the period before the appearance of combined ulcers is taken as a basis for comparison. According to Balfour (1932) about 25% of peptic ulcer patients followed for an average of 10 years will show one or more episodes of bleeding. Emery and Monroe (1935) found an incidence of 26.7% in patients observed for an average of 3.5 years. Gastric ulcers are thought to bleed more often than duodenal ulcers (Ivy, Grossman, and Bachrach, 1950). However, Martin and Lewis (1949), in their follow-up of peptic ulcer patients for more than 10 years, observed bleeding in 26.8% of gastric and 35.2% of duodenal ulcers. In the present series the incidence of bleeding in 59 of 157 patients—that is, 37.6%—followed for a similar length of time, is somewhat higher. Moreover, three-fourths of the haemorrhages took place during the period which represented on the average one-eighth or less of the total ulcer history. It is therefore not surprising that conservative treatment was abandoned in favour of partial gastrectomy in 68 of these patients. In fact, the present findings would suggest that surgical treatment is indicated more often in combined ulcers than in single ulcer, whether gastric or duodenal.

Summary

The combination of chronic gastric and duodenal ulcers or ulcer scars was found in 157 hospital patients during a period of eight years. Cases suffering from prepyloric gastric ulcer were excluded owing to the uncertainty of location.

The observed incidence of combined ulceration was 2.7% based on x-ray investigation. With the inclusion of an estimated 25% of prepyloric ulcers the incidence would reach 3.5%. Thus about one in every seven hospital patients suffering from ulcers of the stomach and 1 in 30 patients having a duodenal ulcer or ulcer scar will be found to show combined ulcers.

With due awareness of the frequent occurrence of combined ulcers, the radiological examination represents a reliable means of their diagnosis.

Combined ulcers run a higher risk of bleeding, making surgical treatment more often advisable than in either gastric or duodenal ulcer occurring alone.

Pyloric stenosis does not appear to be a major factor in the pathogenesis of combined ulcers.

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RECTAL TEMPERATURE IN THE NEWBORN AFTER BIRTH ASPHYXIA

BY

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In a previous investigation (Cross, Tizard, and Trythall, 1955) it was shown that if normal babies were given 15% oxygen to breathe there was a fall in oxygen consumption which was so large that the energy loss would be greater than the energy gain from any anaerobic metabolism which might be taking place. From this indirect calorimetry it was suggested that energy production fell under these experimental conditions, and this seemed to be confirmed when Brodie, Cross, and Lomer (1957) showed that infants breathing 15% oxygen heated the plethysmograph in which they were placed less than when they breathed air, though a consistent fall in rectal temperature was not found when the 15% oxygen was given for periods up to 50 minutes. Young kittens and puppies show a fall in temperature directly after oxygen consumption is reduced in anoxia (Moore, 1956a, 1956b).

In babies the absence of this immediate fall in body temperature along with their fall in oxygen consumption in an atmosphere of 15% oxygen might be connected with a relative thermal inertia compared with the smaller animals. Vascular reactions might also play a part, since skin pallor was noticed in the babies. The probability that factors such as these influenced the findings in short-term observations is supported by Sjöstedt and Rooth's (1957) report that in full-term babies the temperature is "a little lower than normal if kept in 15% oxygen for a week."

Although suggestive, these results might not apply to the infant showing apnoea or cyanosis at or after birth. While cyanosis is evidence of anoxia, it is unlikely that the natural condition is ever a pure "anoxic anoxia." CO₂ retention will probably, although not necessarily, be present. An investigation which would in some measure test whether naturally occurring anoxia causes a fall in heat production of the newborn infant was undertaken. We wished to make the investigation as simple as possible so that it could be fitted into the activities of a busy maternity unit, and decided to divide the babies into those that did and those that did not show asphyxia at birth, and to follow their rectal temperatures. As it became apparent that maternal sedation was a complication the scope of our investigation had to be widened slightly, and finally four groups of infants were studied, but the general scheme was not made more complex in any other way.

Material and Methods

Babies were delivered at a labour-room temperature of 78–80° F. (25.6–26.7° C.), wrapped in a towel, and, after they had been held by their mothers, were transferred to the nursery after a period that varied from 10 to 30 minutes. Resuscitative measures used after birth were oxygen, which was given for a few minutes at the discretion of the obstetrician or midwife in charge, and 1 mg. of N-allyl

morphine by intramuscular injection if delay in breathing could be attributed to maternal sedation with pethidine; some mothers who had received pethidine were given 10 mg. of N-allyl morphine an estimated 30 minutes before delivery. In the nursery, where the temperature was kept between 70 and 74° F. (21.1 and 23.3° C.) throughout the investigation, the infant was covered with two blankets, and after a further interval varying between half an hour and one and a half hours was bathed and dressed.

The rectal temperature was taken two-hourly for 24 hours by the nursing staff with thermometers graduated from 85 to 105° F. (29.5 to 40.6° C.), the thermometer being inserted an inch (2.5 cm.) beyond the anus. A complete record was not always obtained, as will be apparent from inspection of the individual totals in Figs. 1-3. So far as possible, all the babies born in a four-months period were examined, but at busy times the taking of temperatures had to lapse.

The infants were born at term, or possibly later in a minority. None received any special treatment apart from oxygen for the few minutes before the establishment of normal breathing. Babies who needed oxygen for some hours after birth have been excluded from this report.

Asphyxia in this paper means failure to establish respiration within three minutes of birth. While the observations were being made it became clear that maternal sedation with pethidine was a frequent cause of apnoea, and a division was therefore made into the following groups: A ("normals"), 53 babies whose breathing began within three minutes and the mother had received only chloral; B ("pethidine and apnoea"), 29 babies in whom normal breathing was not established within three minutes, the mothers having received pethidine; C ("pethidine, no apnoea"), 35 babies who were breathing normally within three minutes, all the mothers having received pethidine. Group D ("pure asphyxia") is made up of 15 babies. The need for sedation in difficult labour rendered apnoea after birth without maternal pethidine an uncommon event, and explains the small number of observations in this group.

The dosage of pethidine and the time between administration to the mother and birth varied considerably. In order that an infant should qualify for groups B or C it had to be born within three hours of a single dose of 200 mg. or within five hours after 400 mg. (2 × 200 mg.) or more.

The accompanying charts show the mean temperatures for each group, and the vertical lines indicate the 95% confidence limits for each set of two-hourly observations. When

there is no overlapping of these lines the odds against the difference between means being due to chance are greater than 20 to 1.

Results

In Fig. 1 the means of groups A and D are compared. Asphyxia is seen to result in a significantly lower rectal temperature from the second to the sixteenth hour.

In Fig. 2, group B is compared with the normal, and a significant lowering of temperature over the same period is apparent. In group C, however, the fall in temperature occurred after pethidine without the intervention of apnoea (Fig. 3), and it is for this reason that we were careful to exclude the possibility of a drug effect in collecting the data for Fig. 1.

FIG. 2.—Mean rectal temperatures after maternal pethidine and apnoea at birth. Conventions as in Fig. 1. — Group A (normals), 53 babies. - - - Group B (pethidine and apnoea), 29 babies.

FIG. 1.—Mean rectal temperatures after normal birth and after birth asphyxia. The vertical lines are the 95% confidence limits of the means. — Group A (normals), 53 babies. - - - Group D (asphyxia, no pethidine), 15 babies.

FIG. 3.—Comparison of mean rectal temperatures after maternal pethidine with and without apnoea at birth. Conventions as in Fig. 1. - - - Group B (pethidine and apnoea), 29 babies. — Group C (pethidine, no apnoea), 35 babies.

Group C comprised 18 babies who received N-allyl morphine, and 17 who breathed in three minutes without it. These subgroups were analysed separately, and as there was very little difference between them they have been taken together to give the total 35 group C babies. The failure of N-allyl morphine, used as an antidote to pethidine apnoea, to influence the later temperature is the subject of comment below.

There was no clinical disorder in any of the babies, apart from the need for brief resuscitative measures at birth in a minority of the apnoeic ones, as has already been noted. Cyanosis both of the lips and of the extremities occurred to a varying degree, as did variations in respiratory rate.

Discussion

The fact that there is a significant difference in temperature over several hours between group A and group D suggests that asphyxia causes a fall in oxygen consumption and energy production as in the experiments on pure anoxia (15% oxygen) already quoted. It is worth speculating on the degree of anoxia our subjects had met, as Brodie *et al.* noted no fall in rectal temperature in infants breathing 15% oxygen for 50 minutes. The pronounced fall in heat production suggested by the low rectal temperature points to an incident of considerable severity.

There is no apparent difference between the temperatures of the two groups of babies whose mothers had received pethidine (B and C), whether the babies were apnoeic for three minutes after birth or not. Their pattern of temperature change after birth is very similar to that of babies with pure asphyxia. Either the initial asphyxia or mild persisting respiratory depression from the drug could explain the similarity to the group D babies. A second possibility is vasodilatation, since J. Ginsburg (1958, personal communication) has found an approximate doubling of skin-blood flow in the human subject for periods up to an hour after 100 mg. of pethidine intramuscularly. Thus the temperature of babies after maternal pethidine might be lowered both by diminished heat production and by increased heat loss.

To some extent the absence of a difference between groups B and C may be due to artificial selection, because severely asphyxiated babies who were felt to need oxygen for a number of hours after birth have not been included in the series, although some of them had much lower temperatures and these would have enlarged group B.

When the babies in group C were divided according to whether or not they had received N-allyl morphine, the fall in temperature was the same in each subgroup. While the drug proved a very effective antidote to pethidine in the initiation of breathing (Paterson and Prescott, 1954) it did not appear to have any subsequent effect on the course of temperature. Roberts *et al.* (1957) similarly found that the reduction of the baby's minute-volume after maternal pethidine was not influenced by this antidote.

We conclude that a somewhat reduced rectal temperature is a natural phenomenon in babies suffering from asphyxia at birth. It seems probable that this lowered temperature is the result of a period of diminished metabolic rate, caused by the anoxia. If this is so, then the lower temperature may have survival value.

Summary

Neonatal rectal temperature was measured at two-hourly intervals in 53 infants after normal delivery and in 15 after birth asphyxia. Asphyxia was found to cause a significantly lower temperature for 16 hours.

The same effect followed the maternal administration of pethidine independently of apnoea at birth.

The reduced temperature appears to be a natural consequence of anoxia in the baby.

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TREATMENT OF RHEUMATOID ARTHRITIS WITH CHLOROQUINE

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Mepacrine was first observed to have a beneficial effect on the course of rheumatoid arthritis by Page (1951), when treating discoid lupus erythematosus. Two of these patients had associated rheumatoid arthritis, which cleared up under mepacrine treatment. Haydu (1953) two years later published his result of treatment by chloroquine of 28 patients suffering from rheumatoid arthritis. In the dosage of 0.5 g. of chloroquine thrice weekly for six months he found considerable improvement in 21 of the 28 patients with rheumatoid arthritis without encountering toxic symptoms during the trial. Forestier and Certonciny (1954) published a short-term trial of mepacrine in 11 patients and of chloroquine in 17 patients suffering from rheumatoid arthritis for a period of one to six months. Half of the patients in each group responded favourably. Escarpenter-Oriol *et al.* (1955), quoted by Bagnall (1957), treated eight rheumatoid arthritics with mepacrine and 30 with chloroquine, but none of them received more than five months' treatment. Nevertheless, the authors noted an improvement in 29 of the chloroquine cases.

Following an investigation of the unusually high incidence of amoebic infection in patients with rheumatoid arthritis (95% compared with 30% of normal patients in Oregon), Rinehart employed chloroquine together with di-iodohydroxyquinoline ("diodoquin") in these patients (Rinehart, 1955; Rinehart *et al.*, 1957). He noted improvement in both conditions and attributed most of the antirheumatic activity to chloroquine. Eight out of 11 children showed major improvement of rheumatoid arthritis, and 8 out of 14 adults experienced similar benefit. He followed this series by a "double blind study" of two groups of rheumatoid arthritics (33 in all) receiving either chloroquine or an inert substance. He regarded the improvement in the chloroquine group as statistically significant, more than half the patients on chloroquine deriving and maintaining improvement after two months.

Freedman (1956) observed 66 patients, divided into equal groups of similar rheumatoid disease, half of whom received chloroquine (200 to 300 mg. a day) and the remainder dummy tablets. Small doses of salicylates were permitted during the trial, which lasted 16 weeks in the first instance. Subjective and objective progress was assessed and there was appreciable benefit during this period. Subsequently, 50 patients remaining under treatment received chloroquine and 43 became really