

# Klebsiella pneumoniae Pneumonia in Prematures and Young Infants

By

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The incidence among infants of pneumonia due to *Klebsiella pneumoniae* is low as reflected by literature. Description of the disease is incidental in textbooks where the cases reported are quoted as being exceptional in childhood. In a report on four cases in infants [18], the pathogenetic role of *Klebsiella* could be confirmed in one instance only, where recovery was achieved with streptomycin; in the rest, the role of other agents could not be excluded. In a series of 41 infants who had died of respiratory complication of measles, from the lungs of two a pure growth of *Klebsiella pneumoniae* was obtained, while 41 infants who had recovered from pneumonia yielded *Klebsiella* in 5 cases, of which four in a pure culture [4]. In a premature ward, *Klebsiella pneumoniae* appeared in epidemic form, coinciding with a fulminant epidemic of *Klebsiella* enteritis in another ward of the same hospital. In both groups aureomycin proved to be effective and only one of four severely affected infants died [16].

The first cumulative review in the literature presented 30 cases of *Klebsiella pneumoniae* in 1950 [15], while

a total of 36 cases was reported in 1962 [21]. This is a surprisingly low number if one considers the increasing use of new antibiotics, a fact favouring the growing incidence of uncommon pathogens. Development of the diagnostic procedures should also have added to the number of recognized *Klebsiella pneumoniae*. Recent data from Uruguay [2] suggest a more frequent positive bacteriological finding among infants with respiratory infections. Thirtysix out of 58 infants yielded *Klebsiella*; part of the patients suffered from pneumonia, others from asthmatic bronchitis.

While *Klebsiella* infections have been increasingly encountered during epidemic or sporadic enteritis [3, 8, 13, 14, 15, 22, 23] or food poisoning [8], several data suggest a similar increase in the incidence of *Klebsiella pneumoniae*. Our data support this view, and underline the necessity of bacteriological examination in pneumonias of prematures and infants.

## BACTERIOLOGICAL METHODS

The genus *Klebsiella* pertains to the family Enterobacteriaceae. *Klebsiella pneumoniae* used to be known as Friedländer's



bacillus, or *B. mucosus capsulatus*. Several members of the genus are pathogenic. A further subdivision of the strain became possible on the basis of the antigenic structure. There are 5 groups differing in the O antigen, and 72 types differing in the K antigen. The pathologic significance of the different *Klebsiella* strains can be ascertained by serologic methods. More recently, the demonstration of specific phages has attained a diagnostic significance. Specific phages may play a role in turning potential pathogens into actually pathogenic agents [10].

For the identification of *Klebsiella pneumoniae*, chocolate agar, blood agar or Endo medium was inoculated with pharyngeal or subglottic secretion. After 24 hours incubation one of the isolated mucous colonies was transferred to Lányi and Szita's liquid medium to differentiate the strains on the grounds of indol production and urea splitting. In addition, the methyl-red and the Voges-Proskauer tests were carried out, and hydrogen sulphide production was examined. In some cases motility of the organism was observed and phage typing was performed. Selective sensitivity to antibiotics was determined by the disc method and in the case of cefaloridine by the dilution method. The results of these additional examinations confirmed the bacteriological diagnosis in all cases.

## RESULTS

During the period February 10, 1966, to December 31, 1966, a total of 670 bacteriological examinations of pharyngeal and subglottic mucus was performed. *Klebsiella* was cultured 67 times, from 46 patients. A pure culture grew in the case of seven infants with pneumonia, and in eleven cases with spastic bronchitis. In the case of additional four patients with pneumonia, *Klebsiella* grew in a mixed

culture, and clinically the pneumonia did not meet the criteria of *Klebsiella* origin. *Klebsiella* was isolated from further four infants with otitis and from 28 cases without any pathological manifestation.

During the same period pharyngeal secretion of the medical and nursing staff was repeatedly examined. *Klebsiella* was isolated on three occasions from two nurses. Cultures obtained from beds and furniture were always negative.

During the period January 1 to May 10, 1967, 31 out of 400 cultures yielded *Klebsiella*, but only one of the positive patients developed pneumonia. No positive cultures were obtained from faeces.

Table I demonstrates the antibiotic sensitivity of the *Klebsiella* strains. Practically all strains were resistant to sulphadimidine and to oxytetracyclin. Three out of four cases were resistant to streptomycin, and about every second to chloramphenicol. Neomycin and polymyxin proved to be the most effective drugs. Table I also demonstrates the sensitivity of the strains originating from patients with pneumonia. Sensitivity to cefaloridine was examined in two cases. One proved to be sensitive to 5 µg/ml, while the other only to 50 µg/ml. In spite of this, the latter patient responded well to cefaloridine treatment.

## DIAGNOSIS

There is no agreement in the literature on the exact diagnostic criteria of *Klebsiella pneumoniae*. Those suggested



TABLE I  
Sensitivity of *Klebsiella pneumoniae* strains

Antibiotic	67 strains from 46 different patients						17 strains from patients with <i>Klebsiella pneumoniae</i>					
	Sensitive		Relatively sensitive		Resistant		Sensitive		Relatively sensitive		Resistant	
	No.	per cent	No.	per cent	No.	per cent	No.	per cent	No.	per cent	No.	per cent
Oxytetracyclin	2	3	—	—	65	97	—	—	—	—	17	100
Streptomycin	11	16	4	5.8	52	78	3	18	—	—	14	82
Chloramphenicol	30	45	4	5.8	33	49	3	18	1	6	13	76
Neomycin	56	84	4	5.8	7	10	15	88	—	—	2	12
Polymyxin	47	70	4	5.8	16	24	16	94	—	—	1	6
Sulphadimidine	—	—	—	—	67	100	—	—	—	—	17	100
Cefaloridine	—	—	—	—	—	—	1*	—	1*	—	—	—

\* = two tests only.

by PERLMAN and BULLOWA [16] i.e. pulmonary infiltration demonstrated clinically and radiographically; repeated pure cultures of *Klebsiella* from blood or pharyngeal secretion; demonstration of specific polysaccharides and antibodies in blood, cannot be expected to gain general acceptance on account of the limited laboratory facilities in many hospitals. The criteria set by OBRINSKY *et al.* [11], namely, resistance to penicillin and sensibility to streptomycin, are more easy to meet, but since 78% of our cases were resistant to streptomycin, these criteria are insufficient to rely upon. Therefore, we have accepted the criteria of ANDERSON [1], who regards *Klebsiella* as the pathogenic agent, when (i) after death *Klebsiella* can be cultured from the lungs; (ii) the presence of *Klebsiella* can be demonstrated in the acute phase, but not any more during convalescence;

and (iii) *Klebsiella* can be isolated in the acute phase and the patient recovers on adequate antibiotic treatment.

On the other hand, *Klebsiella* cannot be held responsible for the pneumonia if (i) the organism persists after clinical recovery; (ii) *Klebsiella* can be demonstrated transitorily during some other disease, but without causing clinical symptoms; (iii) *Klebsiella* can be isolated only from sputum or a throat swab and the pneumonia responds well to antibiotics to which *Klebsiella* has been resistant; (iv) after death other pathogenic agents can only be isolated; and (v) there is no well defined disease.

#### CASE REPORTS

Seven patients; five prematures and two young infants, suffering from *Klebsiella pneumoniae* have been ob-



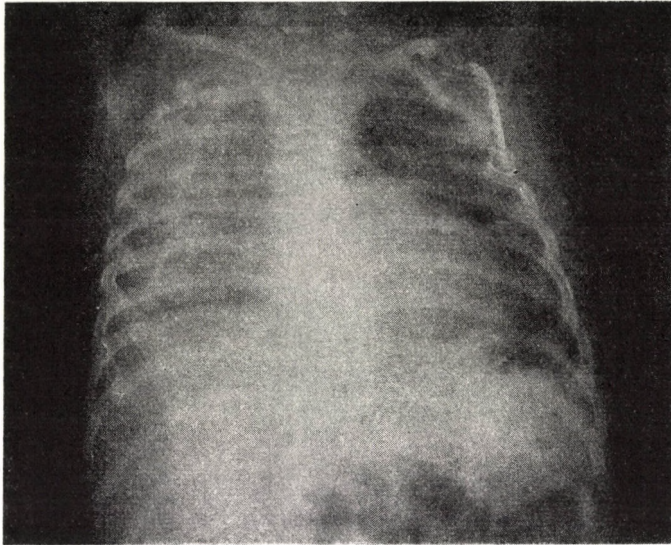


FIG. 1

served in the year 1966. The case of four patients will be reported in some detail, while of three, in brief.

*Case 1.* N. M., a 4-months old infant was admitted on February 17, 1966. History revealed a birth weight of 2500 g, and asphyxia after delivery. Three days prior to admission he had developed fever and cough, X-rays had revealed bronchopneumonia in the right inferior lobe. At admission the infant was wasted, moderately cyanosed, displaying tachycardia, rales over both lungs, harsh breathing over the right inferior lobe, and an enlarged liver. Strophanthin, penicillin, streptomycin and oxygen were administered. The throat swab yielded a pure culture of *Klebsiella*, but the result took four days to arrive. Since the condition was deteriorating and the pneumonia affected further areas of the lung, the possibility of staphylococcal pneumonia was considered, and meticillin and Sigmamycin were prescribed. However, the clinical state deteriorated further, the cough became productive, with an abundant mucous, foamy discharge, and

dullness to percussion appeared over the right lung. Four days later X-rays revealed an increased density over the right inferior and middle lobes, and pleural fluid along the lateral wall of the thorax, reaching up to the apex and compressing the infiltrated right lung (Fig. 1).

A pleural tap resulted in a small amount of serous, sterile fluid. The result of the throat swab was obtained, According to the result of the throat swab, Sigmamycin was discontinued, and streptomycin and kanamycin treatment was instituted. On the sixth day following admission the condition began to improve; temperature, dyspnoea and heart rate decreased, cyanosis disappeared, while the dullness, the auscultatory and radiological findings were unchanged. The laboratory findings were a slightly increased sedimentation rate (27 mm/h), and leucocytosis with a shift to the left. A second throat swab yielded a pure *Klebsiella* culture, which proved to be sensitive to chloramphenicol and to streptomycin.

On this treatment temperature, discharge and dullness soon decreased. By the

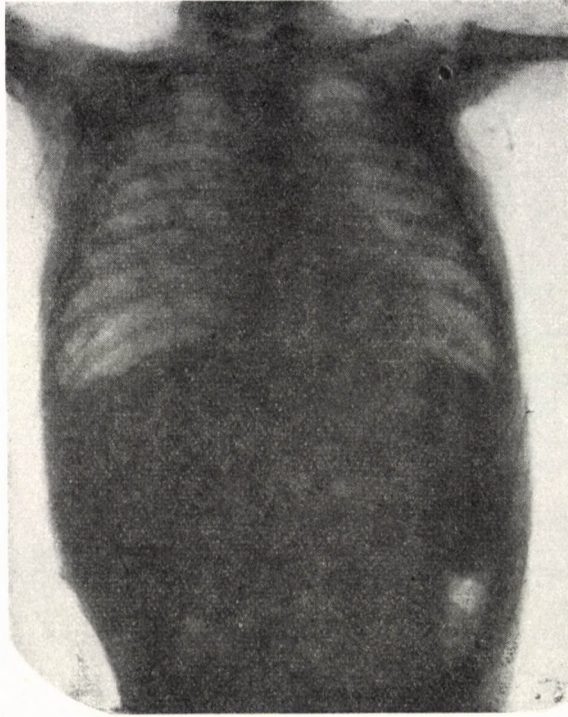


FIG. 2

fourteenth day temperature became normal, the cough stopped and the antibiotics were discontinued. At this time the X-rays revealed a significantly reduced density over the lungs, but the signs of pleural involvement persisted. Four weeks after admission recovery was complete and the baby was discharged.

*Case 2.* M. G. was a premature infant with a birth weight of 2250 g, and with a history of perinatal asphyxia. There had been no incompatibility but owing to hyperbilirubinaemia an exchange transfusion had been carried out. Later, umbilical septicæmia had developed which responded well to antibiotic treatment. Subsequently, anaemia, hepatosplenomegaly and signs of liver damage due to haemolytic disease had been noted. Recovery had been gradual, but at the age of ten weeks the infant was well and weighed 3200 g.

It was then that the patient developed

a temperature, cough, hyperpnoea, with an abundant, mucous, foamy discharge. Bubbling rales were heard over both lungs. Despite streptomycin and Sigmamycin treatment, the condition was deteriorating, crepitan rales appeared over the bases. Cultures taken previously yielded Klebsiella and Pneumococcus. According to their sensitivity, kanamycin (20 mg/kg body weight) was prescribed. This resulted in a gradual improvement.

The chest X-ray revealed initial infiltration of the right upper and middle lobe, with the subsequent development of pleural density and microabscesses (Fig. 2). Radiological regression was observed in a month's time.

Laboratory data: sedimentation rate, 115 mm/h; moderate leukocytosis with a shift to the left.

*Case 3.* V. I., a severely damaged five-month-old premature infant with perinatal



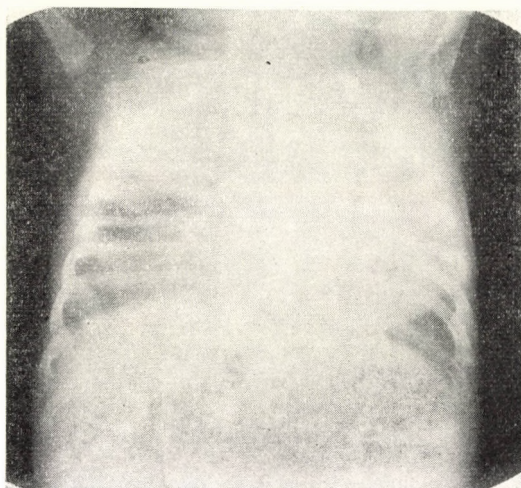


FIG. 3

intracranial haemorrhage was admitted with pneumonia. The course of the pneumonia was atypical and protracted. Throat cultures repeatedly yielded pure *Klebsiella*, even at the end of the second week. As the condition improved, the *Klebsiella* disappeared from the throat, to reappear two weeks later in a mixed culture obtained from the auditory meatus during an episode of suppurative otitis. The pneumonia failed to respond to Sigmamycin, but additional corticosteroid treatment resulted in recovery. The otitis was effectively treated with Sigmamycin.

*Case 4.* Á. E., a premature twin (B) was admitted on the first day of his life, with respiratory distress. The right ear was lacking, the auditory meatus was closed and there was a cavernous haemangioma on the left leg. The lower extremities were oedematous. Cyanosis and tachypnoea disappeared on treatment with glucose and bicarbonate, the oedema after four days treatment with hydrochlorothiazide, 2 mg/kg body weight. The infant began to gain weight, his appetite was good. At the age of two months, anaemia (haemoglobin, 7.0 g per 100 ml) was effectively treated with blood transfusions and with oral iron.

At ten weeks of age tachypnoea with a temperature of 38° C and a respiratory rate of 90 developed. Two days later X-rays revealed small, focal infiltrations in the inferior lobes of both lungs. On the fifth day the throat culture yielded a pure *Klebsiella* growth. Since oxytetracyclin failed to prevent the gradual deterioration, Sigmamycin and cefaloridine (40 mg/kg body weight) were added. On the ninth day the throat swab again yielded *Klebsiella*, which was sensitive to neomycin and polymyxin only. The condition became worse: irritability, forced cough, and an abundant mucous discharge were noted. A severe shock-like state developed, which was successfully treated with prednisone. On the fourteenth day a pure *Klebsiella* culture was again obtained from subglottic secretion. Although the combined administration of prednisone and antibiotics led to some clinical improvement, X-rays showed a progression of the pulmonary process; a confluent density was observed over the upper and lower lobes of both lungs (Fig. 3).

The multiple small, focal infiltrates at the bases raised the suspicion of staphylococcal pneumonia, which was justified by the simultaneous presence of other cases



with staphylococcal infection in the department. Accordingly, oxacillin was started. On the seventeenth day a pure *Klebsiella* culture was obtained again. Then the clinical and radiological state improved and the cultures began to be mixed with *E. coli*. The patient gained weight, rales were no more to be heard over the lungs. It was on the 34th day that the first negative culture was obtained. Four days later the throat culture yielded a normal flora.

Sedimentation rate was within the normal range throughout; leukocytosis with a shift to the left was recorded only initially.

*Case 5.* Á. B., the twin of Case No. 4, was admitted as a premature infant with a birth weight of 1400 g. After overcoming oedema and respiratory distress, she developed normally and attained a body weight of 2500 g. She then contracted a mild bronchopneumonia, simultaneously with his twin sister. Throat cultures repeatedly revealed a pure *Klebsiella* growth, which had the same sensitivity as that of her twin's. Although the pneumonia responded well to oxytetracyclin and erythromycin, throat cultures became negative only on neomycin treatment.

*Case 6.* H. M., a premature infant with a birth weight of 1200 g, developed well despite recurrent *Proteus* pneumonias. With one of the relapses, *Klebsiella* had become to dominate in the throat at a time when a case of *Klebsiella* pneumonia was being treated in the department. Subsequently, *Candida* was repeatedly cultured, giving place to *Proteus* again, two weeks prior to death. In this case *Klebsiella* was isolated on a single occasion and in mixed growth but on epidemiologic and clinical grounds this case may nevertheless be regarded as one due to *Klebsiella*.

*Case 7.* N. E., a premature infant with a birth weight of 1400 g was admitted with oedema and respiratory distress. After he had recovered, and at ten weeks of age attained 2000 g he suddenly developed a pneumonia, with a small infiltrate in the right perihilar area. The pharyngeal secretion yielded *Klebsiella* and *Ps. pyocyanea*,

which were sensitive to cefaloridine and neomycin. These were prescribed together with prednisolone. Improvement was gradual, complete recovery took ten days.

## DISCUSSION

All of our seven patients were premature or young infants, with a low birth weight. In addition, they all had had some previous disease such as pneumonia, haemolytic disease of newborns (2 cases), intracranial haemorrhage (1 case), or umbilical septicaemia (1 case). This seemed to represent a predisposing factor to *Klebsiella* pneumonia, as emphasized also by others [20]. It is well-known that *Klebsiella* pneumonia is more frequent in adults than in children, with an overall incidence of 0.5 to 4% and that chronic alcoholists, sick and old people are much more inclined to contract *Klebsiella* pneumonia than healthy persons [9].

Among our patients, a contact infection occurred only once, in the case of the premature twins, and it was remarkable that one of them developed a mild, while the other a very severe, pneumonia. A similar phenomenon was reported by FERGUSON and TOWER [5] who also observed *Klebsiella* pneumonia in twins; one of them died of the disease while the other had only slight enteritic symptoms.

All but one of our patients had fever, with no characteristic course. Some had temperatures as high as 39–40° C, while in the less severe case only a slight increase could be



observed. The duration of fever ran parallel with the severity of the case. It usually lasted two weeks, and its disappearance was a reliable sign of improvement.

Cough and expectoration were fairly specific. During the first week a short, irritated cough was observed, with a characteristically mucous, foamy and sticky discharge, often by vomiting. This bronchial secretion, though suggestive also of interstitial pneumonitis, was more voluminous and dense than in the case of the latter disease. Fever, cough and expectoration ceased by the end of the second week, parallel with the clinical improvement.

All of our patients displayed dyspnoea and cyanosis during the first ten days of the disease. The cyanosis was characteristic of pneumonia. A most remarkable feature was its early onset and its failure to respond to oxygen inhalation until clinical improvement had become manifest. An increase in the respiratory rate to 75—90 per minute could be observed even before the onset of dyspnoea, showing further elevation on some occasions, and returning to normal simultaneously with recovery.

The special type of cough and the early tachypnoea were the signs drawing attention to the possibility of a *Klebsiella pneumonia* especially in cases, where the auscultatory and the radiological findings were not corresponding to the severity of the condition.

The auscultatory findings did not differ much from those observed in

other types of pneumonias. As our patients developed *Klebsiella pneumonia* in the hospital, we had the opportunity to observe the early signs. During the first few days only a harsh breathing was noted. This was followed by medium and fine rales on the third or fourth day. Crepitant rales could be noticed only from the fourth or fifth day on.

The area affected by the pneumonia was variable. Pleural complications intervened in two cases. Fluid collection was slight in both patients, despite the marked pleural involvement in the first one. The pneumonia extended to several lobes.

The radiological signs were of equal diagnostic value, revealing the presence of small abscesses and focal infiltrations. The clinical course of the disease corresponded to the X-ray findings. In addition to the focal infiltrations some were extending to a whole lobe. Our findings corresponded to the morphological classification of GEFERTH [7] and of RITVO and MARTIN [17]. Radiological changes improved parallel with clinical improvement, but disappeared only about ten days after clinical recovery.

Of the laboratory tests, sedimentation rate was normal or about 20 to 30 mm/hour with the exception of one case, where it attained 115 mm/h. WBC counts ranged between 16,000 and 21,000 during the acute phase, but in some mild cases and in an infant with a grave nervous damage, the count was normal. The differential count always revealed a shift to the left.



## TREATMENT

Antibiotics were immediately started as the first clinical symptoms had appeared (Table I). Once the culture had revealed the antibiotic sensitivity of the *Klebsiella* strain, the adequate antibiotic was introduced. Improvement was attained by kanamycin (15–20 mg/kg) in two cases, by neomycin (10–15 mg/kg) in further two patients, and by cefaloridine (30–50

mg/kg) in the remaining three cases. Kanamycin was the most effective of the drugs. Complete recovery was achieved with neomycin in a mild case.

In view of the serious condition in four of the patients, intravenous prednisone or prednisolone was prescribed, which resulted in an immediate improvement. In Table II, data for antibiotic treatment are summarized.

In addition, strophanthin, oxygen, gamma globulin and vitamins were

TABLE II

Antibiotic treatment of seven patients with *Klebsiella pneumoniae*

No. of case	Treatment applied before sensitivity test	Condition improved on	Duration of treatment days
1	penicillin	streptomycin 26 mg/kg/day	5
N. M.	streptomycin	kanamycin 15 mg/kg/day	5
	meticillin	chloramphenicol 15 mg/kg/day	5
	Sigmamycin, 20 mg/kg/day		
2	streptomycin	kanamycin 20 mg/kg/day	7
M. G.	Sigmamycin, 20 mg/kg/day		
3	penicillin	Sigmamycin 25/mg/kg/day	10
V. I.	streptomycin, 25 mg/kg/day	prednisone 10 mg/day	2
		prednisolone 5 mg/day	10
4	Sigmamycin, 20 mg/kg/day	cefaloridine 50–30 mg/kg/day	13
Á. É.	oxacillin, 100 mg/kg/day	neomycin 10 mg/kg/day	5
		prednisone + prednisolone	9
5	chloramphenicol 25 mg/kg/day	neomycin, 10 mg/kg/day	5
Á. B.	erythromycin 5 mg/kg/day		
6	tetracyclin 40 mg/kg/day	cefaloridine 30 mg/kg/day	14
H. M.	cefaloridine 30 mg/kg/day	chloramphenicol 50 mg/kg/day	4
	erythromycin 50 mg/kg/day	prednisone + prednisolone	11
	neomycin 40 mg/kg/day		
7	erythromycin	cefaloridine 25 mg/kg/day	14
N. É.		chloramphenicol 50 mg/kg/day	7
		prednisolone	11



given. In cases yielding a positive throat culture without clinical symptoms, a 0.5–1% neomycin solution was applied locally during three or four days. This measure was followed by bacteriological negativity.

#### SUMMARY

Five premature and two young infants with *Klebsiella aerobacter* pneumonia have been observed in the year 1966. All but one patient had previously suffered from some severe illness. Pneumonia was mostly grave, but all the patients recovered. One of the premature infants died later of a Pro-

teus pneumonia. The clinical symptoms and course of, and the radiological signs and laboratory data in *Klebsiella* pneumonia have been discussed.

Since, according to literature, *Klebsiella* pneumonia is frequently fatal, the importance of a combined antibiotic treatment has been stressed. In four patients, only the additional use of corticosteroids led to an improvement.

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