cortisone was insufficient to control attacks, although corticotrophin, 50 mg. daily, was effective.

Steroid therapy has so far proved safe in these patients. The usual accepted contraindications were absent. It is, however, interesting that, in Case 2, Stokes–Adams attacks occurred with greater frequency during the first day after starting treatment. Such a phenomenon has not been noted before. There is a theoretical possibility that steroids might interfere with the process of healing after cardiac infarction, but this does not seem to be the case in experimental infarcts in laboratory animals. Furthermore, in such cases treatment for a few days only may be enough.

Summary

Six patients with heart-block and Stokes–Adams attacks have been treated with prednisolone after the failure of conventional measures, and in all six the attacks ceased within 48 hours. Subsequently all patients have remained free from episodes of syncope for a long period.

Similar results have been reported by others, and treatment with adrenocortical steroids appears often to be useful when sympathomimetic drugs are ineffective. In general, a favourable response is most likely when Stokes–Adams attacks occur in a patient with atrio-ventricular block which is unstable. In such cases a return to normal rhythm can be hoped for. Once complete heart-block is established, the rhythm is usually unaffected by steroid treatment, but if it is complicated by syncopal attacks from ventricular stand-still, steroid therapy may still relieve them. Prolonged maintenance treatment is suggested in patients with chronic ischaemic heart disease.

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Dr. J. A. SCOTT, the London County Council's Medical Officer of Health, reports that the number of emergency calls received by the London Ambulance Service increased by more than 10,000 between 1958 and 1960. In 1958 the number of calls was 99,188; in 1959 104,983; in 1960 109,551. Despite the extra journeys the average time taken by ambulances to reach the scenes of accidents was only a fraction of a minute longer than in previous years—6.5 minutes in 1958, 6.8 minutes in 1960. On average, patients were admitted to hospital 21.6 minutes after the calls for help were received. As usual, women about to give birth outnumbered all other kinds of patients (25.2% of the total). Street accident cases came next (20%), displacing from second position cases of illness in public places. There were 22,709 patients who had been involved in street accidents, 1,000 more than in 1959. The number of patients who had been victims of assault rose by nearly 700 to 4,107.

HYPERBILIRUBINAEMIA AND PERCEPTIVE DEAFNESS

BY

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The association between kernicterus and perceptive deafness has been well known since Crabtree and Gerrard (1950) demonstrated that deafness was present in 16 out of 20 cases of athetoid cerebral palsy.

After the identification by Claireaux, Cole, and Lathe (1953) of bilirubin as the pigment in the brain cells in kernicterus, evidence accumulated to incriminate bilirubin as the principal factor in the causation of neurological complications in haemolytic disease of the newborn. This evidence has been reviewed by Lathe, Claireaux, and Norman (1958) and by many others, and hardly needs to be recapitulated. It seemed of importance, therefore, to ascertain by a prospective type of investigation how often perceptive deafness might occur as the sole result of hyperbilirubinaemia and whether this could occur at a bilirubin level lower than necessary to cause athetoid cerebral palsy.

Material

The children selected for this study were infants born at Queen Charlotte's Maternity Hospital between the end of 1953 and the middle of 1957 who suffered from hyperbilirubinaemia.

From the middle of 1954 at Queen Charlotte's Hospital regular daily estimations of total bile pigments and conjugated bilirubin have been performed on all babies showing any sign of jaundice at all, and are repeated on each baby until the bilirubin level begins to fall.

An adaptation of the Evelyn and Malloy technique, as described by Lathe and Ruthven (1958), has been used, but at the beginning of 1957 the factor employed in calculating the bilirubin was altered, as it was found that the readings had been too high by about 20%. The figures given in this paper have therefore been adjusted to make them comparable to the more recent estimations. Accordingly, out of 107 infants, after adjustments as mentioned above, it was found that only 20 reached a bilirubin level of 20 mg./100 ml.

For the purposes of this investigation it was possible to examine 50 children completely. Full assessment of their hearing was carried out, and this study of the relationship of hyperbilirubinaemia to perceptive deafness is based on the special investigation of these 50 children. In this group were 13 with a bilirubin concentration of over 20 mg./100 ml.

Results of Hearing-tests

All these children had a detailed audiological examination, and perfectly normal hearing was found in 41 out of 50. In three there was a significant impairment of hearing of conductive type, but this is not relevant in this context.

In six children bilateral perceptive partial deafness was detected. As seen from the audiographs (see Chart), the

pattern of hearing loss is similar in all but one of the cases. Hearing is either within normal limits or only slightly impaired in the lower range of notes, with a gradually increasing impairment in the higher range. Often the hearing for the highest notes is a little better, with a maximum degree of impairment in the range of 2,000 to 4,000 c/s. This type of hearing loss is characteristic for deafness from haemolytic disease as found in previous studies (Fisch, 1957). Severe deafness, as shown in one of the cases in this series, is comparatively rare. In three of the six children perceptive deafness had been diagnosed before this investigation and appropriate measures were taken for training and rehabilitation at an early age.

In one case deafness was noticed before, but its true nature had not been recognized, probably because of a superimposed conductive hearing loss.

In two cases hearing loss was not suspected at all before this investigation, although in one of these there was marked articulation defect. The other child was seemingly backward, but later it was realized that her I.Q. had been assessed as being low because deafness was not suspected, and consequently the appropriate method for testing intelligence had not been applied.

Clinical Condition and Bilirubin Levels in the Partially Deaf Children

Of the six children suffering from perceptive deafness, two were typical examples of kernicterus resulting from Rh iso-immunization (Cases A and C, see Table), and had a marked athetoid cerebral palsy. Their maximum serum bilirubin concentration was respectively 34 and 30 mg./100 ml.

Details of Children With Perceptive Deafness

Case	Clinical	Max. Bilirubin mg./100 ml.	Synkavit mg.	Birth Wt. lb. oz.	Birth Wt. g.	Maturity in Weeks	Blood
A	Kernicterus.						
	Deafness	34	70	7 12	3,545	37	Rh inc.
B	Deafness	26	15	2 11	1,200	31	No immun.
C	Kernicterus.						
	Deafness	30	Nil	7	3,175	41	Rh inc.
D	Deafness	19·0	50	5 11	2,580	34	No immun.
E	,,	20·3	20	6 14	3,120	38	Anti-A haemolysins present
F	Kernicterus.						
	Deafness	15	30	1 8	680	1 ? 31	No immun.

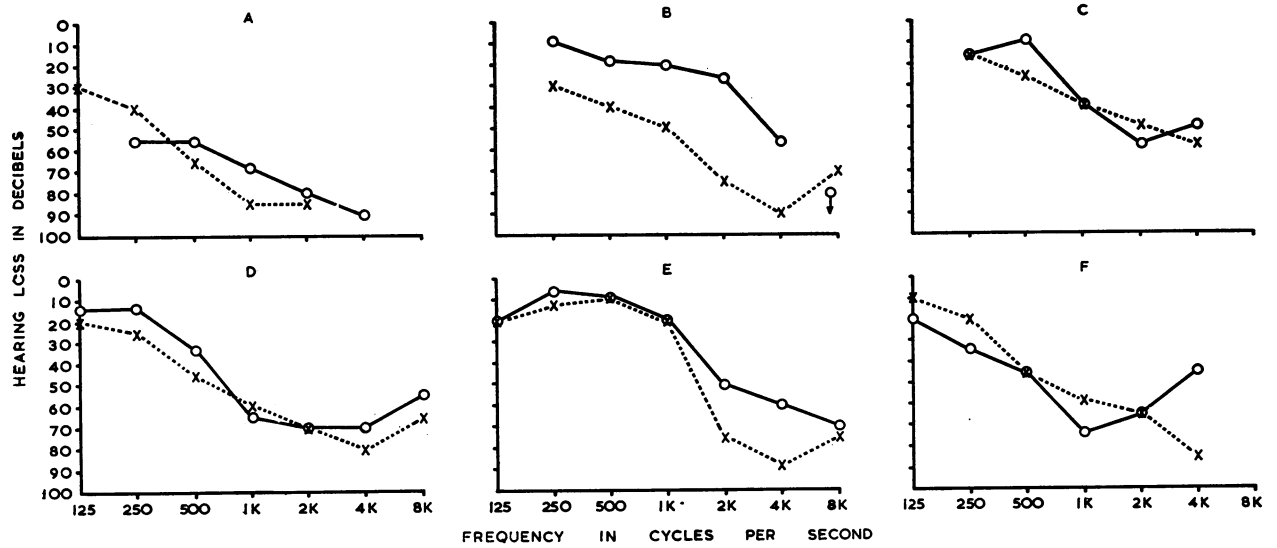
The mother of another (Case E) had alpha-haemolysins in her blood at a low titre, and it is reasonable to assume an A–O blood-group incompatibility as the probable cause of the symptoms.

Three children were premature, with no findings to suggest iso-immunization. One of these (Case F) developed kernicterus and cerebral palsy. The remaining two (Cases B and D) appeared physically normal, although one of us during the examination of hearing, when various tests based on play technique were carried out, observed that all these children had a very mild muscular incoordination in their hands and other parts of the body. They were also regarded by their parents as children who were "restless," "fidgety," and "could not keep still."

It can be seen from the Table that the maximum bilirubin concentration in Cases B, D, E, and F was not very high and would be regarded by many as being well within the range of safety. It was therefore necessary to consider whether any other factors existed which could potentiate the effects of bilirubin.

It was found that all but one (Case C) of the children had received vitamin K in the form of "synkavit." The total dose varied from 15 to 70 mg. in daily amounts of 5 to 20 mg. for the first three to five days. For example Case B, a premature child of 31 weeks' gestation and weighing 2 lb. 11 oz. (1,200 g.) at birth, was given 10 mg. daily for the first three days, and for some odd reason the same amount on the sixth and seventh days. His serum bilirubin rose to 19 mg. on the fifth day. Case E, of 38 weeks' gestation and 6 lb. 14 oz. (3,120 g.) at birth, had a bilirubin concentration of 20.3 mg. on the third day and received 10 mg. of synkavit on the first and third days. Case F, of allegedly 31 weeks' gestation and weighing only 1 lb. 8 oz. (680 g.) at birth, was given 10 mg. of synkavit daily over the first three days of life. The maximum serum bilirubin level was 15 mg. on the sixth day of life.

These babies had therefore all received vitamin K analogue in a high dosage.



Audiographs of six children with perceptive deafness.

Discussion

A prospective study of children who showed signs of jaundice during the neonatal period revealed six cases with congenital perceptive partial deafness. In two of these children the concentration of bilirubin was very high, and both developed kernicterus, athetoid cerebral palsy, and deafness. In four the bilirubin concentration was relatively not high (regarded by many as within the margin of safety). Three of them did not develop clinically detectable kernicterus, had no cerebral palsy, but were affected by perceptive deafness of the type which is known to be associated with haemolytic disease of the newborn. These children received comparatively high doses of synkavit.

Does it mean that the bilirubin concentration regarded as being within the margin of safety (15 mg., 19 mg., 20.3 mg., and 26 mg./100 ml. in these four cases) can still cause a perceptive hearing loss without producing other marked clinical symptoms or signs ? Or does it mean that other contributing factors produced the damage resulting in hearing loss ?

A possibility that vitamin K in the presence of only a moderate degree of hyperbilirubinaemia was responsible for the perceptive deafness cannot be ignored. This may not be the only contributing factor, because several babies had bilirubin concentrations of about the same levels and had also received vitamin K in a similar dosage but did not show any evidence of deafness. On the other hand, the possibility that perceptive deafness in the three cases with a relatively low maximum bilirubin concentration was associated with vitamin K therapy is supported by the fact that no further instances of deafness occurred after the cessation, at the end of 1954, of the habit of giving vitamin K in doses of more than 2 mg.

It is accepted that kernicterus is usually the result of hyperbilirubinaemia (Lathe *et al.*, 1958) and also that kernicterus is more likely to occur in premature infants if vitamin K is given in excessive amounts (Allison, 1955 ; Laurance, 1955).

The relatively low bilirubin concentration which occurred in four of the children with perceptive deafness would suggest that vitamin K did not act, as has been suggested, by causing haemolysis and increasing the degree of hyperbilirubinaemia. Brodie and Ballantine, working on bacteria and not on animals, have suggested that synkavit may uncouple oxidative phosphorylation. This is the same activity that bilirubin is known to possess (Ernster *et al.*, 1957), and if it can be shown to do the same in animals it may explain the damage which the combination of bilirubin and vitamin K may produce.

The hearing loss from hyperbilirubinaemia evidently results from damage to the primary nuclei in the auditory pathway (the cochlear nuclei). No evidence is forthcoming of damage to the peripheral receptor, but various histological studies have shown staining of the cochlear nuclei, and the nuclei in the floor of the fourth ventricle are among the structures most likely to be affected.

There are also physiological reasons why the cochlear nuclei can be selectively damaged, as was pointed out in previous studies (Fisch and Osborn, 1954 ; Fisch, 1955). This is an area which, in the newborn infant, may have the highest metabolic rate of all the structures in the central nervous system. It is now thought that kernicterus is the result of metabolic damage to the central nervous system caused by bilirubin, and vitamin K may act in a similar fashion. It is not surprising, then, that an area which has a very high metabolic rate may be selectively damaged, producing an isolated clinical condition, such as perceptive deafness.

Summary and Conclusions

50 children who were jaundiced at birth, and who had regular daily estimations of total bile pigments and conjugated bilirubin, had their hearing fully tested later, and in six cases a typical perceptive partial deafness was confirmed.

The results showed that perceptive deafness of a characteristic type may occur in jaundiced babies in the absence of athetoid cerebral palsy and at a bilirubin concentration lower than generally regarded as dangerous.

The findings suggest, however, that hyperbilirubinaemia may not have been the sole factor in these cases, and that overdosage with vitamin K may have been partly responsible, although there may have existed some other, so far unsuspected, circumstances which contributed to the damage resulting in deafness.

Further studies will be necessary to find out whether the safety margin of bilirubin levels, applicable to the development of kernicterus and athetoid cerebral palsy, does in fact apply to development of perceptive deafness.

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"If we believe that the typical general hospital of the second half of the twentieth century is the hospital of 400 to 800 beds, affording all the main specialties, and that the little hospitals, often provided with such loving care a century and more ago, are to-day for the most part unfair to the patient and unattractive to staff, then we must dare to express our conviction in the hospital pattern which we plan. None of all this will be easy. We shall find old habits, traditions, prejudices, mistaken loyalties embattled across our path, and the pattern of administration and the complexities of salaries and gradings will add to our difficulties. But against all this we possess a sovereign remedy, and an invincible ally, if we will call it to our aid. It is this. The public do not want a second-rate hospital service. They want the best. They want the most enlightened and effective handling of sickness in all its forms: they want modern methods, modern buildings, modern techniques, modern medicine. Let them only be convinced that these are the standards by which we have framed our plans, and they will brush aside with impatience the opposition of prejudice or self-interest." (Minister of Health, Mr. ENOCH POWELL, addressing the Association of Hospital Management Committees, June 16.)