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Acute Klebsiella, Pseudomonas and Proteus Pneumonia in Childhood

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Summary

Aderele WI, Johnson WBR, Osinusi K, Gbadero D, Adeyemi-Doro FA, Rotowa NA and Okubanjo OA. Acute Klebsiella, Pseudomonas and Proteus Pneumonia in Childhood. *Nigerian Journal of Paediatrics* **1992; 19:80**. The clinical, radiological and laboratory features in 21 children, aged between one and 27 months, with acute pneumonia caused by Klebsiella in 15 cases, Pseudomonas in four cases and by Proteus species in two cases, are presented. Fifty seven percent of the children had received antibiotics before presentation. Sixty-seven percent of those with Klebsiella infection had patchy infiltrates alone or with lobar consolidation, while four of the six cases with Pseudomonas and Proteus infections had lobar consolidation alone or in association with air leak syndromes. Mortality was high at 28.6 per cent and was significantly associated with malnutrition. Although 71 per cent of the cases were malnourished, the clinical features and laboratory data were unhelpful in distinguishing acute pneumonia due to these organisms from that caused by other organisms; by contrast, the radiographic changes were somewhat helpful, as a lobar consolidation with a bulging interlobar fissure would strongly suggest an infection with Klebsiella, while Klebsiella as well as Proteus species must be considered along with *Staphylococcus aureus* as possible aetiological organisms in those with pneumatocoeles.

Introduction

LOWER respiratory infections (LRI) are among the leading causes of childhood morbidity and mortality in developing countries.[1-5] Although most cases of bacterial pneumonia are due to *Streptococcus pneumoniae* and *Haemophilus influenzae*,[2 4 6] a substantial number is also caused by *Staphylococcus aureus*.[7-9] On the contrary, the more virulent gram negative organisms such as Klebsiella, Pseudomonas and Proteus species are rare causes of primary pneumonia in children.[10] Consequently, there is a paucity of information on acute pneumonia caused by these organisms. Furthermore, it is not known if the characteristic features that are described for such pneumonia hold true in developing countries with socio-economic millieu that is different from that in Europe and America where patients with the reported characteristic features reside. Yet, because of their virulence, it is important for physicians to be able to

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recognise, if possible, those features that may suggest pneumonia caused by these organisms in order that early and appropriate management can be instituted. The purpose of the present study was, therefore, to analyse the features of pneumonia in a number of children in whom these organisms were isolated.

Patients and Methods

As part of a prospective study of acute lower respiratory infection (ALRI) of less than four weeks' duration in children aged between two weeks and four years, admitted to the University College Hospital (UCH), Ibadan, over a $2^1/_2$-year period, blood cultures were routinely carried out on cases admitted to the study. Bacterial cultures of pleural fluid, and of lung aspirate in a few cases, were also obtained following an informed and specific parental consent; institutional consent was also obtained from the Ethical Committee of the College of Medicine, University of Ibadan. Standard culture techniques were used to analyse the specimens. Other investigations carried out included full blood count, chest radiographs and virological studies using as specimens, nasopharyngeal aspirates for viral identification by immunofluoresence, while acute and convalescent sera were examined by means of complement fixation tests.

The total number of patients with LRI was 419, but the present report concerns 21 patients in whom either Klebsiella, or Pseudomonas, or Proteus species was isolated from cultures of blood, pleural fluid or lung aspirate. Statistical analysis of the data was carried out, where appropriate, by means of the chi square and Students t tests.

Results

All the 21 positive cultures were pure growths of Klebsiella species in 15, and of Pseudomonas and Proteus species in four and two cases, respectively. The bacterial species that were identified in four cases included three cases of *Klebsiella pneumoniae* and one case of *Proteus mirabilis*. Blood culture alone, was positive in 10 cases (seven for Klebsiella, two for Proteus and one for Pseudomonas); pleural fluid in five cases (three for Klebsiella and two for Pseudomonas), and lung aspirate alone in four (three for Klebsiella and one for Pseudomonas). In the remaining one case, cultures of both blood and lung aspirate yielded Klebsiella species. Viruses were identified in six (four with Klebsiella and one case each, with Pseudomonas and Proteus) of the 21 cases; these viruses were Parainfluenza 3 (three cases), Parainfluenza 1 (one case), Respiratory syncytial virus (one case) and mixed Parainfluenza 3 and Influenza A (one case).

Age distribution

The children were aged between one and 27 months (mean 12.4 months). There was a peak (10 cases) at the age group, 12-23 months. Only one of the 21 cases was older than 23 months while both cases in whom Proteus was isolated, were aged below three months.

Clinical Features

The major presenting symptoms were those expected in children with LRI; fever, cough, anorexia and rapid breathing, were the most prominent (Table I). Vomiting was an associated symptom in eight patients (mean age, 8.1 months), while diarrhoea was associated in seven patients (mean age, 16.4 months). Physical signs consisted mostly of dyspnoea and tachycardia (Table II), while various auscultatory signs of underlying lung pathology were detected in the chest in all the cases. Respiratory rate (RR) ranged from 38 to 100/minute;

TABLE I

Major Clinical Features and Causative Organisms in 21 Cases of Pneumonia

Feature	*Organisms*			
	Klebsiella (n=15)	*Pseudomonas* (n=4)	*Proteus* (n=2)	*Total* (n=21)
Symptoms				
Fever	15	4	2	21
Cough	14	4	1	19
Anorexia	12	4	2	18
Rapid breathing	11	4	1	16
Vomiting	5	1	2	8
Diarrhoea	6	1	-	7
Restlessness	4	2	-	6
Signs				
Respiratory				
Adventitious sound	15	4	2	21
Nasal flaring	14	4	2	20
Chest retraction	13	4	2	19
Respiratory rate>50/min	9	2	2	13
Non-respiratory				
Heart rate> 120/min	15	4	2	21
Temperature > 37°C	14	4	2	20

TABLE II

Chest Radiographic Findings and Organisms in 21 Cases of Pneumonia

Feature	*No. of Cases*			
	Klebsiella (n=15)	*Pseudomonas* (n=4)	*Proteus* (n=2)	*Total* (n=21)
Patchy consolidation	11	1	-	12
Lobar consolidation	6	2	2	10
Hydropneumothorax	4	2	1	7
Pneumatocoele	1	-	1	2
Pneumomediastinum	1	-	-	1
Total	23	5	4	32

the overall mean rate was 65/min, but in only 13 patients (nine with Klebsiella, two with Pseudomonas and the two with Proteus infection), was the RR greater than 50/min. The mean heart rate was 158/min (range 120-200/min), while the temperature ranged between 37°C and 39.7°C; the only patient with a temperature below 37.5°C had Klebsiella infection. The mean temperatures were similar, irrespective of the causative organism. Fifteen (71.4 per cent) of the 21 patients were malnourished; 10 were underweight and two were marasmic, one had kwashiorkor, and two had marasmic-kwashiorkor.

Treatment before hospitalization

Sixteen (76.2 per cent) of the 21 patients had received some treatment before presentation at the hospital; the treatment included antibiotics in 12 cases. Other forms of treatment included antipyretics, antimalarials and cough mixtures. According to the parents, there was no response to the treatment in 10 of the 16, while there was some improvement in the remaining six cases.

Laboratory data

Packed cell volume (PCV) ranged between 23 and 44 per cent (mean 31.8, 29.3 and 41.0 per cent, respectively, with respect to Klebsiella, Pseudomonas and Proteus infections); the overall mean PCV was 32.3 per cent; it was under 30 per cent in six of the 19 cases. Total white blood count (WBC) ranged between 4.1 x 10^9/1 and 31.0 x 10^9/1 (mean 8.46, 19.83 and 3.01 x 10^9/1 respectively); the overall mean was 11.83 x 10^9/1; it was over 10.0 x 10^9/1 in only seven of 15 cases. The overall mean proportions of neutrophils and lymphocytes were 69.2% and 29.4% respectively.

Chest Radiography

The frequency of individual radiographic changes is shown in Table II. Patchy and lobar consolidations were the most common lung le-

sions. Figs. 1-5 illustrate the various radiographic lesions. Of particular interest is Fig. 2 which shows a right upper lobe consolidation with pneumatocoeles and a bulging fissure; cul-

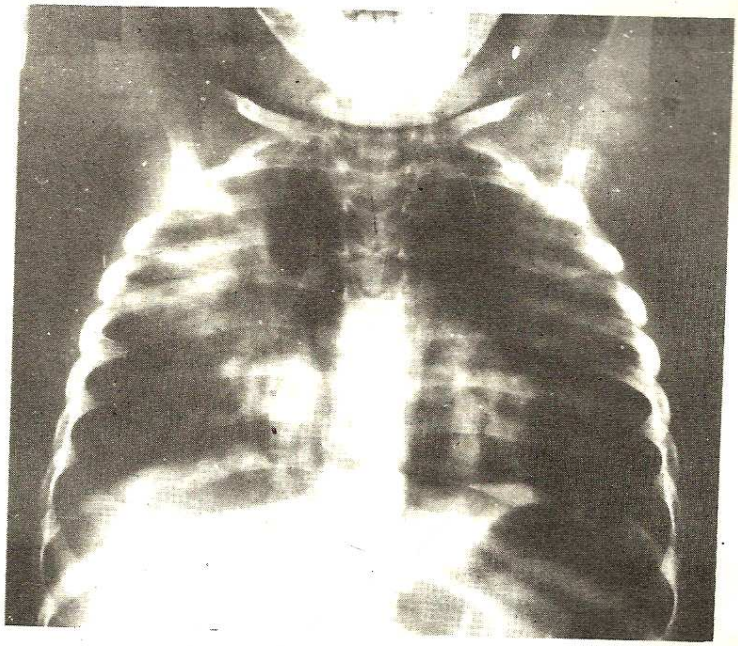


Fig.1. Chest radiograph showing a right upper lobe segmental consolidation with pneumomediastinum. Lung aspirate yielded Klebsiella spp.

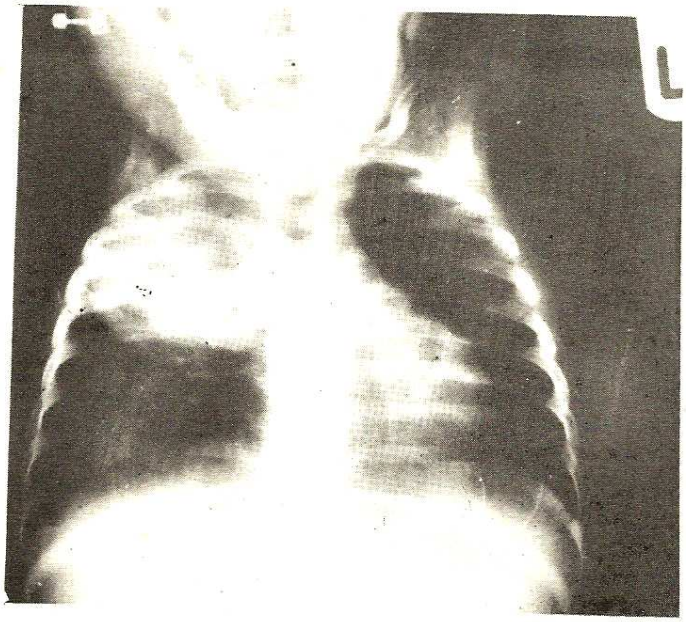
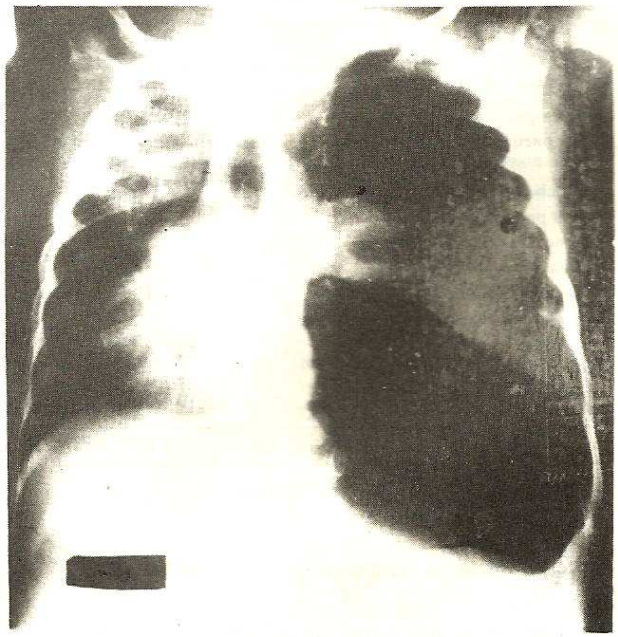


Fig.2. Chest radiograph of a 7-month old underweight girl, showing a right upper lobe consolidation with pneumatocoeles and a bulging interlobar fissure. Cultures of blood and lung aspirate grew Klebsiella species.



g.3. Chest radiograph showing a left tension dropneumothorax and consolidation of the right upper be due to Klebsiella pneumoniae.

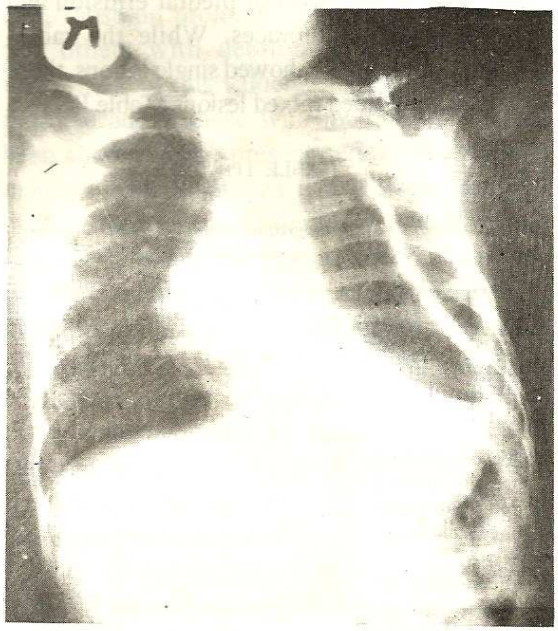


Fig.4. Chest radiograph in a 6-month old boy with a left hydropneumothorax caused by Pseudomonas species.

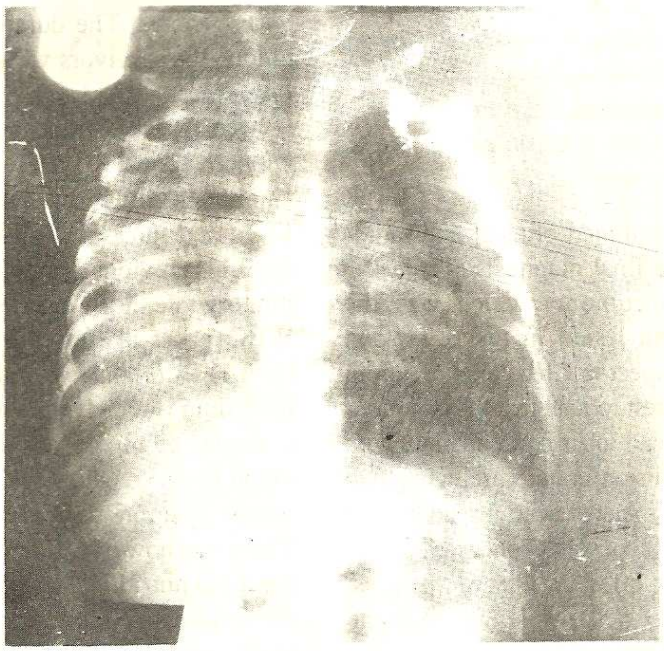


Fig.5. Chest radiograph in a one-month old, underweight boy, showing consolidation of the right lung with pneumatocoeles. Blood culture grew Proteus mirabilis.

tures of blood and lung aspirate in the patient with this radiograph, yielded Klebsiella species. There were seven cases of pleural effusion and associated pneumothoraces. While the radiographs in nine patients showed single lesions, those in 12 others revealed mixed lesions (Table III).

TABLE III

Distribution of Chest Radiographic Findings and Organisms in 21 Cases of Pneumonia

Finding	No. of Cases			
	Klebsiella (n=15)	*Pseudomonas* (n=4)	*Proteus* (n=2)	*Total* (n=21)
Patchy consolidation only	6	1	-	7
Patchy consolidation+ lobar consolidation	4*	-	-	4
Hydropneumothorax	2	1	-	3
Lobar consolidation only	-	1	1	2
Lobar consolidation+ hydropneumothorax	1	1	-	2
Lobar consolidation+ pneumomediastinum	1	-	-	1
Lobar consolidation+ hydropneumothorax+ pneumatocoele	-	-	1	1
Patchy consolidation+ hydropneumothorax	1	-	-	1
Total	15	4	2	21

* Includes one with pneumatocoele

Diagnosis

Based on the combined clinical and radiographic features, the final diagnosis (Table IV) included bronchopneumonia which was the single most common lesion in the series and particularly, with respect to Klebsiella infection; it is however, of interest to note that the two cases of Proteus infection had lobar consolidation, with associated pleural effusion in one case, while two of the four cases associated with Pseudomonas infection also had lobar consolidation. Measles was an associated specific infection in seven patients, six of whom had Klebsiella while the remaining one had Pseudomonas pneumonia.

TABLE IV

Final Diagnosis and Organisms in 21 Cases of Pneumonia

Feature	Organisms			Total
	Klebsiella	*Pseudomonas*	*Proteus*	
Bronchopneumonia	6(2)	1	-	7(2)
Lobar pneumonia	-	1(1)	1	2(1)
Mixed Bronchopneumonia+ lobar pneumonia	4	-	-	4
Pyopneumothorax	2	1	-	3
Lobar pneumonia+ pyoneumothorax	1	1	1(1)	3(1)
Lobar pneumonia+ pneumomediastinum	1(1)	-	-	1(1)
Bronchopneumonia+ pyopneumothorax	1(1)	-	-	1(1)
Total	15(4)	4(1)	2(1)	21(6)

No of deaths in parenthesis

Outcome and its relationship to risk factors

Six (28.6 per cent) of the 21 patients died and this consisted of four of the 15 with Klebsiella, one of the four with Pseudomonas and one of the two cases with Proteus infection; the average duration of hospitalisation before death was 3.4 days. The duration of stay in hospital among the survivors varied between two and 38 days (mean 12.7 days).

Analysis of various risk factors in relation to survival (Table V), showed that there were no significant differences between those who survived and those who died, with respect to age ($p>0.1$), previous antibiotic therapy, mean respiratory rate, heart rate, temperature, PCV, total WBC ($p>0.5$ in each case) or associated measles ($p>0.1$). Mortality was also, not related to the bacterium isolated and whether or not, there was a single, or mixed lesions in the chest radiograph ($p>0.5$), while none of the six patients in whom specific viruses were identified, died. There was however, a significant difference with regard to nutritional status; not only were all the six children who died malnourished, in contrast to nine of the 15 who survivied, a higher propor-

tion of those who died also had the more severe forms of malnutrition (Table V; $p<0.01$).

TABLE V

Risk Factors and Outcome in 21 Cases of Pneumonia

Factor	*Survivors*			*Deaths*			p
	No	*Mean*	*SD*	*No*	*Mean*	*SD*	
Age(yr)	15	10.9	7.9	6	16.0	8.7	>0.1
Resp rate (/min)	15	63.1	16.5	6	68.0	22.2	>0.5
Heart rate (/min)	15	160.0	17.6	6	151.3	30.1	>0.5
Temp (°C)	15	38.5	0.7	6	38.5	0.5	>0.5
PCV (%)	14	32.1	5.2	5	32.6	6.8	>0.5
Total WBC (x10^9/L)	10	11.7	7.8	5	12.0	10.9	>0.5

	No of Survivors	*No of Deaths*	X^2	p
Previous antibiotic therapy				
Yes	8	4	0.097	>0.5
No	7	2		
Associated Measles				
Yes	6	1	1.05	>0.1
No	9	5		
Chest X-ray				
Single lesion	6	3	0.175	>0.5
Mixed lesions	9	3		
Nutritional Status				
Adequate	6	-		
Underweight	8	2	9.24	<0.01
M/Kwash*	1	4		

* M/Kwash = Cases with marasmus, kwashiorkor and marasmic-kwashiorkor

Discussion

This present study was an attempt to identify those clinical, laboratory and chest radiographic features that might help in the early recognition and hence, prompt and specific therapy of lower respiratory infection caused by Klebsiella, Pseudomonas and Proteus, three uncommon but virulent gram negative bacteria. Acute pneumonia caused by these organisms is rare in children with normal immune status; the population of children that are vulnerable to these organisms include the immunocompromised host (children with underlying malignancies, those on prolonged antimicrobial therapy and others with debilitating underlying illnesses);[11 12] to this valnerable group of children must be added those with malnutrition as has been shown in the present series, whereby the majority of the patients had various forms of malnutrition. It is of interest to note that it is precisely in this group of children that common clinical yardstricks for recognising acute infections may not manifest.[13 14] It is thus, tempting to predict that with the current declining economy and the consequent increase in childhood malnutrition in some developing countries, there is likely to be an increase in the incidence of pulmonary infections caused by these virulent organisms.

One of the highlights in the WHO guidelines [15 16] on case management of severe cases of acute respiratory infections (ARI), is the identification of fast breathing and chest retraction as indicative of severity and hence, the need for antibiotics with, or without referral to a higher tier of health care delivery. The strategy proposed for effective case management in the above guidelines include the choice of simple antibiotics for treating suspected bacterial pneumonia at the primary care level. This recommendation was based on the premise that the two common aetilogical organisms of acute pneumonia in developing countries, namely: *Streptococcus pneumoniae* and *Haemophilus influenzae*, are sensitive to the first line antibiotics comprising benzyl penicillin, ampicillin and co-trimoxazole. However, as shown in this and other studies,[17] not only do organisms that are usually insensitive to these antibiltics cause pneumonia in these populations, the recommended practice of relying on the presence of tachypnoea and/or chest retraction in making a decision on the need for antibiotic therapy may be misleading. In this respect, it is noteworthy that as many as 38 per cent of the subjects in the

present series had respiratory rate less than 50/min, while two cases with auscultatory and radiological features indicating severity, did not have retraction of the chest wall.

The therapeutic implication of early identification of acute gram negative bacillary pneumonia (AGNBP) from the presenting clinical features and of hazarding an intelligent guess regarding the particular aetiological agent, is evident. However, it appears from the present series that the clinical features of AGNBP are neither distinctive as a group from those of other bacterial pneumonias nor sufficiently discriminatory amongst the three causative organisms. By contrast, a potentially useful investigation in this regard, is the chest radiograph. For instance, the presence of an interlobar fissural bulge coexisting with a lobar of patchy infiltrative changes, should heighten the suspicion of a Klebsiella pneumonia, whether or not pneumatocoeles are present. Pneumatocoeles which are usually more commonly associated with staphylococcal infection,[18] were also present in two of our subjects with Klebsiella and Proteus pneumonia, respectively. This indicates that, although infection by *Staphylococcus aureus* remains the first consideration in the presence of this radiographic change, the possibility of Klebsiella and Proteus aetiology, should also be entertained. An additional radiographic feature worth highlighting, was the relatively high incidence of lobar consolidation in those with pseudomonas and proteus infection. This observation calls for caution in the choice and continuation of crystalline penicillin in the treatment of pneumonia revealed by radiological lobar consolidation, in the belief that such consolidation is almost always due to *Streptococcus pneumoniae*. The absence of a satisfactory therapeutic response within 72 hours in an apparent pneumococcal pneumonia, particularly in a malnourished child, should lead to the consideration of a more aggressive diagnostic approach which may have to include lung aspiration.

The role of previous antibiotic usage in the development of AGNBP in the present series, was difficult to evaluate. While it is conceivable that some or even most of the patinets who received antibiotics before presentation, developed secondary pneumonia as a result of the elimination of susceptible organisms by the antibiotics, it is also likely that in some, the isolated organisms were the primary aetiological agents, and that the lack of response to initial antibiotic therapy was due to the resistance of the organisms. Similarly, the role of the viruses that were identified in some of the cases is uncertain; the possibility remains that they were opportunistic infections or that they predisposed such children to bacterial invasion.

It seems to us, from the present study and from anecdoctal experiences, that those who are likely to suffer from AGNBP are malnourished children with measles infection, who have mixed radiological lesions and who might have received antibiotics previously. Faced with such patients, early referral to a secondary or tertiary health institution for further investigations and management, is strongly recommended; such investigations would include blood culture, bacterial antigen detection[19] and lung aspiration. Although we did not examine the relative efficacy of the various drugs used in the management of the cases, it is felt that because of the high mortality among malnourished children with AGNBP, as shown in this series, an initial combination of cloxacillin and gentamicin, or the more powerful antibiotics, such as the third generation cephalosporins, should be used in such children, while awaiting results of investigations.

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the light meter to see if their use made any difference to the irradiance. Ten readings at five minute intervals were taken with each setting. Another set of readings was taken with only one phototherapy unit placed directly above the incubator.

Results

The irradiance obtained, using one phototherapy lamp above the incubator and aluminium foil on varying sides of the incubator is shown in Table I, while that obtained using two phototherapy lamps is shown in Table II. Foils applied on two short sides and two long sides improved the irradiance by about 29 percent, using one phototherapy unit and by 33 percent with foil on two short sides and one long side when two phototherapy units were used. The irradiance obtained using the Silver Swaddler was similar. The use of a heat shield made no difference to the irradiance, but there was a reduction of about 0.2mW/cm^2 when the plastic bubble sheet was used.

TABLE I

Irradiance with one Phototherapy Unit over the Incubator

	No of short sides with foil	*No of long sides with foil*	*Number of readings*	*Irradiance mW/cm^2*
A	0	0	20	0.99 ± 0.05
B	1	0	10	1.00 ± 0.01
C	2	0	10	1.04 ± 0.00
D	0	1	10	1.10 ± 0.02
E	0	2	10	1.20 ± 0.01
F	1	1	10	1.13 ± 0.02
G	2	1	10	1.12 ± 0.02
H	1	2	10	1.22 ± 0.02
I	2	2	10	1.32 ± 0.04

No side with foil vs all sides with 33.3 percent increase: t = 18.8; p<0.001

TABLE II

Irradiance with one Phototherapy Unit on top of the Incubator and a second unit against a long side

	No of short sides with foil	*No of long sides with foil*	*Irradiance mW/cm^2*
A	*0*	*0*	*1.50 ± 0.03*
B	*1*	*0*	*1.61 ± 0.02*
C	*2*	*0*	*1.70 ± 0.08*
D	*0*	*1*	*1.75 ± 0.02*
E	*1*	*1*	*1.82 ± 0.02*
F	*2*	*1*	*1.93 ± 0.03*

No foil vs foil on all sides = 29 percent increase t = 30.4; p<0.0001.

Discussion

Phototherapy plays an important role in the management of neonatal hyperbilirubinaemia, although exchange transfusion remains the most rapid method of reducing a very high plasma unconjugated bilirubin concentration. It is important to achieve an adequate dose of light in order to reduce the bilirubin concentration[1-3] and the routine use of a light meter allows the irradiance of phototherapy to be monitored.[1-4] It is now our routine to use aluminium foil so as to increase the irradiance of phototherapy for severely jaundiced babies. This allows the efficient use of only one phototherapy lamp. When two phototherapy lamps are used, the extra reflecting surface is not usually necessary. Silver swaddlers can be used, but these are more expensive than aluminium foil. When a heat conserving device such as a plastic bubble sheet is used, it is important to increase the amount of light. The present results underline the importance of measuring the irradiance when using phototheraphy.[4]

With the use of aluminium foil, the irradi-

ance was significantly increased. The addition of aluminium foil will reduce the demand on phototherapy units, especially in developing countries where this equipment is in short supply and for the number of jaundiced babies that require this type of therapy. Since the effectiveness of phototherapy depends on the intensity of irradiance energy received by the baby,[4] the addition of aluminium foil will improve the efficiency of the phototherapy and therefore, reduce the duration of phototherapy.

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