

Group 2—History of Nephritis

The figures here illustrate well-known facts. Of 36 cases, 12 show complete recovery, with absence of albuminuria; 6 show only orthostatic albuminuria, and in my view should also be considered to have recovered; and 13 still show signs of nephritis, though it is possible that where the history is recent complete recovery may ultimately occur in some cases.

It is probably best, in view of the history, to regard as cases of latent nephritis the 5 with normal findings except for an albuminuria that is not orthostatic, though to those who accept the view that benign albuminuria is not always orthostatic they may be cases which have recovered completely from their nephritis.

Remaining Groups

The number of cases in each of the remaining groups is small and the results call for little comment.

Taking all groups together, the number of cases that can be accepted as being free from renal disease is 118; 18 must be regarded as doubtful; and the remaining 64 show definite signs of renal disease. Thus, approximately 60% of cases referred for the reasons indicated in the table can be accepted as fit for service.

Summary

The examination of recruits who are apparently healthy apart from the presence of albuminuria is described, and the results of such examination in 200 male recruits are given.

The findings in different groups are discussed, and attention is drawn to cases in which it appears that chronic nephritis was the sequel to a subclinical glomerulonephritis following a commonplace infection that is often soon forgotten.

In approximately 60% of the recruits examined the albuminuria could, with reasonable confidence, be taken as benign and the recruits accepted for service.

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In his Annual Report for 1954 Dr. A. ELLIOTT, county medical officer of health for Kent, describes a pilot scheme, undertaken as part of the domestic-help service, for the provision of evening and night attendants for elderly people in the Maidstone and Medway towns area. The attendants' duties include provision of meals, preparations for sleep, attention to fires, and night attendance. The scheme is limited to cases where voluntary help cannot be provided, and the assistance provided may be either continuous or intermittent, depending on available help from relatives or other sources. The scheme was brought into operation on November 1, 1954, and by the end of that year 37 applications had been received, and in 30 of these cases the necessary help was provided by the county council. There has been an appreciable increase in the demand for this service since the end of last year, and it has been decided to continue this pilot scheme for a further period of six months.

STAPHYLOCOCCAL PNEUMONIA IN INFANCY

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Staphylococcal pneumonia in childhood, with its tendency to abscess, empyema, pneumothorax, and cyst formation, has been recognized for many years, but until recently has been regarded as a comparatively rare disease. This is indicated by the small numbers reported in the literature. For example, the largest series, excluding the post-mortem material of Guthrie and Montgomery (1947), deals with 41 cases, and was collected in New York by Kanof *et al.* (1953) from the early sulphonamide era to 1952, a period of more than 10 years.

In contrast to this we have seen as many as 55 cases in a period of 29 months. All our cases were observed at a time when the broad-spectrum antibiotics were freely available, and because of this we wish to discuss some of the problems that arise in the management of the disease at the present time.

Kanof *et al.* (1939) emphasized the frequency of empyema, which occurred in 78%, and stressed the serious nature of the disease, the mortality being 70%. Chaplin (1947), in a review of empyemata in children, noted that the staphylococcus was almost invariably the cause in infants under the age of 6 months. Blumenthal and Neuhof (1946), describing 40 patients, most of whom were treated before the advent of penicillin, drew attention to the importance of surgical measures in lowering the mortality, only 13 (33%) of their cases being fatal. They attributed their good results to the early institution of closed drainage in cases of empyema and pyopneumothorax and deplored the use of repeated aspirations.

With the introduction of penicillin the mortality fell (Chaplin, 1947), but the development of penicillin-resistant strains of staphylococci soon diminished the value of this drug. The discovery of the broad-spectrum antibiotics provided a new weapon, and the results of Kanof *et al.* (1953) suggested that the problem of staphylococcal pneumonia was largely solved. These authors reported 12 consecutive cures with chlortetracycline ("aureomycin") and penicillin, and considered that the need for aspiration of empyemata was almost abolished. This is not our experience.

Cysts have been recognized as a common complication of this condition, but they usually subside without treatment. Potts and Riker (1950) pointed out the importance of distinguishing them from congenital cysts, as these, in contrast, often require major surgery.

Present Investigation

This article deals with 55 cases of staphylococcal pneumonia in infants that occurred over a period of 29 months, and describes briefly the course of the disease, the x-ray appearances, the treatment, and prognosis. Our cases are divided into Group A—a series of 11 fatal cases in which the pneumonia was a terminal event in children with chronic debilitating disease; and Group B—a series of 44 cases corresponding to the primary and secondary pneumonia of other authors.

Group A.—Group A comprises four children with fibrocystic disease of the pancreas, in which the association of staphylococcal pneumonia is well known; two with amyotonia congenita; two with chronic gastro-enteritis; one with epidermolysis bullosa; one with microcephaly; and one with rhabdomyosarcoma of the prostate. All these children had been in hospital for long periods before the onset of the lung infection. This group is included to emphasize the frequency of staphylococcal infections in hospital patients and their commonly fatal nature in debilitated children. No further mention is made of them in the discussion which follows.

Group B.—Of the 44 cases in this group five had osteomyelitis. They therefore corresponded to the secondary pneumonia of other authors. Of the remaining 39, some had evidence of staphylococcal infection elsewhere, but in all of them pneumonia was the predominant feature.

Analysis of Group B Cases

Age Incidence.—All except 10 of the children were under the age of 6 months (Fig. 1).

Seasonal Incidence.—The incidence was greater in the winter and spring of each year (Fig. 2), and in these seasons in 1953 and 1954 there was proved influenza in the community. No virus studies were made in our cases.

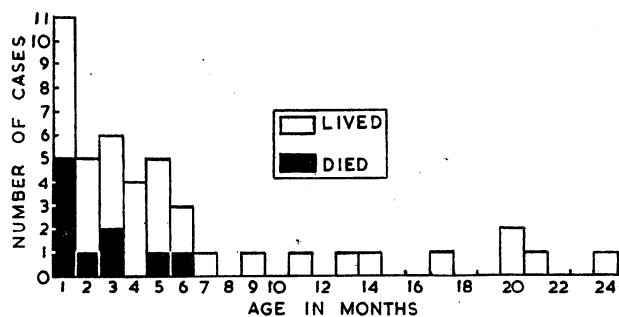


FIG. 1.—Age incidence.

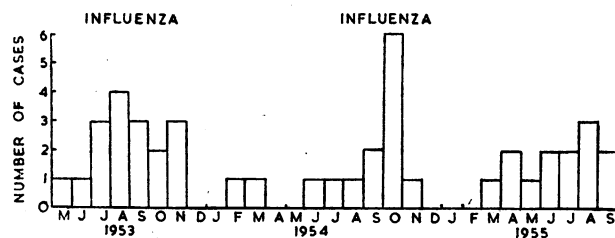


FIG. 2.—Seasonal incidence.

Associated Infections.—In 10 patients (23%) there were associated staphylococcal infections; pustules in four, osteomyelitis in five, and umbilical sepsis in one. In 23 (52%) there was a history of upper respiratory tract infection. Of the 44 patients there were eight whose lungs were passed as normal by the house-physician on admission.

Pyrexia.—The average duration of pyrexia in the surviving cases was 13 days, but in five babies, all under the age of 6 weeks, the temperature never rose above 100° F. (37.8° C.).

X-ray Appearances.—Four patients died before x-ray films could be taken. Of the remainder, pyopneumothorax occurred in 14 (25%), empyema alone in 14 (32%), and pneumothorax alone in 3 (7%). Cysts occurred in 29 (66%), and in seven were present on admission. The average time between admission and the first signs of cyst formation was five days. In 16, regular x-ray examinations were made until disappearance of the cysts, and the average time for this to occur was six weeks.

Laboratory Investigations.—Polymorphonuclear leucocytosis was usual. When possible, sensitivity tests were performed *in vitro* on material obtained from the lungs, pleura, or sputum, but in some cases it was necessary to rely on culture of staphylococci obtained from throat swabs. 92% were completely resistant to penicillin. Resistance to oxytetracycline ("terramycin") was found in 4%, to chlorotetracycline in 3%, to chloramphenicol in 6%, to streptomycin in 3%, and to erythromycin, when tested, in 3%.

Treatment.—Antibiotics were given according to the result of sensitivity tests and clinical response, and the duration of treatment was determined arbitrarily by the duration of pyrexia and the clinical condition. The average was 23 days. Penicillin was not used as the initial treatment in later cases. Surgical treatment was necessary in 21 cases (48%). Aspiration alone was successful in six. Of these five had empyema and one pyopneumothorax. Intercostal drainage was carried out on 13 patients, 11 of whom had pneumothorax or pyopneumothorax and two had empyema alone. One of these patients died. In seven patients the empyema was minimal and surgical intervention was not indicated. The method of intercostal drainage used was the insertion of a catheter through a stab thoracotomy made with a trocar and cannula.

Mortality.—Ten patients died—a mortality of 23%—five of them within 24 hours of admission.

Follow-up.—X-ray films were taken of 29 survivors; all had become normal or showed only minimal pleural thickening.

Case 1

A full-term baby developed furuncles in the maternity hospital. On the fifteenth day, when the skin condition had practically cleared with local treatment, she became difficult with feeds, and the mother noticed grunting respirations. Penicillin and a sulphonamide were given without improvement, and she was admitted here on the seventeenth day.

On admission the temperature was 102° F. (38.9° C.); she was pale, cyanosed, and dyspnoeic, and had a slight nasal

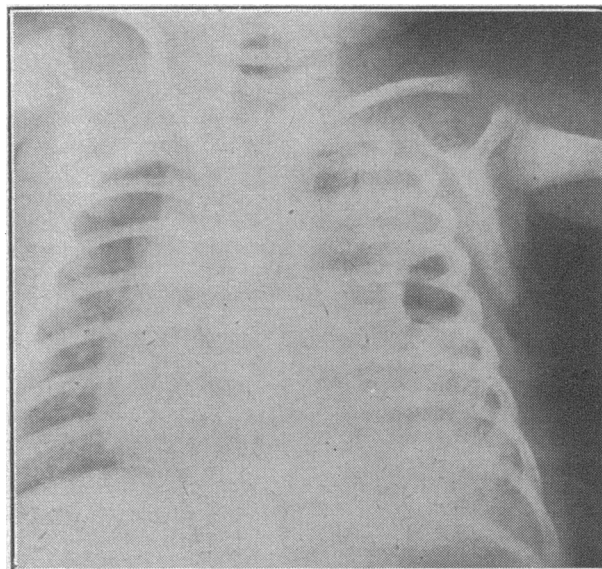


FIG. 3.—Case 1. On admission on October 30. Pyopneumothorax and consolidation.

discharge. There were signs of consolidation on the left side of the chest, and scattered healed furuncles on the thighs. The polymorphonuclear leucocytes numbered 38,800. Staphylococci, resistant to penicillin but sensitive to all other antibiotics, were isolated from the throat swab, and chest x-ray examination showed consolidation of the left lung with early cyst formation and a small pyopneumothorax (Fig. 3).

Chloramphenicol was given and the baby was nursed in oxygen. Respiratory distress continued, and an x-ray examination the following day showed an increase in the amount of fluid. Chest aspiration was performed on the second, third, and fourth days with temporary improvement, approximately 1 oz. (28 ml.) of thin yellow pus being obtained on each occasion. Penicillin-resistant staphylococci were cultured from this.

Five days after admission she was still dyspnoeic and cyanosed, and intercostal drainage was instituted. The immediate improvement following this procedure was maintained, and progressive x-ray films showed gradual re-expansion of the lung with diminution in air and fluid, and

some pleural thickening (Figs. 4 and 5). On the twelfth day, when she had been clinically well for two days, the catheter was removed. Chemotherapy was stopped 14 days after admission, the temperature having been under 100° F. (37.8° C.) for seven days. Cysts were no longer visible radiologically after three weeks, and the pleural thickening gradually diminished until, at 15 weeks, the x-ray film was normal.

Comment.—This infection was probably acquired in the maternity hospital, though not manifest until after the baby returned home. The striking feature of this case was the prompt and dramatic improvement following intercostal drainage.

Case 2

A full-term baby developed pallor and jaundice on the third day. He was slow with his feeds, and vomited twice on the twelfth day, when he was transferred to this hospital. On admission the temperature was normal; he was pale and slightly jaundiced, and had a mildly infected umbilicus. The tissues were lax and he was 20 oz. (570 g.) under his birth weight. He was regarded as having neonatal sepsis and was given chlortetracycline. Staphylococci insensitive to chlor-

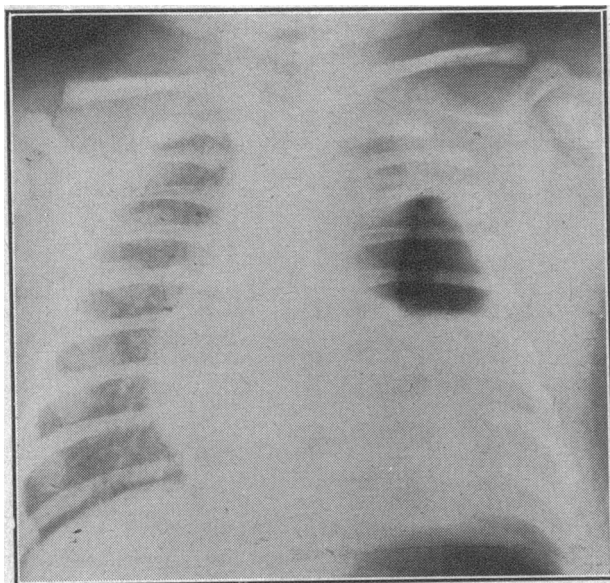


FIG. 4.—Case 1. November 2. Increase in amount of air and fluid.

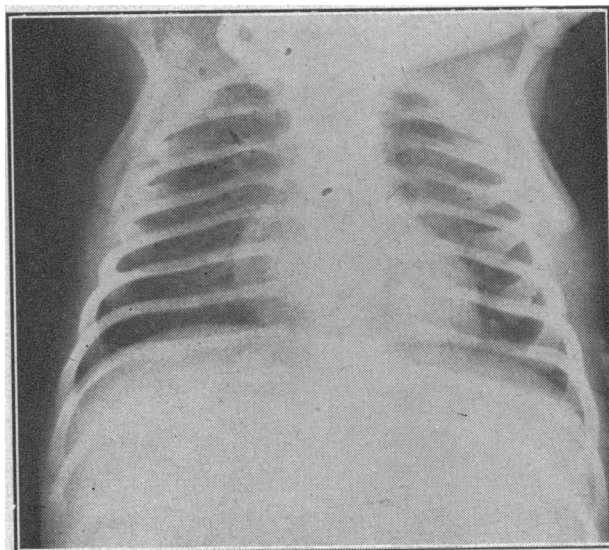


FIG. 6.—Case 2. November 3 (two days after admission). Minimal changes at left apex.

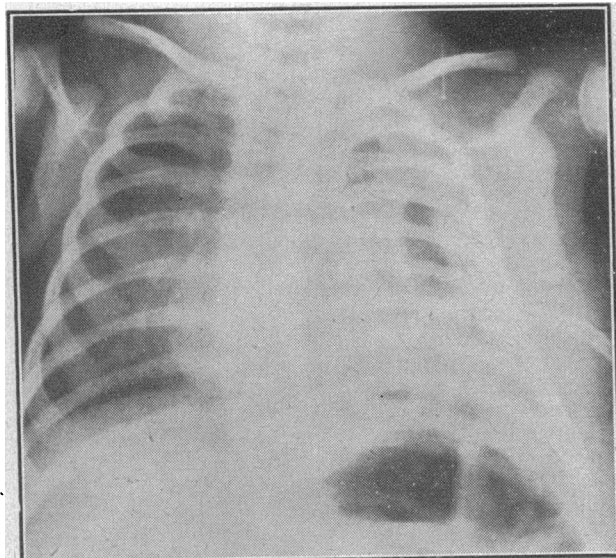


FIG. 5.—Case 1. November 8. Improvement following insertion of intercostal drain; cysts visible.

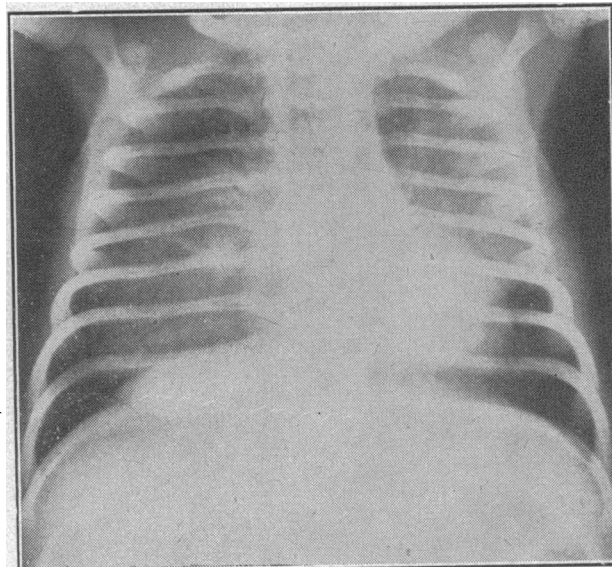


FIG. 7.—Case 2. November 18. Consolidation both sides, cysts visible on right.

tetracycline and to penicillin were grown from an umbilical swab, and chloramphenicol was substituted for the chlortetracycline. A chest x-ray examination two days after admission showed a faint opacity in the left upper zone (Fig. 6). The infant remained lethargic and had mild diarrhoea; then five days after admission, while still having chloramphenicol, his respiration rate increased and he developed a pyrexia and a polymorphonuclear leucocytosis of 44,000. X-ray films showed increased density of the opacity previously seen in the left lung, then one week later a massive opacity on the right side with early cyst formation (Fig. 7). The cysts gradually increased in size and the density lessened, and this was accompanied by clinical improvement.

Three weeks after admission the temperature was normal, he was taking feeds well and was gaining weight, and antibiotics were stopped a week later. Fig. 8, taken seven weeks after admission, shows cysts on both sides when consolidation had cleared. Three months after onset the x-ray film was clear apart from an indistinct cyst on the left side.

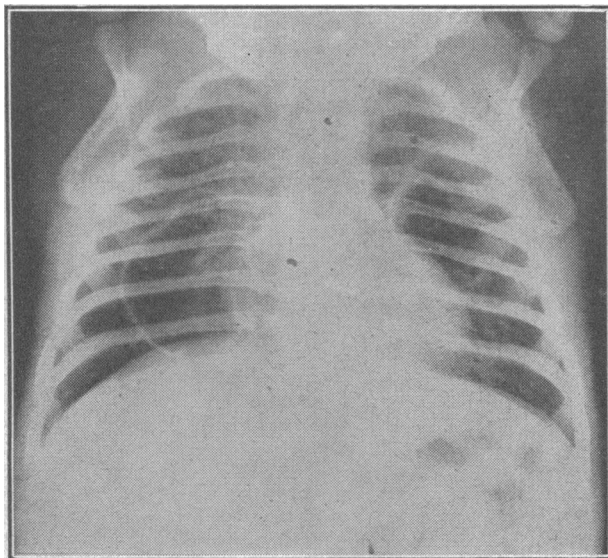


FIG. 8.—Case 2. December 21. Cysts both sides after clearing of consolidation.

Comment.—In this patient antibiotics were administered immediately after admission, when x-ray signs were minimal; yet the disease progressed, extensive lung changes occurred—consolidation first and later cysts—and his illness continued for three weeks.

Discussion

This study was confined to infants under the age of 2 years, but it is a striking fact that more than three-quarters were under the age of 6 months. None of the children over the age of 6 months died.

The increasing frequency of staphylococcal pneumonia has been stressed elsewhere. The cause is not known, but it parallels the growing resistance of the staphylococcus to penicillin and the widespread use of antibiotics. The higher incidence during winter and spring corresponds with that of other respiratory infections, and may be related to the outbreaks of influenza. The frequency of staphylococcal infection in foundling homes and maternity hospitals (Gairdner, 1954) may explain why a number of our cases came from these institutions. In the whole series there were concomitant staphylococcal lesions in nine. The 11 fatal cases (Group A) associated with chronic debilitating disease presumably acquired their infection in this hospital.

Clinical Picture.—Although the respiratory signs may be overshadowed by the toxæmia, in most of the severe cases the appearance was fairly typical, the infant being pale, cyanosed, and tachypnoeic, with distressing cough and grunt-

ing respirations. Occasionally the illness may be fulminating, and one patient included in this series died in transit to hospital after an illness of only 18 hours. The production of thick yellow sputum is common, and it is often possible to obtain a sample of this for culture by provoking a coughing spasm with a spatula. On rare occasions haemoptysis occurs. Abdominal distension and loose motions are sometimes prominent features of the acute stage, at times causing difficulty in the diagnosis. Rupture of an abscess into the pleural cavity is probably responsible for the high incidence of empyema and pneumothorax, and may lead to rapid deterioration. Careful observation and frequent x-ray films are necessary for the early recognition and treatment of these complications, which may develop up to two weeks after treatment is begun.

Antibiotic Treatment.—The work of Chaplin (1947) and McLetchie (1949) and our own experience indicate that the staphylococcus is by far the commonest cause of severe pneumonia and empyema under the age of 6 months. Because of the increasing resistance of this organism to penicillin, Horace Hodes (1952) recommended that one of the broad-spectrum antibiotics be combined with penicillin for treatment of pneumonia in this age group. However, the almost complete failure of penicillin led us to abandon this drug as the initial treatment in later cases. The other drugs used were chlortetracycline, oxytetracycline, chloramphenicol, streptomycin, and erythromycin, the commonest being the tetracyclines. It was not unusual for the antibiotic to be changed during the course of the illness because of the slow clinical response, but there was no evidence of superiority of any one drug or combination of drugs. The value of the broad-spectrum antibiotics and erythromycin appears to be greatest during the early toxæmic stage. The long duration of fever and the extension of pulmonary lesions and empyemata during treatment indicate their relative ineffectiveness against the suppurative foci. A similar trend has been observed by W. N. Gilmour (personal communication) and Dennison (1955) in cases of osteomyelitis. To-day extensive bone destruction is occurring despite the use of chlortetracycline alone or with penicillin, and the spectacular cures of the early penicillin days are no longer seen. Despite the use of these drugs it is disturbing to note that the mortality rate in our series is little better than that of Blumenthal and Neuhof (1946), whose cases were treated before the advent of penicillin and later antibacterial agents.

Surgical Treatment.—When an empyema is demonstrated it is our practice to use simple aspiration, repeated if necessary; but where this is large—or rapidly accumulates after aspiration—intercostal drainage is instituted. The same applies when there is air in addition, because a large broncho-pulmonary fistula may be present. Rib resection was not resorted to in any case and would not appear to be indicated in this condition. Rapid increase in size of a pneumothorax may constitute an acute emergency, and the consequent respiratory embarrassment requires immediate relief. The necessary equipment for intercostal drainage must always be ready for use. Occasionally a cyst may suddenly expand and produce a similar clinical and radiological picture. Conservative treatment is generally recommended in these circumstances, but in two of our cases stab thoracotomy with intercostal drainage was a life-saving measure, and in one was followed by immediate and permanent disappearance of the cyst.

Cysts.—The development of cysts is a unique feature of staphylococcal pneumonia, and their appearance during a lung infection is practically diagnostic of this condition. In the early stages of the disease it is often possible to see small cystic spaces in the consolidated areas radiologically. These are probably abscesses, but these same translucencies may increase in size later and assume the typical thin-walled appearance of cysts. It is difficult to say when an abscess becomes a cyst, and for this reason we have made no distinction between the two, referring to them all as cysts. They occur at an early stage, generally within the first week. As the consolidation clears the cysts often become more

obvious and at the same time tend to enlarge. They are only rarely associated with any respiratory disturbance, and it is surprising how well an infant may be with large cysts in his lung. We do not think it necessary to continue antibiotics until the cysts disappear, and it is our practice to cease treatment when the child is clinically well and the temperature normal.

In a disease which causes such extensive lung changes one would expect sequelae in the form of chronic pulmonary suppuration, but, in the children who survived, the ultimate return of the x-ray films to normal and the invariably normal development of the patient were most gratifying. Bronchograms did not seem to be indicated, and were therefore not done.

Summary

The literature on staphylococcal pneumonia is reviewed briefly. Attention is drawn to an apparent increase in frequency of the disease and its high mortality.

A series of 55 cases in children under the age of 2 years, occurring during a period of 29 months, are discussed. Eleven of them were associated with chronic debilitating disease, the pneumonia being a terminal event (group A). The remaining 44 cases (group B) are discussed in detail with reference to diagnosis, x-ray changes, treatment, and prognosis. Ten patients died—a mortality of 23%.

The relative ineffectiveness of the broad-spectrum antibiotics in controlling the infection is stressed, and the high percentage of penicillin-resistant organisms is noted (92%).

Empyema or pneumothorax was present in 28 cases (64%). Emphasis is laid on the importance of surgical treatment when these complications occur.

Cysts were present in 29 cases (66%).

Follow-up x-ray examinations in 29 out of the 34 survivors showed nothing abnormal, there being no residual signs or symptoms.

APPENDIX: TECHNIQUE FOR INTERCOSTAL DRAINAGE

Apparatus.—Exploring trocar (Allen and Hanburys No. 16920). Jaques catheter, sizes 3-6. Glass connexion and rubber tube for attaching catheter to Woulfe bottle with underwater seal. A small electric suction-pump facilitates drainage. For this purpose we use a low-pressure pump made by the Genito-Urinary Company.

Method.—After locating the site for drainage—a good lateral x-ray film of the chest is essential for this—the skin is infiltrated with a local analgesic. A nick is then made with a scalpel, and the trocar and cannula are inserted quickly into the chest. After withdrawing the trocar the catheter is passed through the cannula, which is then carefully removed. The catheter is then connected to the suction apparatus, approximately 2 in. (5 cm.) being left inside the chest. For small infants a cannula of 9-14 Charrière gauge is satisfactory. Speed is important, as the operation is distressing and the baby may be *in extremis* when it is performed.

We wish to thank the members of the honorary medical staff for allowing us to publish details of cases under their supervision, and Mr. R. Plummer for preparing the photographs.

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EFFECT OF INTRAVENOUS VITAMIN K₁ ON THE ACTION OF PHENINDIONE

BY

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Vitamin K₁ (2-methyl-3-phytyl-1:4:naphthoquinone) when administered orally has been shown to have an antagonistic effect on the action of phenindione (2-phenylindane-1:3-dione) (Toohey, 1952; Perlick, 1953; Chalmers *et al.*, 1954). Because the vitamin is fat-soluble, preparations suitable for intravenous injection have been associated with difficulties in administration (Douglas and Brown, 1952).

While preparations of vitamin K₁ suitable for intravenous administration have been used in America for some time, it is only recently that a new experimental emulsion of vitamin K₁ has become available for trial in this country. This paper records the results of tests performed on volunteers receiving phenindione ("dindevan") who were given intravenous injections of this new vitamin K₁ emulsion.

Material and Methods

1. The vitamin K₁ preparation used was a stable emulsion containing 20 mg. of vitamin K₁ per ml. It was stored in amber-coloured ampoules away from light.

2. Tests were carried out on 24 healthy volunteers, who received 5, 10, or 20 mg. of the vitamin K₁ emulsion intravenously during the administration of phenindione.

3. Using Quick's one-stage technique, "prothrombin activity" estimations were carried out by the method described by Chalmers *et al.* (1954).

4. Prothrombin was estimated by a modification of the globulin assay technique of Douglas and Biggs (1953).

5. Base-line values of prothrombin activity were determined and then phenindione was administered to the subjects for four days, by which time the prothrombin activity was of the order of 10-20%. A single intravenous injection of 5-20 mg. of vitamin K₁ was then given. At varying intervals subsequently, prothrombin activity was determined, with additional controlled tests for prothrombin itself in some of the experiments. The subjects continued to take phenindione in regular dosage until the end of the experiments.

Results

In six volunteers to whom a dose of 20 mg. of intravenous vitamin K₁ was given and in four who were given 10 mg. the prothrombin activity was raised to 100% within 24 hours irrespective of its original level (Figs. 1 and 2).

Fourteen volunteers were given 5 mg. of the vitamin (Figs. 3 and 4). In these the prothrombin activity rose from initial values of 7-19% to maximum figures of between 50 and 100%. In 10 volunteers a maximum figure was reached after 24 hours, in one after 12 hours, and in three after 6 hours.

Estimations of prothrombin activity were not made at such frequent intervals in all volunteers, as their tolerance to venepuncture was limited. However, in 19 experiments prothrombin activity was estimated three hours after dosage with vitamin K₁, and in 12 of these it showed a rise of between 5 and 26%. In seven there had been no elevation by this time. In 16 cases a six-hourly estimation was carried out—in 11 of these the level had risen by between 30 and 65% in this time; in three of the remainder it had risen by at least 14%, whilst in the remaining two there was no increase. In both of these latter patients, however, the level had risen to 100% after 24 hours.