prognosis in infantile dysphagia. The first is the frequency of associated mental retardation, especially in those infants with congenital abnormalities. Illingworth stresses the importance of careful developmental assessment in every case. The second difficulty is concerned with what he has described as the "sensitive" or critical period.[3] He pointed out that if babies are not given solid food—as distinct from thickened feeds—when they have recently learned to chew (average age 6-7 months) they will refuse or vomit solids later. If a baby with dysphagia is not given solid foods at the sensitive period, but is given them subsequently, the vomiting or refusal may be mistaken for the primary condition when in fact it is due to his having passed the critical period without being offered solids.

The third problem is the pseudoretardation from which infants and young children with dysphagia of more than a few weeks may suffer as a result of admission to hospital and separation from their mothers. This may lead to a wrong diagnosis of mental retardation in a mentally normal child. Even if the condition is recognized, it is difficult to foretell how much of the retardation will be reversible after the child returns home.

In summing up his own series of nineteen cases Illingworth writes that he was struck with the low mean intelligence quotient of the neuromuscular group, but that the most notable feature of their follow-up examination was the remarkable improvement many of them showed, with complete recovery at school age in those who had the most severe disabilities in infancy, even in those who had to be tube-fed for several months.

Antilymphocyte Serum and Glomerulonephritis

Antilymphocyte serum or relatively pure antibody globulin fractions prepared from this serum can suppress immunity reactions, thus prolonging the survival of both skin and organ grafts.[1] The action of the antibody globulin fractions is still far from completely understood, but it includes a toxic effect on lymphocytes, and these fractions certainly inhibit cell-mediated immune responses more powerfully than they do the production of circulating antibody.[2]

The use of antibody globulin fractions (A.L.G.) in the treatment of glomerulonephritis thought to be initiated or rendered chronic by immune mechanisms might seem attractive, but it has not been reported for a variety of reasons. Evidence has been lacking that cell-mediated immune mechanisms play a part in glomerulonephritis in man. Doubts have also been felt about the use of antibody globulin fractions when alternative treatments might be available. For the antibody globulin is itself a foreign protein able to produce a serum-sickness type of nephritis;[3] it has side-effects (such as thrombocytopaenia) dependent on its present lack of specificity;[1 4] its potency and dosage are difficult to assess;[1 5] severe local and systemic reactions are frequently encountered in the use of horse antisera;[6] and, finally, it is thought to be capable of inducing, both at the site of injection[7] and elsewhere,[8] tumours of the lymphoid series of cells.

These doubts have resulted in the continuing use of corticosteroids and immunosuppressants such as azathioprine. However, both these preparations[9 10] have proved much less effective than was initially hoped,[11] particularly for those forms of nephritis showing extensive formation of periglomerular crescents and for necrotic glomerulitis running a rapidly progressive course. The most severe forms of progressive nephritis associated with systemic lupus erythematosus may also respond poorly or not at all to treatment.

Recently B. Pirofsky and his colleagues[12] reported favourably on their experiences with goat antithymocyte and antilymphocyte globulin in three cases with severe progressive nephritis unresponsive to large doses of corticosteroids and, in two of the cases, azathioprine in addition. The first patient had a clinical picture typical of Goodpasture's syndrome, with rapid decline of his creatinine clearance to 23 ml./min. despite treatment with high doses of prednisolone and azathioprine. Unfortunately immunofluorescent studies on the renal biopsy specimen are not reported and the histology is briefly described as "focal glomerulonephritis." Goat A.L.G. was given for 98 days, with reduction of the prednisolone dosage but maintenance of the azathioprine. The pulmonary lesions resolved completely, and the creatinine clearance rose to over 60 ml./min., at which level it remained eight months after A.L.G. treatment. The second patient was a young woman with long-standing systemic lupus erythematosus with nephritis. Reduction of prednisone in high dosage resulted in rapid decline in her creatinine clearance to 23 ml./min., which did not respond to restoration of prednisolone and azathioprine in addition. A.L.G. was given over 147 days, with return of creatinine clearance to 100 ml./min. and reduction in proteinuria from 22 to 2 g./day. Meanwhile the prednisolone was decreased but the azathioprine continued. Again the improvement was maintained up to 3½ months after the end of A.L.G. treatment. The third patient also had lupus nephritis, and became anuric despite treatment with dexamethasone. She died, still anuric, after 30 days' treatment with A.L.G.

These results, while encouraging, are difficult to interpret. In the two successfully treated patients azathiopine was continued throughout. The nephritis of Goodpasture's syndrome has been shown to depend in part on circulating antibody to glomerular basement membrane,[13] while that of systemic lupus erythematosus has been thought to arise principally from circulating complexes containing antibody, complement, and deoxyribose nucleic acid. Pirofsky and his colleagues performed a variety of tests on their patients, showing that ability to produce antibody was intact but cell-mediated immune responses were depressed.

The results of their treatment could be interpreted as an indication that the nephritis apparently responding to the A.L.G. was produced or maintained by cell-mediated mechanisms, though the authors do not themselves discuss

1 *British Medical Journal*, 1968, **2**, 507.
2 James, K., *Clinical and Experimental Immunology*, 1967, **2**, 615.
3 Dixon, F. J., Feldman, J. D., and Vazquez, J. J., *Journal of Experimental Medicine*, 1961, **113**, 899.
4 Gray, J. G., Monaco, A. P., Wood, M. L., and Russell, P. S., *Journal of Immunology*, 1966, **96**, 217.
5 Jeejeebhoy, H. F., and Vela-Martinez, J. M., *Transplantation*, 1968, **6**, 149.
6 Iwasaki, Y., *et al.*, *Surgery, Gynecology and Obstetrics*, 1967, **124**, 1.
7 Deodhar, S. D., Kuklinca, A. G., Vidt, D. G., Robertson, A. L., and Hazard, J. B., *New England Journal of Medicine*, 1969, **280**, 1104.
8 Penn, I., Hammon, W., Brettschneider, L., and Starzl, T. E., *Transplantation Proceedings*, 1969, **1**, 106.
9 Berlyne, G. M., and Baker, S. B. de C., *Quarterly Journal of Medicine*, 1964, **33**, 105.
10 Sharpstone, P., Ogg, C. S., and Cameron, J. S., *British Medical Journal*, 1969, **2**, 533.
11 White, R. H. R., Cameron, J. S., and Trounce, J. R., *British Medical Journal*, 1966, **2**, 853.
12 Pirofsky, B., Bardana, E. J., jun., Bayracki, C., and Porter, G. A., *Journal of the American Medical Association*, 1969, **210**, 1059.
13 Lerner, R. A., Glassock, R. J., and Dixon, F. J., *Journal of Experimental Medicine*, 1967, **126**, 989.
14 Lewis, E., Rocklin, R. E., and David, J. R., presented at the meeting of the European Society for Paediatric Nephrology, Helsinki, June 1969.

this point. Although a dense cellular infiltrate has consistently been observed in glomerulonephritis, particularly in active and progressive forms of the disease, little attention was paid to this observation until the resemblance to infiltrate found in allografted kidneys undergoing rejection was seen. E. Lewis, R. E. Rocklin, and J. R. David[14] have now shown that most patients with rapidly progressive glomerulonephritis have circulating lymphocytes sensitized against kidney, as well as antibody against glomerular basement membrane. The spectrum of activity and clinical course in lupus nephritis is so wide that several mechanisms, including this one, may be operating in the most severe forms.

These observations of Pirofsky and Lewis and their colleagues would suggest that cautious evaluation of A.L.G. in patients with rapidly progressive glomerulonephritis unresponsive to other forms of treatment is justified, even though present antisera and our knowledge of their action leaves much to be desired. They would also suggest that, in transplantation into patients with this form of nephritis, immunosuppression should include A.L.G.

Blue Light and Jaundice

Light may reduce serum bilirubin levels in neonatal jaundice,[1 2] and two controlled trials[3 4] have renewed interest[5-8] in this effect, especially in the U.S.A. J. F. Lucey and his colleagues[3] found that a "light chamber" attached to the incubator substantially reduced physiological jaundice of prematurity. F. Giunta and J. Rath[4] achieved significant but less marked reduction simply by increasing the normal intensity of nursery illumination. Current knowledge on the effect of light in neonatal jaundice was summarized last year at a symposium in Chicago.[8]

Vision, photosynthesis, and the photo-periodism of plants, which governs their season of flowering, all depend on biochemical effects of light. Light consists of streams of photons, which have the properties both of particles and of electromagnetic waves. Biological molecules which can be activated by light have systems of alternating single and double bonds; their energy state can be altered by absorption of photons, making them more chemically reactive or unstable. The bilirubin molecule resembles very closely the phytochrome molecule of plants which is responsible for photo-periodism.[9] Bilirubin solutions absorb light maximally at wave lengths around 450 nm. and it is probable,[1 10] though not certain,[8] that blue light of wave length close to this is most effective in activating the bilirubin molecule. The activated molecule is probably oxidized to biliverdin, which is in turn converted to a series of other water-soluble compounds, though there are some uncertainties about the chemical processes concerned.[8 10]

Despite enthusiastic claims for the value of phototherapy,[3-6] it is generally agreed that its usefulness is limited to "physiological" hyperbilirubinaemia, which is a major problem only in premature infants. Phototherapy is not likely to be effective in jaundice due to haemolytic disease of the newborn, where the rate of bilirubin production is very much higher.[1-3 7] Reduction of hyperbilirubinaemia of prematurity might have two possible advantages: it might lessen the need for exchange transfusions or diminish a possible adverse effect on the brain of bilirubin levels below those at which exchange transfusions are usually done to prevent kernicterus. If the latter situation was a real one it would be a strong argument for phototherapy. T. R. Boggs and his colleagues,[11] in a much-quoted paper, have claimed that motor performance at eight months is inversely related to the neonatal serum bilirubin level, even at levels below those usually considered toxic. However, this study was not controlled for gestational age: immature infants would tend to be more jaundiced, and would also be at a disadvantage at eight months of chronological age because of their lower age from conception,[12] as well as their higher incidence of motor handicap from causes other than hyperbilirubinaemia.[13] Other studies have shown no evidence of bilirubin toxicity at serum levels below 20-25 mg./100 ml.[14-19] except in infants with severe hypoxia, acidosis, hypothermia, or other special circumstances[20] in which phototherapy is unlikely to be adequate treatment. Early feeding has limited the need for exchange transfusions in jaundice of prematurity to fewer than 1% of babies of low birth weight;[12] the further reduction which could be achieved by phototherapy must be very small.

Phototherapy has two possible dangers—the photochemical products of bilirubin might themselves be toxic,[21] and light might have other deleterious effects on the newborn.[8] The evidence on possible toxicity of the products of photodecomposition of bilirubin is reassuring but not conclusive. The toxic effect of high levels of serum bilirubin depends on the fact that a fraction of this lipid-soluble substance is not bound to plasma protein and may penetrate the brain to cause kernicterus. The products of bilirubin decomposed by light in vitro are water-soluble, and therefore should not readily penetrate the brain.[1 8 22] This has been confirmed in guinea pigs.[23] However, the effect of light on bilirubin metabolism in the human infant cannot be firmly established from experiments in vitro or on animals.[8]

The possibility that light may have adverse effects on the infant unconnected with bilirubin metabolism is more worrying, for the information is even less complete. Light profoundly affects pineal function, sexual maturation,[24] and circadian rhythms. Bright light may be injurious to the eyes of premature babies.[25] Though light can penetrate deep into the brain,[26]

Cremer, R. J., Perryman, P. W., and Richards, D. H., *Lancet*, 1958, **1**, 1094.
[1] Broughton, P. M. G., Rossiter, E. J. R., Warren, C. B. M., Goulis, G., and Lord, P. S., *Archives of Disease in Childhood*, 1965, **40**, 666.
[2] Lucey, J., Ferreiro, M., and Hewitt, J., *Pediatrics*, 1968, **41**, 1047.
[3] Giunta, F., and Rath, J., *Pediatrics*, 1969, **44**, 162.
[4] Lucey, J. F., *Developmental Medicine and Child Neurology*, 1968, **10**, 521.
[5] Lucey, J. F., *Pediatrics*, 1969, **44**, 155.
[6] Lester, R., and Troxler, R. F., *New England Journal of Medicine*, 1969, **280**, 779.
[7] Behrman, R. E., and Hsia, D. Y. Y., *Journal of Pediatrics*, 1969, **75**, 718.
[8] Hendricks, S. B., *Scientific American*, 1968, **219**, 174.
[9] Sisson, T. R. C., *et al.*, *Pediatric Research*, 1969, **3**, 380.
[10] Boggs, T. R., jun., Hardy, J. B., and Frazier, T. M., *Journal of Pediatrics*, 1967, **71**, 553.
[11] Davies, P. A., *Lancet*, 1969, **2**, 273.
[12] McDonald, A., *Children of Very Low Birth Weight*, London, Spastics Society/Heinemann, 1967.
[13] Koch, C. A., *Journal of Pediatrics*, 1964, **65**, 1.
[14] Wishingrad, L., *et al.*, *Pediatrics*, 1965, **36**, 162.
[15] Vuchovich, D. M., Haimowitz, N., Bowers, N. D., Cosbey, J., and Hsia, D. Y. Y., *Journal of Mental Deficiency Research*, 1965, **9**, 51.
[16] Ose, T., Tsüruhara, T., Araki, M., Hanaoka, T., and Bush, O. B., jun., *Pediatrics*, 1967, **40**, 196.
[17] Hyman, C. B., Keaster, J., Hanson, V., Harris, I., Sedgwick, R., Wursten, H., and Wright, A. R., *American Journal of Diseases of Children*, 1969, **117**, 395.
[18] Drorbaugh, J. E., In *12th International Congress of Pediatrics*, Mexico, Impresiones Modernas, 1968.
[19] Stern, L., and Doray, B. H., In *12th International Congress of Pediatrics*, Mexico, Impresiones Modernas, 1968.
[20] Franklin, A. W., *Lancet*, 1958, **1**, 1227.
[21] Blondheim, S. H., and Kaufmann, N. A., *Journal of Laboratory and Clinical Medicine*, 1965, **65**, 659.
[22] Diamond, I., and Schmid, R., *Archives of Neurology*, 1968, **18**, 699.
[23] Wurtman, R. J., and Axelrod, J., *Scientific American*, 1965, **213**, 50.
[24] Riley, P. A., and Slater, T. F., *Lancet*, 1969, **2**, 265.
[25] Ganong, W. F., Sheperd, M. D., Wall, J. R., Van Brunt, E. E., and Clegg, M. T., *Endocrinology*, 1963, **72**, 962.
[26] O'Connell, B., *Archives of Disease in Childhood*, 1969, **44**, 647.