Leucocyte alkaline phosphatase in neonatal infections

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Summary
The leucocyte alkaline phosphatase (LAP) score was estimated in healthy and infected neonates. A leucocyte band count was also done simultaneously. The infected group showed a significant ($P<0.001$) decrease in the LAP score and a significant ($P<0.001$) increase in the band count. These findings are discussed.

Introduction
Interest in the activity of alkaline phosphatase of human leucocytes has grown rapidly with the increasing number of reports demonstrating significant shifts of activity in different clinical states. Leucocyte alkaline phosphatase (LAP), determined by cytochemical methods, is increased in bacterial infections of the adult, but to the best of the author’s knowledge, there are no data concerning infections in the neonatal period. The main purpose of this study was to determine if LAP levels undergo alterations during the course of neonatal bacterial infections, and to compare the results with conventional haematological methods.

Material and methods
Fifty-five neonates, ages ranging from 3 to 28 days were divided into 2 groups:

Group A—A control group, composed of 32 healthy newborn infants whose birth weights ranged from 2500 to 4500 g.

Group B—The infected group, composed of 32 newborn infants whose birth weights ranged from 1170 to 5300 g. All these neonates had severe bacterial infection such as septicaemia, meningitis or pulmonary infections.

Diagnostic criteria of bacterial infection
The difficulty in establishing a diagnosis of infection during the neonatal period is well known. Clinical grounds usually included a history of a long interval between membrane rupture and birth; abnormal behaviour such as recurrent apnoea, failure to suckle well, and lethargy appearing in previously normal infants. The final evidence of bacterial infection, however, rested on laboratory evidence. The criteria employed in general were as follows:

1. For septicaemia—a positive blood culture or isolation of the organism from 2 or more cultures from different sites, and a clinical syndrome suggesting sepsis.
2. For meningitis—the presence of 2 or more of the following findings simultaneously: positive culture of cerebrospinal fluid; more than 20 cells, predominantly neutrophils, in CSF; CSF glucose level < 50% of glycaemia simultaneously tested; presence of bacteria in CSF (Gram’s technique).
3. For pneumonia—clinical respiratory distress; and chest radiograph consistent with pneumonia.
4. For urinary tract infection—bacterial count of $10^8$ organisms obtained on culture of a clean cath specimen.

Capillary blood samples were taken from each neonate for conventional haematological procedures and cytochemical methods. Total leucocyte count was performed by the standard dilution technique using a Neubauer chamber. Two peripheral smears were made simultaneously from each infant and stained with Jenner-Giemsa stain. Band counts were estimated from the first hundred neutrophils in each slide and results were averaged. In infected infants, all determinations were performed before starting antibiotic therapy.

LAP activity was studied using the method of Kaplow (1963). The alkaline phosphatase in the cytoplasm, which is presumably in the granular leucocytes, splits the phosphate from the sodium $\alpha$-naphthyl phosphate, allowing coupling of the residue with the fast Blue RR, and the formation of a granular black precipitate. The cytoplasm of the granular leucocytes may fail to stain, or may stain in a non-uniform manner—varying in colour from pale brown to black. One hundred consecutive segmented neutrophils were examined in each smear and rated 0 to 4 according to the intensity of the granular precipitate in the cytoplasm. Normal adult scores in the author’s laboratory are 72±11 (mean±s.d.).
Results

Absolute neutrophil and blood counts in healthy infants were significantly different from those in infected infants ($P<0.001$); $63\%$ of infected newborn infants had levels above $6.5 \times 10^9/l$ and $94\%$ of the same group had levels above $1.0 \times 10^9/l$. Healthy infants had leucocyte alkaline phosphatase scores significantly different ($P<0.001$) from those of infected newborn infants 206 and 108 respectively (Table 1); $100\%$ of healthy newborn infants had LAP score ranging from 144 to 244, whereas all infected newborn infants had LAP scores <132. There was no significant difference in LAP score between infected infants who survived and those who died. LAP score did not show significant correlation with either neutrophil or band counts. Toxic granulation was the commonest cytoplasmic abnormality and was seen in $83\%$ of infected neonates.

Discussion

These observations using conventional haematological methods are in agreement with the work of Akenzua et al. (1974) indicating that the band count is the most helpful test for the diagnosis of bacterial infection during the neonatal period.

There has been a considerable amount of controversy as to the diagnostic value of total neutrophil count in bacterial infections of the newborn. Xanthou (1970) noted a significant fall within 3 days of birth while Gregory and Hey (1972) reported a neutrophil leucocytosis immediately after birth which had usually disappeared 3 days later. There is a lack of unanimity in the neutrophil count, even in the remainder of the neonatal period; however, the majority of authors feel that there is relatively little day-to-day fluctuation between the ages of 3 and 28 days and that most healthy infants display a stable neutrophil count. Despite this, the total neutrophil count during this period has not been found of significant use mainly because of an unpredictable response of the neonate to infections.

Activity of LAP in healthy newborn infants is usually above normal adult level (Sudovsky et al., 1975). To the best of the author's knowledge, the LAP score for infected newborn infants has not been reported. Elevated activity in polycythaemia vera, leukaemoid reaction and stress; and decreased activity in paroxysmal nocturnal haematuria, idiopathic thrombocytopenic purpura; infectious mononucleosis, pernicious anaemia, aplastic anaemia and erythroblastosis fetalis have all been reported (Tanaka, Valentine and Fredricks, 1960; Halbrecht and Shabtay, 1972). The function of this enzyme in the neutrophil is as yet poorly understood, but one might infer from some of the available evidence that its variability is probably due to multiple factors.

Evidence in the literature suggests that in the haemopoietic apparatus, the activity of alkaline phosphatase resides principally in the polymorphonuclear leucocytes and that the polymorphonuclear leucocytes are richer in the activity of alkaline phosphatase than their precursors, the myeloblasts and myelocytes. Trubowitz et al. (1959) reported that bone marrow neutrophils show $50\%$ less LAP levels than do circulating neutrophils. They also suggested that LAP activity might be a cell maturation index. Based on such observation, the present findings of low LAP activity in infected newborn infants could be explained by a rapid release of functionally immature neutrophil by the bone marrow.

References

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