the social security system in cases of need). One or other of these alternatives is needed. The last Conservative budget cut health expenditure;[5] a further effective cut by abolition of prescription charges would accelerate the spiral of economic decline that is already evident. A second-rate service will attract only second-rate recruits and Britain will join the ranks of countries which export their doctors and nurses overseas.

Unpopular decisions can be made at a time of acknowledged economic adversity by a government at the start of its term of office. The electorate is certainly expecting them. What is not acceptable any longer is a bland reassuring attitude at the Department of Health claiming that all is well and the N.H.S. is the envy of Europe. It may have been in the 50s—it isn't any more.

[1] B.M.A. Press Conference, 5 February 1974.
[2] *British Medical Journal*, 1973, 4, 369.
[3] *British Medical Journal*, 1974, 1, 335.
[4] *British Medical Journal*, 1974, 1, 335.
[5] *British Medical Journal*, 1974, 1, 47.

Pre-eclampsia and the Kidney

Medical students learn half-a-dozen explanations for pre-eclampsia, and the theories change from year to year; there are plenty to choose from.[1] Amid this speculation one mechanism appears well supported by clinical and experimental observations and must be fitted into any aetiological concept—the role of uteroplacental ischaemia.[2]

Pre-eclampsia is common in first pregnancy, twin and multiple pregnancies, and hydatiform mole, all situations in which the growth of the uteroplacental unit is likely to outstrip the development of an adequate blood supply. It is relieved by bed rest, which prevents the deleterious effects of exercise on uterine blood flow; these are exaggerated in pre-eclampsia.[3] Arteriography during pregnancy shows that the gravid uterus is supplied by a rich vasculature derived from dilated uterine, ovarian, and other collateral arteries; a much poorer blood supply is visualized in patients with pre-eclampsia.[4] The well established familial tendency to pre-eclampsia and eclampsia in first pregnancy has not been explained on any vascular basis, but pre-eclampsia in later pregnancies is a predictor of essential hypertension and diabetes.[5,6] The predisposition of such women and of those with established hypertension, diabetes, and chronic renal disease could be explained by their possession of vessels incapable of the massive dilatation required for normal pregnancy, though this suggestion has not been confirmed experimentally. Impaired placental function, shown by poor fetal growth, reduced excretion of oestrogens, and declining plasma level of placental lactogen are characteristic of late pre-eclampsia and important harbingers of intrauterine death.[7,8] The best animal models of pre-eclampsia are pregnant dogs and primates whose uterine blood flow has been reduced by constricting the uterine arteries and severing the collaterals.[9,10] Uteroplacental ischaemia is clearly the primary event in these animals, and it probably plays the same role in the human disease.

Agreement ends when a link is sought between placental insufficiency and the manifestations of pre-eclampsia—oedema, hypertension, proteinuria, and renal insufficiency. Oedema is common in normal pregnancy, and there is wide overlap between normal and pre-eclamptic women in visible oedema and measured sodium and water retention.[11] The idea that hypersecretion of aldosterone might be the cause of sodium retention and hypertension was attractive while it lasted; but the plasma concentration of aldosterone is in fact lower in women with pre-eclampsia than in matched controls,[12] and the occurrence of pre-eclampsia in patients with Addison's disease[13] makes it unlikely that aldosterone is an essential factor in the disease. There is an astonishing lack of agreement about the effect of sodium restriction, diuretics, and sodium supplements on the course of the disease.[2]

Renin is produced in the chorion[14] and uterine muscle.[15] Hypersecretion of uterine or renal renin has been blamed for the hypertension and nephropathy of pre-eclampsia; Sophian[1] called it "*the* aetiological factor." Plasma levels of renin, renin substrate, and angiotensin II are, however, no higher in pre-eclampsia than in normal pregnancy and may be lower[12] except perhaps at the very end of pregnancy.[16,17] It is difficult to blame angiotensin deficiency[18] for any of the features of pre-eclampsia when plasma angiotensin II levels are not raised above those in normal pregnancy. Pre-eclamptic women have poorly distensible arterioles,[19] and many of their abnormalities could be explained by a circulating pressor agent other than renin.[12] Apparently their blood has a pressor effect when retransfused after pregnancy,[20] though this observation awaits confirmation and comparison with normal pregnancy. The typical sequence of events—hypertension, renal lesions, proteinuria—[21] is compatible with the possibility that the pressor agent, if any, causes the renal lesion, but other explanations for the nephropathy are more popular.

Proteinuria in pre-eclampsia is of glomerular origin and moderately selective[22,23] but electron microscopy does not show the changes in podocytes found in most other glomerulonephropathies causing proteinuria, though one description mentions epithelial swelling.[24] The typical findings are endothelial swelling, obliteration of capillary lumina, subendothelial deposits, and enlargement of mesangial cells.[24,27] The subendothelial deposits are the most characteristic lesion and are very similar to those which are found in the rabbit after intravacular coagulation.[27] Fluorescence microscopy shows abundant fibrin in the glomeruli.[28] This has led to the dominant theory, that the renal lesions are the result of intravascular coagulation caused by some substance released from the damaged placenta. Intravascular coagulation is present in pre-eclampsia[29,31] and in animal models[32] as judged by the presence of fibrin degradation products in plasma and urine, low platelet counts, and increased fibrinogen turnover. It may be responsible for the changes in lung function in pre-eclampsia which are reversed by heparin.[33]

An alternative explanation for the renal lesion is suggested this week by Dr. O. M. Petrucco and his colleagues (p. 473). On fluorescence microscopy they have detected IgM and IgG in the glomeruli of pre-eclamptic women, in proportion to the severity of the disease, and found complement in arterioles and sometimes in glomeruli. They suggest that the negative findings reported by previous authors may have been due to lack of specificity in the antisera employed. They suggest that immunological mechanisms may be concerned in the nephropathy of pre-eclampsia and draw analogies with transplant rejection. A number of observations do not readily fit this theory. Serum complement is raised in pregnancy, and pre-eclamptic women are no different from normals.[34] The clinical manifestations and the renal lesion remit rapidly after delivery on a very different time scale from the resolution of, for instance, poststreptococcal glomerulonephritis. However, these conflicts of evidence apply to all current theories, and

the findings of Petrucco and his colleagues will lead to re-examination of present evidence and further studies.

[1] Sophian, J., *Pregnancy Nephropathy*. London, Butterworths, 1972.
[2] Speroff, L., *American Journal of Cardiology*, 1973, **32**, 582.
[3] Morris, N., Osborn, S. B., Wright, H. P., and Hart, A., *Lancet*, 1956, **2**, 481.
[4] Bieniarz, J., Yoshida, T., Romero-Salinas, G., Curuchet, E., Caldeyro-Barcia, R., and Grottogini, J. J., *American Journal of Obstetrics and Gynecology*, 1969, **103**, 19.
[5] Chesley, L. C., Annitto, J. E., and Cosgrove, R. A., *American Journal of Obstetrics and Gynecology*, 1968, **101**, 886.
[6] Chesley, L. C., Annitto, J. E., and Cosgrove, R. A., *Obstetrics and Gynecology*, 1968, **32**, 303.
[7] Campbell, S., Kurjak, A., *British Medical Journal*, 1972, **4**, 336.
[8] Lindberg, B. S., and Nilsson, B. A., *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 1973, **80**, 1046.
[9] van Bouwdijk Bastiaanse, M. A., and Mastboom, J. L., *Gynaecologia*, 1949, **127**, 1.
[10] Cavanagh, D., Rao, P. S., Tung, K., and Gaston, L. W., *Obstetrics and Gynecology*, 1972, **39**, 637.
[11] Hytten, F. E., and Thomson, A. M., *British Medical Bulletin*, 1968, **24**, 15.
[12] Weir, R. J., *et al.*, *Lancet*, 1973, **1**, 291.
[13] Normington, E. A. M., and Davies, D., *British Medical Journal*, 1972, **2**, 148.
[14] Skinner, S. L., Lumbers, E. R., and Symonds, E. M., *American Journal of Obstetrics and Gynecology*, 1968, **101**, 529.
[15] Ferris, T. F., Stein, J. H., and Kauffman, J., *Journal of Clinical Investigation*, 1972, **51**, 2827.
[16] Gordon, R. D., Symonds, E. M., Wilmshurst, E. G., and Pawsey, C. G. K., *Clinical Science*, 1973, **45**, 115.
[17] Hoffman, C. M., Karu, A. E., and Dev, J., *American Journal of Obstetrics and Gynecology*, 1973, **117**, 537.
[18] Tapia, H. R., Johnson, C. E., and Strong, C. G., *Lancet*, 1972, **2**, 847.
[19] Duncan, S. L. B., and Ginsburg, J., *American Journal of Obstetrics and Gynecology*, 1968, **100**, 222.
[20] Tatum, H. J., and Mule, J. G., *American Journal of Obstetrics and Gynecology*, 1962, **83**, 1028.
[21] Altchek, A., *Circulation*, suppl. 2, 1964, **30**, 43.
[22] MacLean, P. R., *et al.*, *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 1972, **79**, 321.
[23] Simanowitz, M. D., MacGregor, W. G., and Hobbs, J. R., *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 1973, **80**, 103.
[24] Pirani, C. L., Pollak, V. E., Lannigan, R., and Folli, G., *American Journal of Obstetrics and Gynecology*, 1963, **87**, 1047.
[25] Hopper, J., Farquhar, M. G., Yamauchi, H., Moon, H. D., and Page, E. W., *Obstetrics and Gynecology*, 1961, **17**, 271,
[26] Paul, R. E., Hayashi, T. T., Pardo, V., and Fisher, E. R., *Obstetrics and Gynecology*, 1969, **34**, 235.
[27] Thomson, D., Paterson, W. G., Smart, G. E., MacDonald, M. K., and Robson, J. S., *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 1972, **79**, 311.
[28] Morris, R. H., Vassalli, P., Beller, F. K., and McCluskey, R. T., *Obstetrics and Gynecology*, 1964, **24**, 32.
[29] Henderson, A. H., Pugsley, D. J., and Thomas, D. P., *British Medical Journal*, 1970, **3**, 545.
[30] Bonnar, J., McNicol, G. P., and Douglas, A. S., *British Medical Journal*, 1971, **2**, 12.
[31] Birmingham Eclampsia Study Group, *Lancet*, 1971, **2**, 889.
[32] Wardle, E. N., *Angiologica*, 1973, **10**, 173.
[33] Littler, W. A., Redman, C. W. G., Bonnar, J., Beilin, L. J., and Lee, G. de J., *Lancet*, 1973, **1**, 1274.

Management of Neonatal Jaundice

Exchange transfusion is the most effective means of preventing kernicterus from neonatal jaundice, but it is hazardous and costly in time and materials.[1] Phenobarbitone[2 3] and phototherapy[4 5] are also effective; yet their place in the management of this condition is not yet certain. Anxiety arises from a number of well-reviewed factors,[6] principally the non-specific effects of phenobarbitone on many aspects of metabolism,[7] the possible adverse effect of phototherapy itself and of the photodegradation products of bilirubin,[8] and continued uncertainty about the concentration of bilirubin which causes brain damage in an individual infant. Of particular concern is the prophylactic use of these agents in low-birth-weight infants.

The combined effect of phototherapy and phenobarbitone in small infants has been well studied in a recent report from the Birmingham Maternity Hospital.[9] By random selection low-birth-weight infants with bilirubin levels of over 15 mg/100 ml were allocated to treatment with phototherapy for 60 hr; or ten doses of intramuscular phenobarbitone (8 mg/kg/24 hr, three times a day); or a combination of both. Phototherapy alone or in combination caused an equal fall in bilirubin within 24 hr. Infants treated with phenobarbitone had significantly higher serum bilirubin levels throughout the period of study, except in those weighing more than 2·5 kg, in whom levels fell to those of the other groups in the last 24 hr of the study. Of 21 infants receiving phenobarbitone alone rising serum bilirubin levels caused four to receive other treatment, as did one infant in the combined group. No advantages from combined treatment were demonstrated, in keeping with earlier studies in which treatment had started in infants at the age of 24 hours.[10 11] Treatment may have contributed to delay in diagnosis of meningitis and septicaemia in two infants in the combined treatment group; both infants died. It is noteworthy that the authors do not consider that a control group was ethically justifiable, since in a previous study one third of such a group had required "other treatment" when the serum bilirubin level rose towards 20 mg/100 ml. The other treatment is not specified, but presumably carried greater risks than those in the trial. But what of the risks of phototherapy?

Increasing clinical use of phototherapy has led to the recognition of a number of side-effects. Perhaps most frequent is the increased insensible water loss,[12] which if not balanced by increased water intake (preferably as a 5% or 10% glucose solution) may lead to dehydration. Diarrhoea has been reported, but where detailed observations have been made with appropriate controls[13] the incidence of loose stools has not been increased. Alimentary transit times are unchanged[14] and 5-hydroxy indole acetic acid excretion is normal.[15] Forceful expulsion of a fluid green stool by an active infant is no doubt more striking if the infant is undressed and much of the incubator soiled repeatedly. Skin reactions include maculopapular rashes,[16] tanning of negro infants,[17] and bronzing of the skin[18] with acute haemolysis[19] in infants with liver disease. These side-effects are, however, rare and less hazardous in practice than the uncritical use of therapy to banish jaundice without determining the underlying cause or aggravating factors. Phototherapy will not prevent kernicterus in small acidotic premature infants even when the bilirubin remains low,[20] and its use does not allow any relaxation in standards of perinatal care and indeed may complicate observation.

It has been postulated that neonatal hyperbilirubinaemia may cause not only the serious well-recognized neurological sequelae of kernicterus, such as cerebral palsy with extrapyramidal features or severe mental retardation, but also perhaps a continuum of brain damage including minor intellectual impairment. The difficulty in confirming this is shown by an excellent report from Vancouver[21] in which well-matched low-birth-weight infants with maximum recorded bilirubins of less than 11 mg/100 ml, 11-19 mg/100 ml, and greater than 20 mg/100 ml were assessed at between 4 and 11 years of age. No statistically significant differences in I.Q., verbal, or performance scores were found. There is thus reason for caution in the widespread use of phototherapy in the management of non-haemolytic jaundice in low-birth-weight infants. An easily available precise indicator of the risks of kernicterus would be an important advance. Meanwhile, the comment that "if light came in a bottle, the Food and Drugs Administration wouldn't allow it to be marketed" remains an indictment of our ignorance of the effects of phototherapy rather than a criticism of that agency.

[1] Kitchen, W. H., *The Australian Paediatric Journal*, 1970, **6**, 30.
[2] McMullin, G. B., Hayes, M. E., and Arora, S. G., *Lancet*, 1970, **2**, 949.