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

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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.

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Volume-dependent Essential Hypertension?

Though an increase of sodium in the diet can expand the volume of plasma, blood, and extracellular fluid and raise blood pressure in animals,[1 2] the role of volume expansion in clinical hypertension is not clear. Certainly there are hypertensive syndromes in which volume is expanded. Chronic renal failure,[3 4] the hypertension which sometimes develops after bilateral nephrectomy,[5 6] and primary hyperaldosteronism[7 8] are examples, and in each instance reduction of volume is associated with a fall of arterial pressure. But in contrast there are occasional cases of severe or malignant hypertension with depletion of sodium and water and reduction of volume.[9 10]

Between these extremes lie the large group of patients with essential hypertension. Most studies of the condition indicate that plasma or blood volume is not increased. Some show mean values for hypertensive patients that are significantly lower than the normal mean though still well within the normal range.[11-15] In other studies the difference is not significant.[16-18] An inverse relation between plasma volume and blood pressure is also reported in essential hypertension.[12 14 15] That observation was made originally by R. C. Tarazi and colleagues.[14] Classifying their patients in a rather different way they found the correlation became less significant.[19] They now propose[20] that blood pressure in certain types of essential hypertension is volume-dependent. During both sodium loading and sodium deprivation blood pressure and plasma volume correlated directly but, in the control period when untreated, there was no significant relation. Also needing explanation is the interesting paradox that blood pressure fell most during sodium deprivation in the group of patients with the lowest initial plasma volume. The case for volume-dependent essential hypertension is not, therefore, clear-cut.

Some of these problems might be more clearly understood if evidence could be obtained in essential hypertension to support or refute the autoregulation theory.[21 22] According to this theory, which derives mainly from observations on animals, there is retention of sodium and water and expansion of volume in the early stages of hypertension. Increased cardiac output is mainly responsible for raising blood pressure at this stage. Later, peripheral resistance rises (autoregulation of tissue perfusion), cardiac output falls, and plasma volume decreases. So it seems a period of volume expansion is followed by a more prolonged period of increased resistance. If this process occurs in patients with hypertension, the chances are that they will be clinically examined during the second phase, when volume is normal. It is of interest therefore that when peripheral resistance is raised in patients with essential hypertension plasma volume tends to be normal, and when cardiac output is high plasma volume tends to be high also.[12 15 23] But much remains to be done before it is clear whether autoregulation occurs in essential hypertension and, if it does, whether it can account for the variations in plasma volume.

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Turner's and Noonan's Syndromes

During the past 35 years much has been learned about Turner's syndrome[1] of webbing of the neck, cubitus valgus, and sexual infantilism in females. Additional features, such as short stature and congenital lymphoedema described by O. Ullrich[2] in an earlier paper, together with dysgenetic "streak" ovaries and abnormalities of the skin, kidneys, bones, and cardiovascular system are now generally recognized, and it is clear that there is considerable variation in the clinical expression of the syndrome.[3] Early chromosome studies in such patients indicated that their cells carried a single X chromosome,[4] but subsequent work has shown that mosaicism or a range of abnormalities of one sex chromosome may be present.[5] It appears that the Turner phenotype is probably related to loss of genetic material on the short arm of one X chromosome or corresponding areas of a Y chromosome.[5]

One aspect of Turner's syndrome which has been difficult to explain has been the occurrence in males of features of the syndrome similar to those originally described in women.[6] In some cases, particularly those with ambiguous external genitalia, XO/XY mosaicism has been present, but in the