.[11]

Treatment is unsatisfactory and in one respect paradoxical. Plasma volume is already low; further depletion by diuretics is likely both to worsen symptoms attributable to hypovolaemia and to reinforce the compensatory sodium and water retention. This latter effect may be particularly undesirable in the occasional woman who seems persistently to overcompensate for reduced plasma volume and who, after an initial worsening of the oedema, may paradoxically lose her oedema altogether when diuretics are stopped.[12] A diuretic is usually necessary, but the dose should be as small as possible: a preparation such as chlorthalidone should be chosen to achieve a mild and prolonged diuresis, aided perhaps by a potassium-sparing diuretic such as amiloride or spironolactone. Diuretics should be withdrawn from time to time to establish whether the tendency to oedema has spontaneously remitted, but the patient must be prepared for her oedema to get worse initially.

Constipation, a frequent feature of the idiopathic oedema syndrome, is likely to be intensified by diuretic-induced dehydration and hypokalaemia. Laxatives further threaten potassium conservation. Patients sometimes discover that excessive