weight gain and composition of new tissue. It would thus be prudent to ensure an adequate zinc intake during rehabilitation from severe malnutrition to match the demands of rapid growth.

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Relevance of Performing a 'Sepsis Screen' in a Surgical Neonate

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The early signs of neonatal sepsis may be subtle and non-specific, especially in the neonate who has undergone major surgery, where features of sepsis may mimic post-operative physiological derangements. Rapid presumptive diagnosis of sepsis can be made at the bedside using the 'sepsis screen'. These tests may help to guide the need for antibiotic therapy and in some cases surgical intervention. The four commonly used parameters of the screen namely total leukocyte count (TLC), immature to total neutrophil ratio (IT ratio), micro-erythrocyte sedimentation rate (μESR) and C-reactive protein assay (CRP) are essentially manifestations of an acute phase response(1). Surgical intervention - a trauma would thus appear to alter these 'screen' parameters and impair their ability to aid in diagnosis of infection(2). This study was undertaken to define the relevance of the 'sepsis screen' in the management of new-borns undergoing major surgery.

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Subjects and Methods

A test battery incorporating a, b, c and d below, constituted the sepsis screen. The 'screen' was positive and indicative of infection, if two or more of these parameters were deranged. The test battery comprised: *(a)* TLC using a Coulter cell counter. Values <5000/mm^3 or ≥ 20,000/mm^3 (after the 1st week of life) were taken as abnormal and indicative of infection; *(b)* IT ratio using peripheral blood smear stained with Leishman's stain. A ratio of ≥0.20 was considered abnormal; (c) µESR-the method advocated by Alder and Denton(4) was followed using a heparinized capillary tube of standard dimension (5) (75 mmx1.1 mm, internal diameter). Neonates with hematocrit less than 40% were corrected to 40% using the Wintrobe correction chart(6). I0.ESR ≥10 mm in 1st hour was considered abnormal and indicative of sepsis(5); and *(d)* CRP using the Rhelax latex agglutination test (Tulip Diagnostics, India). Being a semiquantitative assay, a positive test with undiluted serum indicated CRP levels ≥6 mg/L and with 1 in 4 dilution of serum a positive reaction indicated serum CRP concentration of ≥24 mg/L(7). Appropriate bacterial cultures were also taken at the same time and an infant was labelled infected if he/she had: *(i)* Positive blood, CSF or urine culture; and /or (ii) Suggestive clinical picture (e.g. tachypnea) with a chest radiograph showing infiltration and positive tracheal aspirate culture; and/or (iii) pus in peritoneal or thoracic cavity at operation or autopsy.

Forty neonates admitted to the Neonatal Surgical Intensive Care Unit were included in the study between September 1993 to February 1994. Pre-operative, 24 h post-operative and subsequently as and when required sepsis screen was performed upto a maximum of 72 h postoperatively. The neonates were assessed daily for clinical evidence of sepsis by a Registrar in Pediatric Surgery and on such suspicion blood samples were drawn for the screen parameters and appropriate cultures. The screen was also performed on 16 healthy neonates matched for gestational age, sex and postnatal age who served as controls. Thus 3 groups of neonates were formed: *(A)* No evidence of sepsis- only surgical trauma; (B) Sepsis and surgical trauma; and (C) Controls- healthy neonates, not undergoing surgery. The routine measures of validity, namely, sensitivity, specificity and positive predictive value were calculated for analysis.

Results

Forty newborns included in the study underwent surgical procedures for a spectrum of conditions which included esophageal atresia with distal tracheoesophageal fistula (8 cases), anorectal malformations (10 cases), meningomyeloceles (8 cases), intestinal obstruction other than ano-rectal malformations (7 cases) and others. Their average weight on admission was 2.30 kg (range 1.3 to 3.4 kg), average gestational age was 38 weeks (range 33-41 weeks) and mean postnatal age was 3.79 days (range 1 to 12 days). Mortality was very high in the infected group of operated neonates (Group B, n=13) with eight of the 13 infants in this group succumbing to infection. There was no mortality in the uninfected surgical neonates (Group A, n=27).

Following surgery there was a rise in uESR as compared to preoperative values (mean preoperative µESR 5.33 mm 1st h compared to postoperative mean value of 9.0 mm 1st h; $p < 0.01$). (µESR was also higher in the Group B patients compared to either Group A or Group C patients. This difference was statistically significant (Kruskal Wallis test; $p < 0.05$). For the other sepsis screen parameters (TLC, IT ratio and

CRP), the difference in values between the 3 groups and the pre-operative versus postoperative values did not reach statistical significance.

The sensitivity, specificity, positive and negative predictive accuracy of the various screen parameters and for the sepsis screen score > 2, in the group of surgical neonates was calculated *(Table I). Table I* also compares the results of earlier studies in neonates with early and late onset sepsis(8,9) who did not undergo any surgical trauma.

Discussion

It is well known that neonatal sepsis may present with subtle or apparently nonspecific signs and symptoms especially after major surgery. Confounding matters further, surgical trauma itself produces an acute phase response and would, therefore appear to impair the ability of many of the tests recommended as screen for sepsis in the neonate. Reference values and the details of these screening tests have been extensively reviewed(3,8,9,10). A scoring system was recommended by Philip and Hewitt using a 5 part test(8). Although initially used in the 1st week of life, these tests also proved reliable beyond the 1st week in the neonate(9). In this subset of patients, a TLC above 20,000/mm^3 was also considered abnormal and indicative of sepsis.

Out of 13 surgical neonates with evidence of infection, according to the criteria listed earlier, 11(84.6%) could be detected by a positive sepsis screen. The screen remains fairly specific for infection (77.8%) and has a high negative predictive accuracy (91.3%) in surgical neonates. These values are compared to earlier descriptions(8,9) of newborns who had not undergone any surgical trauma *(Table I).* The IT ratio and TLC show impaired sensitivity and this probably can be attributed to the fact that many of the surgical neonates were beyond the 1st week of life. This ob-

TABLE I– *Value of Individual Tests and of the Sepsis Screen Score (≥2) in Neonates with Early(8) and Late(9) Onset Sepsis Compared with Surgical Neonates in the Present Study.*

Parameter	Sensitivity (%)			Specificity (%)			Positve predictive value (%)		Negative predictive value (%)	
	I	II	Present study	I	II	Present study	I	Present study	I	Present study
IT Ratio	90	58	53.8	78	79	70.4	26	46.6	NM	76
TLC	50	33	30.7	94	90	92.6	40	66.6	NM	75.8
CRP	47	75	100	86	71	66	22	59	NM	100
µESR	30	25	53.8	97	86	88.8	43	70	NM	80
Screen score	93	100	84.6	88	69	77.8	39	64.7	98	91.3

I - Early onset sepsis; II-Late onset sepsis
Positive and negative predictive values not quoted in Literature for II.
NM - Not mentioned
Due to limitations of small sample size, little variations in numbers will influence percentages to a greater extent.

servation has been confirmed by other investigators as well(9,10).

The CRP test was performed with undiluted serum (positive agglutination implies serum CRP concentration ≥ 6 mg/L) and with serum diluted 1:4 (positive agglutination implies serum CRP concentration ≥ 24 mg/L). Performing the test in dilute serum reduced the sensitivity, although it became more specific for infection (specificity 88.9%). However, as a screening test in the surgical neonate, the CRP latex agglutination test should be performed with undiluted serum, when the sensitivity and negative predictive accuracy reached 100% in our study.

The μESR in this study has shown better than reported(8,9) sensitivity (53.8%) and reasonable specificity (88.8%) for detection of sepsis in neonates even after surgery.

In conclusion, surgery and sepsis appear to alter the sepsis screen parameters in the same direction, although this difference reached statistical significance only for HESR. Even though the sensitivity and specificity of the sepsis screen are somewhat blunted in surgical neonates, it retains a high negative predictive value. Hence, a negative screen can be quite reassuring in the postoperative period in neonates. Accepting, serum CRP concentration ≥ 24 mg/L as abnormal enhances the specificity of the test but impairs its negative predicitive value. Therefore for the purpose of screening for sepsis, a serum CRP concentration ≥ 6 mg/L should be taken as abnormal.

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