Leucocyte Blood Picture in Healthy Full-term and Premature Babies During Neonatal Period

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Xanthou, M. (1970). *Archives of Disease in Childhood*, 45, 242. **Leucocyte blood picture in healthy full-term and premature babies during neonatal period.** Serial leucocyte counts were done on 15 full-term babies during the first 10 days of life and on 14 prematures during the first 30 days. In addition a single count was done on the total of 53 babies around the 96th hour of life. Absolute values of each cell type are given for each postnatal age examined. The main changes in the leucocyte counts during the neonatal period were found to be as follows: (a) An increase in polymorphonuclear neutrophils after birth, reaching a peak at 12 hours, thereafter dropping to a figure which remains fairly constant from 72 hours onwards. (b) A decrease in polymorphonuclear neutrophil precursors. (c) A drop in lymphocytes reaching a minimum at 3 days of age, and thereafter rising to a steady level at about 10 days. The mean values $\pm$ 2SD for each cell type at 96 hours of life are as follows. *Polymorphonuclear neutrophils*: Mean = 4100/cu.mm., M + 2SD = 6900/cu.mm., M - 2SD = 1400/cu.mm. *Eosinophils*: Mean = 700/cu.mm., M + 2SD = 1900/cu.mm., M - 2SD = 200/cu.mm. *Lymphocytes*: Mean = 3900/cu.mm., M + 2SD = 7100/cu.mm., M - 2SD = 2200/cu.mm. *Monocytes*: Mean = 1000/cu.mm., M + 2SD = 1800/cu.mm., M - 2SD = 200/cu.mm.

Bacterial infections in the newborn still account for a considerable morbidity and mortality. This is partly because the newborn and especially the premature are prone to serious infections by organisms, especially Gram-negative, that are non-pathogenic in older people, and partly because the signs of these infections, both local (inflammatory) and general (fever, etc.) may be absent or minimal and hard to detect. Thus fatal septicaemia may occur with little warning.

The white cell count routinely used in the detection of bacterial infection in children and adults is also thought to be of little value in the newborn.

In reviewing papers written in English, it appears that this subject has not been studied since the late 1930s (Agress and Downey, 1936; Bauza, 1933; Forkner, 1929; Hosen, 1933; Lippman, 1924; Lucas *et al.*, 1921; Rogatz, 1930, 1933; Sanford, 1929; Washburn, 1935; Wollstein, 1938). From 1940 onwards interest seemed to fade; a few

studies were published (not in English) and these remained more or less unnoticed in the English medical literature (Hinglais and Hinglais, 1949; Klees, Schlagetter, and Wokittel, 1958; Kumar, 1944; Lee, 1943; Muhl, 1949; Napp, 1950; Nassar and Verga, 1955; Uklonskaya, 1953; Upadhyay, 1945).

The main conclusion drawn by authors of modern textbooks comes from the studies of the 1930s, and it is that the leucocyte blood picture in the normal newborn is so variable and unpredictable that normal values cannot be established.

For instance, Wintrobe (1967), referring to Washburn (1935), states, 'during infancy, however the leucocyte count may be very irregular and until the 26th week of life, variations from 5000-24,000 may occur in the absence of demonstrable disease'. Clement Smith (1959) says, 'an exact account (of the white cell count in the newborn) is not only unnecessary here but might be more confusing than valuable, so wide are the ranges of normal variation'. This view does an injustice to some of these studies but nevertheless they were unsatisfactory in several respects.

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The practice of reporting the differential leucocyte count as a total with percentages of each cell type is scientifically correct since this is, after all, the method by which the leucocyte count is made. However, it is confusing when serial changes are being described, and it is much clearer to express the results in terms of absolute values for each cell type. In some of the older studies only the total counts or the differentials are given. Besides this, only small numbers of babies were studied or only a limited number of counts was made on each baby.

Some of these defects are repaired in the later papers, and Klees *et al.* (1958) and Straková (1964) provide evidence for a constant pattern of changes in the first few days of life.

However, no investigator has published a systematic study of the dynamics of blood leucocytes in the neonatal period, or studied sufficient numbers to establish biological ranges for each cell type over this period of life.

The purpose of the current study was, therefore, to establish the leucocyte picture of the healthy full-term and premature baby. The changes seen with illness are the subject of a separate communication.

Material and Methods

Studies were made on 69 healthy babies, capillary blood being obtained from a free-flowing heel-prick. The 69 babies included the following groups.

Group A (15 full-term babies). The first sample was collected in the first half hour following delivery, thereafter 6-hourly for the first 72 hours of life and then daily until the 7th–10th day.

Group B (14 babies, with birthweight less than 2500 g.). 13 were born before the 39th week, 1 was a small-for-dates baby of 40 weeks' gestation, whose white cell counts did not differ significantly from the others. Again the first sample was obtained within half an hour of delivery, and thereafter samples were collected every 6 hours in the first 24 hours of life and then daily until the 20th–31st day of life; in addition 6-hourly collections were made on a day chosen at random after the 10th day of life in order to look for diurnal variations.

Group C (40 full-term babies). Because the number of healthy babies was too small to show if the counts of each leucocyte cell type were normally distributed, the blood picture of an additional 40 full-term babies was studied around the 96th hour of life; the time at which the neutrophil count has stabilized.

Total white cell counts were made on a Coulter electronic counter which has an instrumental error of up to 2%. The total error of the method, however, including heel-prick collection, pipetting, and diluting has been estimated as up to 8%.

The films were stained by the combined May-

Grünwald + Giemsa method and cover slips were used.

For the differential examination 2 sets of 100 cells were counted with a repeat examination of a further 200 if the difference between the original counts in respect of any cell-type was greater than 10%.

Results

There is little to be learnt from the total white cell count in any subject and especially in the newborn baby; therefore the results reported below are in terms of individual cell types.

(A) Neutrophils

Polymorphonuclear neutrophils. At birth the polymorphonuclear neutrophils were the predominant cells found in the blood. Each baby showed a marked increase in the absolute value during the first 24 hours of life, reaching a peak at 12 hours.

In full-term babies the mean value was 8000/cu.mm. at birth, rose rapidly to 13,000/cu.mm. at 12 hours of age, and dropped almost as rapidly to 4000/cu.mm. by 72 hours of age, thereafter remaining stable over the period studied (Fig. 1).

FIG. 1.—Means, ranges, and means ± 1 SD of neutrophils on 15 full-term healthy babies during the first 10 days of life.

In premature babies the mean value at birth was 5000/cu.mm., at 12 hours 8000/cu.mm., and at 72 hours 4000/cu.mm. Thereafter there was a gradual fall in the mean count, reaching 2500/cu.mm. by the 28th day of life (Fig. 2).

It is worth noting that both in full-term and in premature babies after the first 72 hours of life the absolute values of polymorphonuclears never exceeded 7000/cu.mm. and remained remarkably steady in each baby, so that, in general, daily differences in polymorphonuclear neutrophil counts

TABLE I
Means and Standard Deviations of Daily Differences in Absolute Values of Polymorphonuclear

Days	4-5	5-6	6-7	7-8	8-9	9-10	10-11	11-12	12-13	13-14	14-15	15-16	16-17
Means	-277	-111	-133	+78	-142	-126	+78	-28	-28	-23	-83	-175	-193
SD	611	476	565	619	342	303	386	309	240	321	236	270	284

FIG. 2.—Means, ranges, and means ± 1 SD of neutrophils of 14 healthy babies during the first month of life (13 premature + 1 small for dates).

were within the range of experimental error (Table I).

The range of the absolute values of polymorphonuclear neutrophils after the 3rd day of life (Fig. 1 and 2) is due to the differences in values between babies and not to the fluctuations of the value in individual babies.

From Table II it can be seen that there are no obvious changes in neutrophil counts in healthy premature babies from the 10th to the 30th day of life.

TABLE II

Absolute Values of Polymorphonuclear Neutrophils 6-hourly on Random Day after 10th Day of Life

Babies	Age (dy.)	Hours				
		12	18	24	6	12
1	10	2600	3000	2800	2600	2900
2	10	5200	5300	5200	4800	4600
3	11	2900	3000	2900	2700	2900
4	12	6200	6000	5800	5600	5700
5	12	2000	2100	2200	2100	2300
6	13	6600	6700	6600	6400	6300
7	13	1100	1000	1100	1100	1000
8	15	2100	2100	2200	2000	2000
9	16	3200	3300	3100	3400	3300
10	18	3900	3800	3600	3700	3700
11	20	3700	3600	3700	3500	3000
12	22	3900	4100	3900	4100	4000
13	24	2800	3000	2900	2900	2700
14	26	2900	2800	2800	2600	2700

The 96-hour values of Group A were added to Group C for analysis of distribution of neutrophil counts at this age.

As seen in Fig. 3, the distribution of neutrophil counts appears to be slightly skewed to the right. However, the χ^2 test shows that it is compatible with an arithmetic normal distribution.

The mean of the absolute values at 96 hours of age was 4100/cu.mm. and the standard deviation 1400/cu.mm.; thus the mean $+2$ SD is approximately 6900/cu.mm. and -2 SD 1300/cu.mm.

Of the observed values all but four fell within the range 2500 to 6500/cu.mm.; the lowest was 1400/cu.mm. and the highest was 10,200/cu.mm. However, this latter count, the only one to exceed 7000/cu.mm., was from a baby who had suffered intrapartum asphyxia and meconium aspiration and who, though well at 96 hours, should not perhaps have been regarded as normal. Since this baby was not excluded in advance, his white cell count has been included in the study.

Band forms. It was found that, in the first 2-3 days of postnatal life, a varying proportion of neutrophils, sometimes half of them, presented as band forms (Fig. 4), but their number decreased thereafter so that by the end of the first week they usually

FIG. 3.—Histogram of neutrophils on 53 healthy full-term babies.

Leutrophils on 29 Full-term and Premature Babies from 4th to 30th Day of Life

7-18	18-19	19-20	20-21	21-22	22-23	23-24	24-25	25-26	26-27	27-28	28-29	29-30	30-31
-100	-190	-40	+80	-80	-60	-80	+11	-33	+44	+57	-83	-116	-125
194	448	397	187	161	257	339	261	250	343	127	204	183	50

represented a small percentage of the total neutrophil count.

Metamyelocytes. Metamyelocytes in full-term babies were found in greater numbers during the first 3 days of life and practically disappeared by the end of the first week. As shown in Fig. 5, counts of up to 2000/cu.mm. were found to be normal during the first 72 hours of life.

Premature babies gave approximately the same picture as full-term babies but with somewhat higher counts during the first 72 hours of life, the upper range approaching 3000/cu.mm. occasionally. In premature, as well as full-term babies, metamyelocytes had almost entirely disappeared towards the end of the first week of life (Fig. 6). After the first 72 hours of age a metamyelocyte count of over 500/cu.mm. was very unusual both in premature and full-term babies.

Myelocytes. In healthy full-term babies myelocytes were found within a range from 100 to 750/cu.mm. during the first 3 days of life, while

an occasional one was seen up to the end of the first week of life.

Premature babies presented similar findings but with a range of up to 1000/cu.mm. during the first 3 days of life, and in the prematurely born an occasional myelocyte was found up to the 30th day of life.

Promyelocytes. An occasional promyelocyte was sometimes seen in the blood of a healthy newborn baby. This was more frequently noticed during the first days of life and in premature rather than full-term babies.

Blast cells. An occasional blast cell was also encountered in healthy newborns, and as with promyelocytes, more frequently during the first days of life and in premature rather than full-term babies.

(B) Eosinophils. The numbers of eosinophils during the first week of life were variable, ranging

FIG. 4.—A neutrophil band form and a normoblast in the blood of a 24-hour-old baby.

FIG. 5.—Means and ranges of metamyelocytes of 15 full-term healthy babies during the first 10 days of life.

from 100–2500/cu.mm. both in full-term and premature babies (Fig. 7 and Fig. 8).

The distribution of the eosinophils of 53 healthy full-term babies at the 96th hour of life was logarithmically normal (Fig. 9).

Logarithmic transformation gives the following figures: Mean = 700/cu.mm., $M + 2SD = 1900$ /cu.mm., $M - 2SD = 200$ /cu.mm. The upper figure observed at that time was 1900/cu.mm. and the lowest 200/cu.mm. In the group of premature babies a steady rise was found after the first week of life, the mean being under 600/cu.mm. during the first week, 800/cu.mm. at the end of the 2nd week, and just over 1000/cu.mm. by the end of the first month (Fig. 8).

(C) Basophils. Basophils were encountered in very small numbers both in premature and full-term babies. Their numbers tended to follow the rise or fall of the eosinophils.

FIG. 6.—Means and ranges of metamyelocytes of 14 healthy babies during the first month of life (13 premature + 1 small for dates).

FIG. 7.—Means and ranges of the eosinophils of 15 healthy full-term babies during the first 10 days of life.

(D) Lymphocytes. The absolute values of lymphocytes tended to fall during the first 3 days of life and then rise up to the 10th day both in premature and full-term babies (Fig. 10 and 11).

The distribution of the lymphocytes of 53 healthy full-term babies at the 96th hour of life was logarithmically normal (Fig. 12).

Logarithmic transformation gives the following figures: Mean = 3900/cu.mm. $M + 2SD = 7100$ /cu.mm. $M - 2SD = 2200$ /cu.mm. The highest number observed at that time was 9100/cu.mm. and the lowest 2000/cu.mm.

In premature babies the absolute numbers of lymphocytes remained steady after the first 10 days of life.

(E) Monocytes. The absolute values of monocytes showed a rise at 12 hours of life, with a subsequent gradual fall until the third day of life both in premature and full-term babies. After this there was a further rise up to the 7th day of life (Fig. 13 and 14).

The distribution of the monocytes of 53 healthy

FIG. 8.—Means and ranges of eosinophils of 14 healthy low birthweight babies during the first month of life (13 premature + 1 small for dates).

FIG. 9.—Histogram of eosinophils of 53 healthy full-term babies.

full-term babies at the 96th hour of life was normal using arithmetic values (Fig. 15).

The mean value was 1000/cu.mm. and the SD 400/cu.mm. The observed upper figure at that time was 2100/cu.mm. and the lowest 300/cu.mm.

In prematures the mean and ranges were quite steadily maintained after the 10th day of life up to the end of the first month.

Discussion

There are obvious and significant trends in the peripheral blood of the numbers of the various white cell types in the first few days of postnatal life.

In theory, the number can be increased by: (1) increased production in the marrow; (2) displacement from storage areas, especially the marginal layer of vessels; (3) increased life time in

FIG. 10.—Means and ranges of lymphocytes of 15 healthy full-term babies during the first 10 days of life.

FIG. 11.—Means and ranges of lymphocytes of 14 healthy low birthweight babies during the first month of life (13 premature + 1 small for dates).

the blood; (4) decreased passage into tissues; and (5) haemoconcentration.

The reverse of these five situations will decrease the number of white cells in the peripheral blood.

Since the main purpose of this study was to establish normal values, the dynamics of white cell fluctuation will not be discussed in detail. However, certain striking features call for comment.

The most striking change is the enormous rise in neutrophils, which takes place on the first postnatal day (Bayer, 1881; Agress and Downey, 1936; Lippman, 1924; Lucas *et al.*, 1921). This rise fully accounts for the increase in total white cells which has so often been reported.

Since there is a simultaneous decrease in the numbers of lymphocytes and no commensurate

FIG. 12.—Histogram of lymphocytes of 53 healthy full-term babies.

FIG. 13.—The mean and range of the monocytes of 15 healthy full-term babies during the first 10 days of life.

increase in other white cells, it seems most improbable that haemoconcentration, so often invoked to explain this phenomenon (Oski and Naiman, 1966; Schiff, 1892; Wollstein, 1938), is the true explanation.

Since there is only a small rise in neutrophil precursors, it also seems improbable that increased marrow production is the cause of the rise.

The most plausible explanation seems to be the displacement of neutrophils from the marginal layer of vessels. This is known to happen after violent exercise in adults (Boggs, 1967), and in the newborn may well reflect his personal labours in childbirth which is by no means a passive process.

Another striking feature as regards neutrophils is that the absolute values of polymorphonuclears both in full-term and premature babies after the first 72 hours of life never exceeded 7000/cu.mm. or fell below 1000/cu.mm., and remained remarkably steady in each individual baby, so that daily differences in counts were found to be within the range of experimental error. As regards the absence of diurnal changes in polymorphonuclear neutrophil counts in the newborn, this is in keeping with other observations on the absence of diurnal rhythms in the newborn.

FIG. 14.—Means and ranges of monocytes of 14 healthy low birthweight babies during the first month of life. (13 premature + 1 small for dates).

FIG. 15.—Histogram of monocytes of 53 healthy full-term babies.

The other obvious changes in the neonatal period, viz. a drop in the numbers of neutrophil precursors (myelocytes, metamyelocytes) (Agress and Downey, 1936; Forkner, 1929; Kato, 1935; Lippman, 1924; Sanford, 1929; Washburn, 1935; Wollstein, 1938), the marked drop in lymphocytes in the second and third day (Forkner, 1929; Kato, 1935; Lippman, 1924; Wollstein, 1938), and the rise in eosinophils towards the end of the first month (Medoff and Barbero, 1950; Burrell, 1953), are harder to explain.

As regards the latter trend Medoff and Barbero (1950) have suggested that this could be due to recovery from the hyperadrenal or shock state of birth to the subsequent neonatal hypoadrenalism.

Also noteworthy is the high level of monocytes in the neonatal period, usually exceeding that found in adults (Forkner, 1929; Kato, 1935; Klees *et al.*, 1958; Uklonskaya, 1953).

The most important finding from this study has been the demonstration that quantitative and qualitative changes of white cells in individual healthy full-term and premature newborn babies follow a remarkably constant pattern during the neonatal period.

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