ADR Ultrasound (Tempe, Arizona) supplied the ultrasound equipment.

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Correspondence to Dr L Ch de Crespigny, University of Melbourne, Department of Obstetrics and Gynaecology, Parkville, Victoria 3052, Australia.

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Normal values for mature and immature neutrophils in very preterm babies

B W LLOYD AND A OTO

Department of Paediatrics and Neonatal Medicine, Hammersmith Hospital, London

SUMMARY Serial leucocyte counts were made on 24 babies of less than 33 weeks' gestation during the first 5 days of life. The values for mature neutrophils show two important differences from those obtained by previous workers studying term babies, in that the counts were much lower on the first day of life and showed a wider range of values at all ages. In contrast, immature neutrophil counts, expressed either as absolute values or as a proportion of the total neutrophil count (the I/T ratio), were similar to those found in previous studies and had a considerably narrower range.

Neutrophil counts are widely used to help diagnose infection in newborn babies.¹⁻⁴ Published reference ranges have been largely constructed using data from term or fairly mature preterm babies.²⁻⁶ It has been suggested¹⁻⁵⁻⁷ that the neutrophil counts of preterm babies differ from those of term babies, casting doubt on the usefulness of these ranges when dealing with the very immature. Previous work on preterm babies has been with fairly mature infants¹⁻⁵ (M Xanthou and E Hey, 1981, personal communications), so we set out to determine the range of mature and immature neutrophil counts in healthy babies of not more than 32 weeks' gestation.

Patients and methods

Twenty-four babies admitted to the neonatal intensive care unit at Hammersmith Hospital between June 1979 and August 1980 were studied with their parents' written consent and the approval of the hospital's ethical committee. All were 32 weeks' gestation or less according to their mothers' dates, and gestational assessment by the method of Dubowitz *et al.*⁸ Mean gestational age was 30.4 weeks (range 26-32) and mean birthweight 1510 g (range 900-1900).

Certain conditions were fulfilled to ensure that the infants could reasonably be considered healthy. There were 3 babies born after prolonged rupture of membranes and 8 with very mild and short-lived respiratory distress who had no clinical or laboratory evidence of infection.

Blood was taken from each baby at 1, 12, 24, 48, 72, 96, and 120 hours, although specimens were not obtained at every age from all. A total of 124 specimens was taken from 24 babies using capillary blood from the heel; 0.2 ml of blood was taken into a tube containing 0.3 mg of dipotassium EDTA. A total leucocyte count was performed using a Coulter counter. A blood film was stained using a standard May Grunwald (Giemsa)

Table Values for mature and immature neutrophils and I/T ratios in the first 5 days of life

Age (hours)	Mature neutrophils ($\times 10^9/l$)		Immature neutrophils ($\times 10^9/l$)		I/T ratio	
	Median (range)	Mean	Median (range)	Mean	Median (range)	Mean
(n=10)	4.64 (2.20-8.18)	4.57	0.11 (0-1.5)	0.30	0.04 (0-0.35)	0.09
12 (n=17)	6.80 (4.0-22.48)	8.61	0.27 (0-1.6)	0.48	0.04 (0-0.21)	0.06
24 (n=17)	5.60 (2.61-21.20)	7.64	0.14 (0-3.66)	0.47	0.03 (0-0.17)	0.05
48 (n=20)	4.98 (1.02-14.43)	6.24	0.13 (0-2.15)	0.44	0.02 (0-0.17)	0.05
72 (n=22)	3.19 (1.28-13.94)	4.63	0.16 (0-2.42)	0.38	0.03 (0-0.25)	0.05
96 (n=21)	3.44 (1.37-16.56)	5.33	0.23 (0-3.95)	0.45	0.05 (0-0.37)	0.07
120 (n=17)	3.46 (1.27-15.00)	4.98	0.25 (0-2.89)	0.44	0.05 (0-0.21)	0.07

method. A differential count was performed on 100 leucocytes. A band cell was defined as a neutrophil in which the width of the narrowest segment of the nucleus is not less than one-third of the broadest segment.³

Results

Mature neutrophils. There was a wide range of values at each age particularly on the first day of life (Table). The values are not normally distributed; a few high values skew the mean upwards, so that at each age, except at one hour, the median is lower than the mean.

The median mature neutrophil count rises from $4.64 \times 10^9/l$ (range 2.20-8.18) at one hour to a peak at 12 hours of $8.61 \times 10^9/l$ (range 4.00-22.48) and levels out at $3.19 \times 10^9/l$ (range 1.28-13.94) by 72 hours. The values obtained from the 8 babies with mild respiratory distress lay evenly within the range of the other 16 babies.

Immature neutrophils. All band cells and cells less mature than band cells were classed together as immature neutrophils. The Table shows the results obtained at each age. There is no peak at about 12 hours comparable with that seen with the mature neutrophils. All but 15 of the 124 values were less than $1.0 \times 10^9/l$.

The proportion of immature (I) to total (T) neutrophils—the I/T ratio—was also calculated for each blood count. The values obtained are shown in the Table. Only 13 counts had an I/T ratio exceeding 0.14, of which only 5 exceeded 0.2.

Discussion

Our study is thought to be the first on healthy babies

of such immaturity. Our results show broad similarities to those obtained from term babies in the studies mentioned above,^{2,5,6} but there are two important differences.

The peak in mature neutrophil values seen at 12 hours was considerably lower in our babies than that shown by other workers with term infants.^{1,2,5,6} Akenzua's median at about $13.5 \times 10^9/l$ is nearly double ours. Xanthou found a mean of $13.0 \times 10^9/l$, although when she studied 14 preterm babies of considerably greater gestation than ours (M Xanthou, 1981, personal communication), the mean was very similar to ours at about $8.0 \times 10^9/l$. Manroe found that at 12 hours 90% of her counts were within the range of $8.0-14.4 \times 10^9/l$; 70% of our babies had values below this lower limit.

After age 48 hours our median and mean values are close to the values obtained by others,^{2,5,6} but the range of neutrophil counts at each age is much wider in our babies.^{5,6} At every age from 12 hours, at least 30% of our babies had counts outside both Xanthou's and Manroe's ranges. Out of a total of 124 counts, 63 were outside Xanthou's range and 64 were outside that of Manroe; that is just over half of our counts are abnormal when compared with these ranges. In the first 48 hours most of these 'abnormal' values were below these two ranges, thereafter more were above them.

These findings cast considerable doubt on the widespread practice of comparing mature neutrophil counts obtained from preterm babies with reference standards based largely on data from term babies. Furthermore, their value depends on the experience of the technicians performing them.

In contrast, our values for immature neutrophils are not greatly different from those obtained by others.^{2,5,6} Several workers^{2,3,6} have suggested that the immature neutrophil count, either as an absolute value or expressed as the proportion of the total neutrophil count (the I/T ratio), is of more help in the diagnosis of infection than is the mature neutrophil count. Our results, showing a considerably narrower range of normal for both immature neutrophils and I/T ratios, support this idea.

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Correspondence to Dr B W Lloyd, Department of Paediatrics, New Cross Hospital, Wolverhampton WV10 0QP.

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Oral converting enzyme inhibitor in malignant hypertension

WILLIAM GRISWOLD, RICHARD McNEAL, DAN O'CONNOR, VIVIAN REZNIK, AND STANLEY MENDOZA

Department of Pediatrics, University of California, San Diego, USA

SUMMARY Malignant hypertension, which developed in a 9-year-old boy after an episode of haemolytic uraemic syndrome, could not be controlled with antihypertensive agents. However, treatment with oral converting enzyme inhibitor (captopril) was effective in controlling the blood pressure and it averted bilateral nephrectomy. No adverse effects from the drug were noted.

Captopril (SQ 14225), an orally active inhibitor of angiotensin converting enzyme, has been used for the control of hypertension in adults. The following case shows the striking effectiveness of captopril in a child with malignant, high renin, drug-resistant hypertension.

Case report

This 9-year-old boy had been in good health until December 1977 when he developed haemolytic uraemic syndrome. In the hospital, the patient was anuric for 17 days and required peritoneal dialysis. As urine output resumed the blood pressure increased to 150/100 mmHg requiring antihypertensive therapy. The patient was discharged after one month with a serum creatinine concentration of 1.6 mg/100 ml (142 μ mol/l).

However one month later blood pressure rose to 150/110 mmHg and the patient was readmitted with papilloedema, plasma urea 29 mmol/l, and creatinine 4.4 mg/100 ml (392 μ mol/l). Despite treatment the blood pressure was poorly controlled and serum

creatinine levels remained high. Urinary vanillyl-mandelic acid was normal. Intravenous pyelogram and technetium renal scan showed decreased renal function but were otherwise normal. Peripheral venous renin was greatly increased at over 100 ng/ml per hour (normal 0-5). Renal biopsy showed evidence of nephrosclerosis with severe endothelial proliferation in the arterioles. Bilateral selective renal angiograms showed loss of corticomedullary junction and interlobular arteries suggesting glomerular disease. Renin was 81.9 in the right renal vein and 111 ng/ml per hour in the left.

His subsequent course was difficult, complicated by persistent hypertension despite treatment with various combinations of the following; propranolol 480 mg/day (26 mg/kg per day), hydralazine 400 mg/day (22 mg/kg per day), prazosin 12 mg/day (0.6 mg/kg per day), methyldopa 1500 mg/day (82 mg/kg per day), clonidine 0.8 mg/day (0.04 mg/kg per day), minoxidil 40 mg/day (2.2 mg/kg per day), guanethidine 100 mg/day (5.5 mg/kg per day), and frusemide 400 mg/day (22 mg/kg per day). Heart size was persistently enlarged on chest x-ray film; echocardiogram showed left ventricular hypertrophy and pericardial effusion. Weight decreased to 18.2 kg. He was depressed and anorectic. There were 2 episodes of hypertensive encephalopathy. He underwent pericardiectomy for treatment of persistent effusion, probably due to minoxidil, in September 1978.

In late December 1978, permission to use captopril for this patient was obtained from Squibb via a humanitarian protocol. Other antihypertensives were