

Blood Neutrophil Response to Bacterial Infection in the First Month of Life

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Gregory, J., and Hey, E. (1972). *Archives of Disease in Childhood*, **47**, 747. **Blood neutrophil response to bacterial infection in the first month of life.** Serial white blood cell counts were undertaken on 100 babies who required admission to hospital in the first 4 weeks of life. Severe neutropenia was seen in 3 babies who died with overwhelming septicaemia, but a significant and early rise in the absolute polymorphonuclear neutrophil count was detected in 9 of the remaining 11 cases of septicaemia. A similar neutrophil response was seen within 24 hours of the onset of symptoms in 5 babies with meningitis, 10 babies with urinary infection, and 5 babies with pneumonia. Raised neutrophil counts were seen in only 9 of the remaining 66 babies, and all 9 had undergone major surgery.

In more than 98% of healthy babies the neutrophil count is within the range 1350 to 8840 cells/mm³ after the first 4 days of life; counts outside this range nearly always occur during serious bacterial infection.

It seems to be generally believed that white cell counts are so variable as to be of negligible diagnostic value in the neonatal period. Clement Smith wrote in 1945 in his book *The Physiology of the Newborn Infant*:

'To describe in mathematical detail the interrelationships of the various white blood cells immediately after birth would require a long discussion. So well has the subject been reviewed by Wollstein (1938), Lippman (1924), Lucas *et al.* (1921), Forkner (1929), and most recently Washburn (1935), that an exact account is perhaps unnecessary; indeed a detailed tabulation might be more confusing than valuable so wide is the latitude of normal variation.

'... Perhaps the most useful conclusion that can be drawn from this evidence is that one should be very hesitant to apply testimony from the white blood cell count to any clinical problem occurring in newborn life.'

Smith found no reason to change his views when he came to prepare the third edition of his book in 1959, and Oski and Naiman (1966) and Wintrobe (1967) have echoed similar views in their recently published texts. However, such a sweeping conclusion does scant justice to the available data: a consistent, if transient, polymorph leucocytosis in the first 48 hours of life is followed by a rapid fall in the total white cell count and the appearance of progressively more marked relative lymphocytosis after the first week (Aitken, 1902), and Klees,

Schlagetter, and Wokittel (1958), Straková (1964), and Xanthou (1970) have recently quantified these changes very precisely. In the light of this evidence we decided to challenge the assumption that white cell counts lacked diagnostic value by studying 100 young babies serially throughout their stay in the Babies' Hospital, Newcastle. Nearly 10% of the babies admitted to this small unit show evidence of infection on admission, while postoperative sepsis is always a real risk in those requiring surgery.

Patients and Methods

White blood cell counts were undertaken on all babies less than 28 days old at the time of admission. The first specimen was obtained on admission, and further specimens were collected at regular intervals until the babies left hospital. The first 50 babies were taken into the study between 1 March and 20 August 1970. Blood specimens were obtained on admission and thereafter at least 3 times each week (but more frequently when there was clinical evidence of possible infection). A further 50 consecutive babies were taken into the study between 1 November 1970 and 3 May 1971. Blood specimens were obtained from these babies once a day for at least the first 10 days after admission (and for longer where there were signs of possible infection); further specimens were taken on alternate days until the babies left hospital.

Two specimens of blood were also taken from 100 healthy term babies and 100 healthy preterm babies

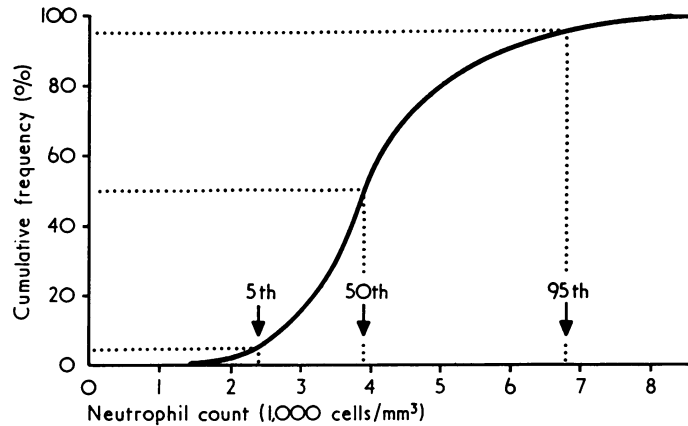


FIG. 1.—Range and distribution of the absolute neutrophil count on the 5th day of life. Constructed from 400 counts on 100 healthy babies.

36 hours, 5 days, and 10 days after delivery in the local maternity hospital. Duplicate counts were performed on each specimen, giving a total of 4 counts on each baby at each age.

Haematology. Capillary blood was obtained from a free-flowing heel prick and 0.02 ml was diluted in normal saline without delay so that a total white blood cell count could be obtained using a Model A electronic Coulter Counter. Films were made and stained with Leishman's stain; these slides were then labelled in code and stored for 3 to 13 days before a differential white cell count was undertaken by one of the authors. (This arrangement was adopted in order to eliminate bias in the counting procedure, and minimize the influence of our research findings on the management of the infants being studied.) Two sets of 100 cells were counted, and a further 200 cells were counted if the difference between the 2 original neutrophil counts was more than 4%. The white cell studies were supplemented by haemoglobin and platelet counts wherever there was clinical evidence to suggest sepsis or disturbed haemostasis.

Bacteriology. Appropriate specimens were collected from each baby without delay wherever there was clinical evidence of possible infection. Less than a quarter of all the specimens of CSF, blood, and urine sent for examination revealed evidence of infection.

Freshly voided specimens of urine obtained after thorough skin cleansing were examined under a microscope and sent for bacteriological examination within an hour of being passed. On 4 occasions it proved impossible to obtain a clean-catch specimen of urine within a reasonable time: urine was then obtained by percutaneous bladder aspiration. Urinary infection was only diagnosed where the colony count exceeded 100,000 organisms/ml.

Blood for bacteriology was obtained from the femoral vein after first cleaning the skin with iodine.

Results

Normal neutrophil count.

Term babies. The total white cell count of the 100 healthy babies we examined at 1½, 5, and 10 days after birth had a skew distribution like that seen by Garrey and Bryan (1935) in older children and adults. The neutrophil count had a similar scatter (Fig. 1), but the logarithm of the count was symmetrically distributed about the mean at each age.

Many authors have published data showing how the mean neutrophil count varies with age, but few have studied more than 30 subjects or published their results in a way that makes it possible to define the normal range for the absolute count. However, analysis of the available European and North American figures revealed reasonable agreement and an almost constant coefficient of variation during the first 4 weeks of life; it also provided additional evidence that the neutrophil count probably has a log-normal distribution. At least 90% of these counts fell within the limits given in the Table. On the assumption that neutrophil counts have a log-normal distribution and a constant coefficient of variation, it can be calculated that less than 1% of healthy babies should have a count of more than 8840 cells/mm³ after the first 4 days of life, and that less than 1% should have a count of less than 1350 cells/mm³ at any time in the first 4 weeks of life.

Preterm babies. Neutrophil counts appear similar to those found in term babies except that the perinatal peak is less marked (see also Straková, 1964; Xanthou, 1970). 5% of the healthy preterm babies examined during the present study had a

TABLE

Changes in Polymorphonuclear Neutrophil Count of Healthy Term Babies with Age (cells/mm³)*

Postnatal Age	5th Centile	Median	95th Centile
Birth	4120†	7750	14600
6 hours	6640†	12500	23500
12 hours	6640†	12500	23500
18 hours	6370†	11000	20700
24 hours	4830†	9100	17100
36 hours	3820†	7200	13400
48 hours	3080†	5800	10900
3 days	2550	4800	9040
4 days	2260	4250	8000
5 days	2040	3850	7250
7 days	1800	3400	6400
10 days	1730	3250	6120
2 weeks	1700	3200	6020
3-4 weeks	1650	3100	5840

*Assembled from the present data and data given by Lucas *et al.* (1921), Lippman (1924), Forkner (1929), Washburn (1935), Magnusson (1939), Nasso and Verga (1955), Marks, Gairdner, and Roscoe (1955), Klees *et al.* (1958), Straková (1964), and Xanthou (1970), assuming a log-normal distribution and a constant coefficient of variation.

†About 5% of healthy preterm babies probably have a neutrophil count of less than 3000 cells/mm³ at this age.

count of less than 3000 cells/mm³ at the age of 36 hours.

Neutrophil response to bacterial infection. Infection appeared to provoke the same qualitative

white cell response in the baby as in later life, and the simplest index of this change appeared to be the *absolute* polymorphonuclear neutrophil count: changes in the total white cell count or in the percentage of neutrophils were of less help because of the variable lymphocyte count. We have only considered a neutrophil count abnormal when there was less than a 5% chance of it being normal (i.e. the count lay outside the limits given in the Table).

Meningitis. 2 babies less than 10 days old had coliform meningitis and abnormally high neutrophil counts on admission. 2 babies with spina bifida developed meningitis at the age of 1 week (1 staphylococcal, 1 enterococcal); there was an immediate and sustained neutrophil leucocytosis that subsided only when the infection was brought under control. A further baby suddenly became irritable and pyrexial and started to vomit while in hospital at the age of 3 weeks. Cultures taken within 8 hours of the onset of symptoms revealed a coliform meningitis and septicaemia. The neutrophil count was abnormally low at this time, but it rose to 8200 cells/mm³ the next day and remained abnormally high for 10 days. The neutrophil counts at the time of diagnosis are shown in Fig. 2.

Septicaemia. Septicaemia without evidence of

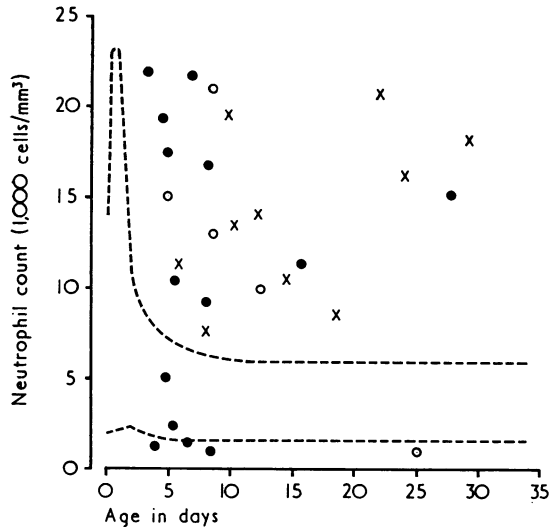


FIG. 2.—Blood neutrophil count in 5 babies with meningitis (○), 14 babies with septicaemia (●), and 10 babies with urinary infection (x) on the day infected CSF, blood, or urine was first obtained. Dotted lines enclose the region within which 90% of all normal neutrophil counts are found.

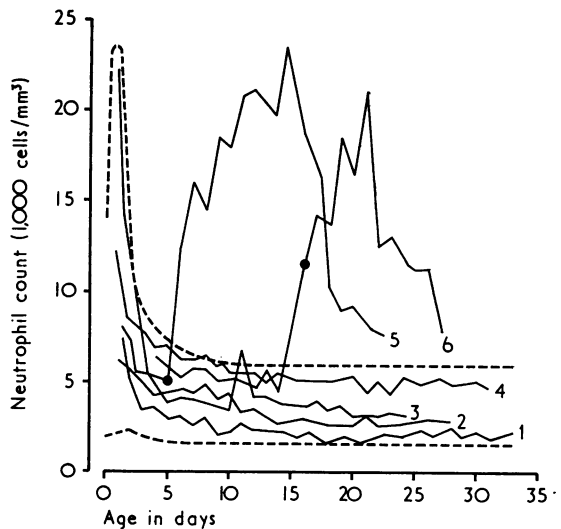


FIG. 3.—Serial neutrophil counts in 4 of the babies who remained free of infection throughout their stay in hospital, and 2 babies who developed septicaemia (●) while in hospital (Cases 5 and 6). Cases 1 and 5 were operated upon on the 2nd day of life; Cases 3 and 6 were operated upon on the 3rd day of life.

meningitis was detected in 14 babies (2 had additional evidence of pyelonephritis and 2 of broncho-pneumonia). 1 baby with ileus was admitted for laparotomy at the age of 4 days and found to have septicaemia on admission; the remainder developed septicaemia after admission.

Three babies had abnormally low neutrophil counts at the time septicaemia was detected (Fig. 2); these babies developed a progressively more severe neutropenia and died despite appropriate antibiotic therapy. 2 babies had a normal neutrophil count when septicaemia was detected on the fifth day of life but developed a neutrophil leucocytosis within 24 hours. The daily neutrophil count in 1 of these 2 babies is shown in Fig. 3 (Case 5); the neutrophil count in the other halved on the day before septicaemia was detected but then rose in a similar manner. The remaining 9 babies had abnormally high neutrophil counts at the time septicaemia was first detected (Fig. 2). In each case there had been a marked rise in the neutrophil count in the preceding 24 hours (e.g. Fig. 3, Case 6).

Urinary infection. 3 babies had severe coliform infections when admitted at the age of 3 to 4 weeks. Blood cultures were sterile, but the blood neutrophil count exceeded 15,000 cells/mm³ in each case. 7 other babies developed coliform urinary tract infections without evidence of septicaemia while in hospital. 5 had pyuria and a neutrophil count of more than 9000 cells/mm³ in the blood. The urine of the other 2 babies also contained over 100,000 organisms/ml but only a small number of

cells; these 2 babies had a significant but less marked leucocytosis.

The rise in the neutrophil count coincided in each case with the onset of signs of infection. This is well illustrated by Fig. 4 which shows the daily neutrophil count throughout the first 8 weeks of life in a preterm baby with an imperforate anus and a congenital rectourethral fistula. A defunctioning colostomy was made on the day after birth, prophylactic antibiotics were started, and a close watch was kept for evidence of urinary infection. Three separate episodes of significant bacterial infection were documented: there was a prompt and sustained rise in the neutrophil count on each occasion.

Pneumonia. 5 babies developed clinical and radiological evidence of pneumonia without septicaemia. In 2 babies who died and a third baby who required thoracotomy the diagnosis was confirmed by histology as well as bacteriology. 2 of these babies had coliform infections and the third a staphylococcal pneumonia. A fourth baby developed signs of consolidation and a pseudomonas empyema that required aspiration on 3 occasions after the repair of a tracheo-oesophageal fistula. A fifth baby who had meconium ileus at birth developed clinical and radiological evidence of pneumonia when 3 weeks old. All these babies had high neutrophil counts (<9000 cells/mm³) by the time clinical signs of pneumonia were detected.

Other factors provoking a neutrophil leucocytosis. The results from the remaining 66 babies were analysed to see how frequently a high

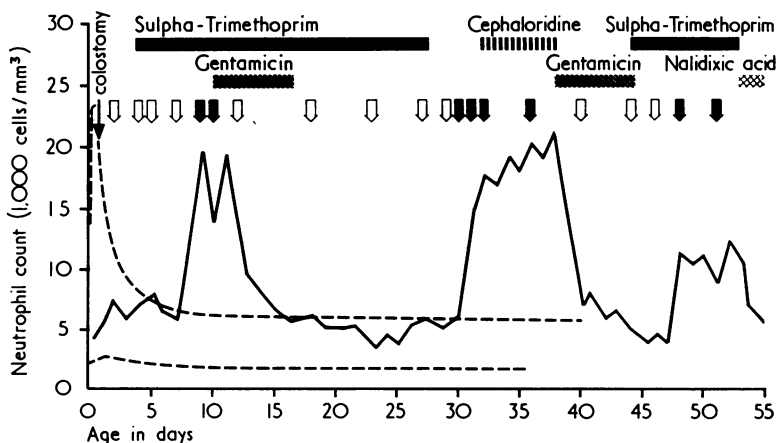


FIG. 4.—Neutrophil response to 3 separate episodes of urinary infection in first 8 weeks of life. The white arrows indicate dates on which clean-catch specimens of urine were examined; black arrows indicate occasions on which coliform infections were detected.

neutrophil count occurred in the absence of unequivocal evidence of significant infection. 49 of these babies required surgery; 17 did not. None of the babies in the latter group had a significant neutrophil leucocytosis though 1 had a sub-mandibular abscess and 2 had localized omphalitis. Serial counts revealed a slow progressive fall in the neutrophil count with little day-to-day fluctuation (e.g. Fig. 3, Cases 1 to 4).

Surgery. A brief leucocytosis was sometimes observed for 1 to 2 days after operation, but most of the 49 babies who underwent surgery had normal neutrophil counts throughout their stay in hospital, even when there was superficial wound sepsis. Apart from this transient postoperative response, a neutrophil count of more than 9000 cells/mm³ was seen only after the third day of life on 9 occasions: a prolonged neutrophil leucocytosis was seen in 3 babies with a gastroschisis or exomphalos that was covered with a silastic pouch and closed in stages, and a similar response was seen after thoracotomy on 3 occasions in the absence of any evidence of significant infection. In the other 3 babies a short-lived neutrophil leucocytosis was seen 6 to 10 days after an operation involving bowel resection.

A neutrophil count of less than 1350 cells/mm³ was seen during the last 1 to 3 days of life in 3 of the 8 babies who died after surgery without antemortem or postmortem evidence of sepsis or gangrene.

Discussion

The neutrophil count of the healthy newborn baby is not as variable as is sometimes thought, if due allowance is made for the transient neutrophil leucocytosis seen during the first few days of life. The constancy of the neutrophil count during the remainder of the neonatal period (Kato, 1935; Xanthou, 1970) has often been overlooked largely, perhaps, because it has been traditional to report the percentage rather than the absolute count. There has also been a tendency to quote a minimum and maximum value without at the same time showing the actual distribution, and this has tended to obscure the fact that the vast majority of counts lie within $\pm 50\%$ of the mean count at any given age (Fig. 1).

The reason for the neutrophil leucocytosis at birth has been the subject of much speculation. Explanations in terms of neonatal haemoconcentration are almost certainly erroneous. The maternal neutrophil count is raised throughout pregnancy (Andrews and Bonsnes, 1951), probably as a result of increased oestrogen excretion (Cruikshank *et al.*, 1970), and the maternal count rises further during

labour (Andrews and Bonsnes, 1951) as it does in other forms of strenuous muscular exertion (Garrey and Bryan, 1935). The white cell count of the baby at birth mirrors that of the mother in many respects, the neutrophil count (and the proportion of immature cells) after delivery being highest in babies subjected to prolonged labour and a difficult delivery (Straková, 1964). The further transient postnatal rise is probably largely caused by the displacement of neutrophils from the reserve 'pool' of cells that are normally sequestered in the vascular bed. This neutrophil leucocytosis is usually over within 3 days of birth (Table), but may be prolonged in babies with evidence of cerebral injury or aspiration and pneumonia at birth (Straková, 1964). There is relatively little day-to-day fluctuation in the neutrophil count during the remainder of the neonatal period, though there is nearly always a slow, progressive fall in the absolute count throughout the first 3 weeks of life (Xanthou, 1970). Some healthy babies display a stable neutrophil count that is 3 times as high as others for many days on end (Fig. 3). Within 1 week of birth lymphocytes usually predominate in the peripheral blood, as they do for the remainder of the first 3 years of life (Kato, 1935), and as they appear to have done throughout development *in utero* (Playfair, Wolfendale, and Kay, 1963).

The Czech writer Straková has recently commented on the diagnostic value of a differential cell count in babies with signs of bacterial infection, and others have drawn attention to the neutrophil leucocytosis that accompanies neonatal meningitis (Debré, Grumbach, and Mozziconacci, 1948; Ziai and Haggerty, 1958). High blood neutrophil counts have been a feature of some case reports of urinary infection and septicaemia accompanied by jaundice (Hamilton and Sass-Kortsak, 1963; Kenny *et al.*, 1966; Seeler and Hahn, 1969; Rooney, Hill, and Danks, 1971), but it is not generally recognized how frequently a neutrophil leucocytosis accompanies uncomplicated neonatal urinary tract infection. High white cell counts are frequently present by the time septicaemia is diagnosed (Nyhan and Fousek, 1958; Keuth, 1967), but few reviews of neonatal septicaemia include data on the differential cell count. Such information is, however, available for 24 of the babies with 'sepsis of obscure origin' reported by Silverman and Homan in 1949, and it is clear in retrospect that 16 of these babies had abnormal neutrophil counts at the time of investigation.

The prospective longitudinal study that we undertook has confirmed that the newborn baby normally

responds to infection in the same way as does the older child or adult, and has shown that the total neutrophil count is an effective index of this response. An increase in the proportion of immature polymorphonuclear cells is known to provide a sensitive index of the bone marrow's response to infection (Marsh *et al.*, 1967); changes of this nature were noticed quite often during the present study, but they were seldom detected before there had also been a significant rise in the neutrophil count. These changes can, however, be of diagnostic significance (Xanthou, 1972). Infection seldom seemed to cause thrombocytopenia, but 2 of the septicæmic babies who died with neutropenia suffered from severe thrombocytopenia ($<50,000$ platelets/mm³) during the last 60 hours of life.

Nearly all the babies we studied had neutrophil counts outside the normal range (as defined in the Table) by the time clinical signs of infection were detected (Fig. 2); indeed most of the babies had neutrophil counts that exceeded 9000 cells/mm³, and less than 1% of healthy babies had counts that were as high as this after the first 4 days of life. We would not, however, wish to suggest that an abnormal neutrophil count is ever, by itself, diagnostic of neonatal sepsis. In the first place, 1 in every 20 healthy babies will, by the definition we have adopted, have a neutrophil count above the limits set by the Table, and, since these counts have a skewed distribution, a few babies will have counts that are very significantly above these limits. Perinatal events will influence the neutrophil count immediately after birth, while the effects of exchange transfusion (Xanthou *et al.*, 1972) and surgery will sometimes cloud the issue later on. Babies born with severe haemolytic disease often show a marked leucocytosis, which may persist for a week or more (Diamond, Blackfan, and Baty, 1932; Straková, 1964). Of rather more consequence, the white cell count is sometimes normal despite unequivocal evidence of early septicaemia (Smith, Platou, and Good, 1956; Buetow, Klein, and Lane, 1965), though in our experience a second specimen will nearly always reveal an abnormal count some hours later (Fig. 3, Case 3; see also Fig. 4, day 30). We would, nevertheless, claim that a careful differential count provides useful information that should not be neglected. A baby with an abnormal neutrophil count should receive further investigation, and serial counts can be of help in an infant with vague and nonspecific symptoms.

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REFERENCES

- Aitken, J. (1902). Blood-counts in the new-born. *Journal of Obstetrics and Gynaecology of the British Empire*, **1**, 414.
- Andrews, W. C., and Bonsnes, R. W. (1951). The leucocytes during pregnancy. *American Journal of Obstetrics and Gynecology*, **61**, 1129.
- Buetow, K. C., Klein, S. W., and Lane, R. B. (1965). Septicæmia in premature infants. The characteristics, treatment, and prevention of septicæmia in premature infants. *American Journal of Diseases of Children*, **110**, 29.
- Cruikshank, J. M., Morris, R., Butt, W. R., and Crooke, A. C. (1970). The relationship of total and differential leukocyte counts with urinary oestrogen and plasma cortisol levels. *Journal of Obstetrics and Gynaecology of the British Commonwealth*, **77**, 634.
- Debré, R., Grumbach, R., and Mozziconacci, P. (1948). Le leucocytose à polynucléaires dans les septicémies à germes intestinaux du nourrisson. *Archives Françaises de Pédiatrie*, **5**, 173.
- Diamond, L. K., Blackfan, K. D., and Baty, J. M. (1932). Erythroblastosis fetalis and its association with universal edema of the fetus, icterus gravis neonatorum and anemia of the newborn. *Journal of Pediatrics*, **1**, 269.
- Forkner, C. E. (1929). Studies on the living blood cells of the newborn. *Bulletin of the Johns Hopkins Hospital*, **45**, 75.
- Garrey, W. E., and Bryan, W. R. (1935). Variations in white blood cell counts. *Physiological Reviews*, **15**, 597.
- Hamilton, J. R., and Sass-Kortsak, A. (1963). Jaundice associated with severe bacterial infection in young infants. *Journal of Pediatrics*, **63**, 121.
- Kato, K. (1935). Leukocytes in infancy and childhood. A statistical analysis of 1,081 total and differential counts from birth to fifteen years. *Journal of Pediatrics*, **7**, 7.
- Kenny, J. F., Medearis, D. N., Jr., Klein, S. W., Drachman, R. H., and Gibson, L. E. (1966). An outbreak of urinary tract infections and septicæmia due to *Escherichia coli* on male infants. *Journal of Pediatrics*, **68**, 530.
- Keuth, U. (1967). Zur Neugeborenensepsis. *Zeitschrift für Kinderheilkunde*, **101**, 278.
- Klees, E., Schlagetter, K., and Wokittel, E. (1958). Die Bedeutung des Neugeborenenblutbildes in der geburtschilflichen und pädiatrischen Praxis. *Zeitschrift für Geburtshilfe und Gynäkologie*, **151**, 73.
- Lippman, H. S. (1924). A morphologic and quantitative study of the blood corpuscles in the new-born period. *American Journal of Diseases of Children*, **27**, 473.
- Lucas, W. P., Dearing, B. F., Hoobler, H. R., Cox, A., Jones, M. R., and Smyth, F. S. (1921). Blood studies in the new-born. Morphological; chemical; coagulation; urobilin and bilirubin. *American Journal of Diseases of Children*, **22**, 525.
- Magnusson, J. H. (1939). On the white blood picture during the first year of life, especially with regard to its course. *Acta Paediatrica*, **23**, 14.
- Marks, J., Gairdner, D., and Roscoe, J. D. (1955). Blood formation in infancy. Part III. Cord blood. *Archives of Disease in Childhood*, **30**, 117.
- Marsh, J. C., Boggs, D. R., Cartwright, G. E., and Wintrobe, M. M. (1967). Neutrophil kinetics in acute infection. *Journal of Clinical Investigation*, **46**, 1943.
- Nasso, S., and Verga, A. (1955). Le variazioni numeriche dei globuli bianchi durante le prime ore e i primi giorni di vita. *Minerva Pediatrica*, **7**, 735.
- Nyhan, W. L., and Fousek, M. D. (1958). Septicæmia of the newborn. *Pediatrics*, **22**, 268.
- Oski, F. A., and Naiman, J. L. (1966). *Hematologic Problems in the Newborn*, p. 14. Saunders, Philadelphia.
- Playfair, J. H. L., Wolfendale, M. R., and Kay, H. E. M. (1963). The leucocytes of peripheral blood in the human foetus. *British Journal of Haematology*, **9**, 336.
- Rooney, J. C., Hill, D. J., and Danks, D. M. (1971). Jaundice associated with bacterial infection in the newborn. *American Journal of Diseases of Children*, **122**, 39.
- Seeler, R. A., and Hahn, K. (1969). Jaundice in urinary tract infection in infancy. *American Journal of Diseases of Children*, **118**, 533.
- Silverman, W. A., and Homan, W. E. (1949). Sepsis of obscure origin in the newborn. *Pediatrics*, **3**, 157.

- Smith, C. A. (1945). *The Physiology of the Newborn Infant*, p. 113. Thomas, Springfield, Illinois.
- Smith, R. T., Platou, E. S., and Good, R. A. (1956). Septicemia of the newborn: current status of the problem. *Pediatrics*, **17**, 549.
- Straková, M. (1964). The white blood count in newborns. (Czech.) *Acta Universitatis Carolinae*, **10**, 261.
- Washburn, A. H. (1935). Blood cells in healthy young infants. III. A study of 608 differential leucocyte counts, with a final report on 908 total leucocyte counts. *American Journal of Children*, **50**, 413.
- Wintrobe, M. M. (1967). *Clinical Hematology*, 6th ed., p. 261. Lea and Febiger, Philadelphia; Kimpton, London.
- Wollstein, M. (1938). *Handbook of Hematology*, Vol. II, p. 923. Ed. by H. Downey. Hoeber, New York; Hamish Hamilton, London.
- Xanthou, M. (1970). Leucocyte blood picture in healthy full-term and premature babies during neonatal period. *Archives of Disease in Childhood*, **45**, 242.
- Xanthou, M. (1972). Leucocyte blood picture in ill newborn babies. *Archives of Disease in Childhood*, **47**, 741.
- Xanthou, M., Tsomides, K., Nicolopoulos, D., and Matsaniotis, N. (1972). Leucocyte blood picture in newborn babies during and after exchange transfusion. *Paediatric Research*, **6**, 59.
- Ziai, M., and Haggerty, R. J. (1958). Neonatal meningitis. *New England Journal of Medicine*, **259**, 314.

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