THE INVESTIGATION OF AN OUTBREAK OF PSEUDOMONAS PYOCYANEAE INFECTION IN A PÆDIATRIC UNIT

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The introduction of potent antimicrobial agents has resulted in the lesser frequency of potentially fatal infections caused by β-haemolytic streptococci and pneumococci, but the greater frequency of staphylococcal, fungal and other bacterial infections of the coliform and related gram-negative species. *Pseudomonas pyocyanea* or *Ps. aeruginosa* owing to its notorious resistance to therapy occupies a unique position.

Charrin (1890) first recognised pseudomonas as a pathogen in man and recently many descriptions of the disease have been given. Curtin (1957), a leader in the Lancet (1961), Rogers (1960), Markley, Audmendi, Charez and Bazan, (1957), Sussman and Stevens (1960), Williams (1960), Lubsen (1961), Curtin, Petersdros and Sennott (1961), and McCabe and Gee Jackson (1962), all warn of the frequency of the infection in young and debilitated patients, in burns, in orthopaedic cases, in urinary problems, in gram negative septicaemia, in geriatric patients, in premature infants and those with congenital abnormalities. Deaths were frequent in most of the series.

Clinical Material

Between July, 1960 and March, 1964 some 73 cases of *P. pyocyanea* infection have been seen in pediatric units in various hospitals in Cardiff. The patients could be placed in the following groups:

1. *Associated with prematurity*—49 patients with nine deaths including two infants with congenital abnormality of the urinary tract and one cleft palate with other congenital abnormalities, (trisomy 18). These occurred in a premature unit (A).

2. *Associated with congenital abnormalities*—16 patients. (a) 12 meningomyeloceles (7 died) in a paediatric unit (B) (b) one child with cleft lip and palate (trisomy 15-17) (who died later but not of the disease) in a paediatric unit (C) (c) one child with hydrourer and hydrenephrosis (alive) in a paediatric unit (C) (d) two children with abnormal hearts (large patent ductus; pulmonary atresia) (both died) in a paediatric unit (D) of a chest hospital.

3. *Associated with leukaemia*—two patients (who died later but not of the disease) in a paediatric unit (C).

4. *Associated with chronic disease*—two patients with fibrocystic disease (both died later but not of the disease) in a paediatric unit (C).

5. *Chance findings*—four patients:—two with infected urine (in a paediatric unit), one neonatal infant with no obvious abnormality who survived (in a paediatric unit) and one neonatal infant with no obvious underlying abnormality (transferred from a neonatal paediatric unit with a chest infection to a chest unit) who died of pyocyaneae infection of lungs.

In these various infants, positive swabs were obtained from umbilicus (4), urine (29—including two at post mortem), lung (10—all at post mortem), rectal swabs and stools (51), skin (3), ear (3), eye (3), nose and throat (34), meninges (two—at post mortem) and pericardial fluid (one—at post mortem).

Classical Symptoms and Signs

*Of the premature infants in group* 1, 30 were admitted from home or from outside maternity units, whilst 19 were born in the hospital containing the premature unit. The weights lay between 2 lbs. 4 ozs. (1,023 g.) and 5 lbs. 5 ozs. (2,360 g.). The disease commenced at the age of one to fifteen days and deaths occurred from one to twenty-three days after birth. 19 infants had signs of respiratory distress syndrome within eight hours of birth and it was difficult to recognise when the respiratory problem had altered to one of a generalised infection. Later cases showed a fall in temperature (from 95°F to 87°F), a gradual increase in cyanotic attacks and, in some cases a peculiar type of diarrhoea with a brownish-black stool, semi solid in character, sometimes with slime or blood. Some infants had an odd membrane on the mouth, starting with thrush-like white patches, but proceeding to small brown
lesions with black centres. These lesions spread to cheek and oropharynx and later to the anus, the rectal margin often being everted. Occasional infants had convulsions (only one being associated with meningitis). The infants regurgitated easily, became anorexic and often died after vomiting blood. The abdomen showed the picture of ileus with distension and ladder patterning. Oedema was a prominent feature.

Various skin lesions were seen, a toxic erythema (like erythema multiforme); "eczthyma gangrenosum" with a characteristic macule changing to an indurated area with a black necrotic centre; generalised purpura (in one proceeding to ecchymoses); pustular lesions (being clusters of vesicles growing Ps. pyocyanea) and small pink nodules.

The blood picture showed little. Anaemia and leucocytosis were rarely seen, the common finding being the presence of toxic granules with a neutrophilic shift to the left. Thrombopenia was noted in two cases.

Sixteen cases had had previous antibiotic therapy (13 methicillin or cloxacinilin and three ampicillin) and of these four died, whereas five died of the remaining cases not given antibiotics previously.

In the 16 patients in Group 2, the infection developed at the operation sites which became brown-black and necrotic. Meningitis appeared with the usual physical signs (pyrexia, neck stiffness, bulging of fontanelle, lethargy, vomiting, cyanotic attacks and convulsions. Occasionally patients seemed to live in symbiosis with the organism. Death was from septicaemia and meningitis. Antibiotics had been previously used. The patients in the chest unit were considered to be cardiac problems, in one instance with a superadded pulmonary infection. Skin lesions developed in one just before death, whilst in both the organism was only found at death (again antibiotics had been used).

In groups 3 and 4, infective episodes were shown to be due to Ps. pyocyanea infection, but the patients survived. All patients had been on antibiotics, the leukæmia patients also having had steroids and methotrexate.

In group 5 one mature infant died at the age of five weeks in a chest unit after transfer from a neonatal unit. Multiple antibiotics had been given for a chest infection, but ventilation become inadequate even after tracheostomy.

Post Mortem Findings

The characteristic lesion on the tongue showed an area of muscle necrosis and infiltra-

Fig. 1.—Skin, showing arteritis of vessel in dermis. 
H & E X 80.

tion. Gram stains showed numerous gram negative bacilli in the necrotic areas. The lungs showed intra-alveolar and intra-bronchial polymorphonuclear exudates and hæmorrhage. In places there was necrosis and abscess formation with gram negative bacilli. The walls of small blood vessels showed acute inflammatory arteritis (Fig. 1) the thrombosis secondary to this leading to arterial occlusion and small infarct-like areas (Fraenkel, 1917). The affinity of the organism for the walls of small vessels was seen in all tissues showing lesions, i.e., skin, lung, brain and kidney. (Fig. 1).

In the gut necrotic non-exudative lesions were seen with a yellowish opaque centre and deep red margins.

Investigation of Epidemics

In the premature unit involved, cases have occurred over a period of more than three-

and-a-half years. Conditions in such a unit are conducive to epidemics in that infants are in debilitating situations, often being very small, occasionally having congenital abnormalities liable to high levels of bilirubin with resultant lethargy and difficulty in feeding, while the unit is liable to sudden increases in numbers in the ward with overcrowding of nurse/patient ratio. Such patients are prone to respiratory difficulties and tend to be treated with an "antibiotic cover" to prevent possible infection or deal with apparent infection. Again being small and in poor condition they tend to be nursed in an incubator with a relatively high humidity atmosphere. (Hoffmann & Finberg, 1955). The ambient temperature and humidity in a premature unit tends to be higher than average. All these conditions produce a situation in which infections like Monilia
The number of swabs taken was inadequate. Quaternary thermometers being used dust at as a look for cleaning tubing, left was meters, fluid etc.

(3) incubators-from the All incubators.

1). (Table Procedures Lumbar puncture Intravenous tubes)

No positive swabs were found initially in any part of the unit except in the incubators which had held a case. Later swabs were positive in various sinks.

A general investigation in various wards in the hospital (including the labour ward), and nearby hospitals, showed that there was no uniform policy in any section with regard to sterilization. For thermometers sterilization (Table 2) involved the use of some six different materials—some of which looked nice but were of no value from a sterilization point of view. Brushes were cleaned in a variety of substances; rubber tubing was treated with one of seven different media. In general the antiseptic used related to the material which the sister in charge of a ward had been accustomed to using in her training hospital. With regard to strength of solution used, it could be taken as a general rule that wherever solutions were made up on the ward from a stock solution which required diluting, the final solution: was usually dependent on how the person making up the solution felt about the colour rather than on suggested dilutions needed.

In the chest unit where the two children were infected, about eight adult chest cases were also infected. Here positive swabs were obtained from the noses of radiographer, physiotherapist, nurses, orderlies, cleaner, laboratory technician and one doctor, as well as in the rubber tubing attached to anaesthetic apparatus, sucker, nozzle, a brush from a cleaning bottle, the outside of a pulmoflator and also on plates put in the post-operative ward. Positive swabs were obtained from a sink and from a wall.

In the unit with the meningomyeloceles, the positive swabs were obtained from the sink disposal unit, but not from the atmosphere or any personnel.

In the units concerned an attempt was first made to assess the value of antiseptics in common use. Dilutions of antiseptic in terms of the active ingredient after a 24-minute

<table>
<thead>
<tr>
<th>TABLE 1</th>
<th>MODES OF SPREAD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Airborne particles</td>
<td>Dust { Previous cases Methods of cleaning } Humidifiers { Incubators, Air-conditioning } Nose</td>
</tr>
<tr>
<td>Contact</td>
<td>Hands Dressings Suction tubes, oxygen supply “Sterilising” materials (quarternary compounds, etc.)</td>
</tr>
<tr>
<td>Procedures</td>
<td>Injections Lumbar puncture Intravenous tubes</td>
</tr>
</tbody>
</table>

albicans and Ps. pyocyanea tend to flourish.

All the cases concerned in the unit had been in incubators. Those admitted from other units could not have been initially affected in this way. All methods of spread were considered (Table 1).

Swabs were taken (1) from skin, nose and throat of all personnel (doctors, nurses, techni-
cians, cleaners, mothers), (2) piped oxygen sets. (3) Floors, walls, basins and sinks (4) incubators—from the water in the humidity tank as well as walls and floor of the apparatus. Plates were put out in the unit.

All chemical antiseptic procedures were reviewed—the fluid in the tube holding thermo-
meters, for keeping polythene tubes for feeding, for cleaning tubing, for cleaning incubators, etc.

Drying procedures, the use of hot air hand driers, towels, both ordinary and paper, were looked at as a possible source of infection.

Techniques used were found to be inadequate. Quaternary compounds were being used in many places (incubator, thermometer tubes, Woolf bottles, for damping dust and cleaning tubing). Rubber tubing was left attached to suction apparatus and found to contain moisture.

<table>
<thead>
<tr>
<th>TABLE 2</th>
<th>THERMOMETERS</th>
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</thead>
<tbody>
<tr>
<td>Hospital 'A'</td>
<td>Hospital 'B'</td>
</tr>
<tr>
<td>Roccal (5)</td>
<td>Glycothymoline (13)</td>
</tr>
<tr>
<td>Glycothymoline (3)</td>
<td>Glycothymoline (7)</td>
</tr>
<tr>
<td>Savlon (2)</td>
<td>Hibitane (5)</td>
</tr>
<tr>
<td>Bradosol (4)</td>
<td></td>
</tr>
<tr>
<td>Dettol (1)</td>
<td></td>
</tr>
<tr>
<td>Hibitane (2)</td>
<td></td>
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</tbody>
</table>

(The number represent the numbers of wards using material)
October, 1964  JACOBS: Investigation of Outbreak of Pseudomonas Pyocyanea Infection

contact test of antiseptic and bacteria were noted (Table 3). Table 4 shows the ratio between dilution for complete kill and recommended strength.

A change was made in the premature unit to the use of hibitane, C.T.A.B. and hexachlorophene, as well as savlon (a mixture of chlorhexidine 1.5 per cent. w/v, and cetrimide 15 per cent). *Ps. pyocyanea* has been shown to survive in cetrimide alone ("Cetavlon"), (cetyltrimethylammonium cro-mide) (Robinson 1957) especially when bark corks were used in the bottles. Anderson (1959) grew the organism in the humidifying water in an operating theatre ventilation plant. Coliform bacteria have also been found at the same site, also in incubators and where lumbar puncture needles have been inadequately cleansed. McLeod and Mason (1963) have shown how topical antibiotics ("polybactrin" polymyxin 0.4 per cent., neomycin 1 per cent and bacitracin 1 per cent) are superior to chlorhexidine or domiphen as local methods of killing bacteria.

### Treatment

The tendency of *Ps. pyocyanea* infections to occur in damaged ischaemic and fibrotic or debilitated patients (premature infants, congenital abnormality, "poor genetic material"—trisomy 15-17, 18 etc.)" (Smith 1963) makes therapy difficult. The most important part of treatment is prevention of the entry of the organism into the patient, but as the organism is ubiquitous this means keeping a careful check on the conditions of susceptible patients and their surroundings. (Table 5). Regular surveys must be taken of personnel, apparatus, procedures and antiseptics in use. Great thought must be taken before antibiotics are prescribed and their use in prophylaxis abandoned. "Chemotherapy without bacteriology is guesswork." Serious considerations should be given to the use of disposable apparatus of all kinds—brushes, tubing, syringes, needles and so on, so that the need for the use of antiseptics will diminish.

A relief can be obtained by closing down a particular unit and fumigating with formaldehyde vapour. In the premature unit involved this procedure has had to be repeated for only temporary relief has been obtained, and the infection has continued for almost four years. The sinks have given an intermittent positive finding of organisms to a degree that one wondered whether the U-tube part of the drainage might represent a constant source of re-infection. An attempt to sterilize this area by use of Phenoxetol (phenoxyethanol) in strength above one per cent or Wescodyne Fluid (iodine-detergent complex (idophor) from 1/160 (one ounce to a gallon) to 1/20 (eight ounces to the gallon)), Dettol and Lysol have had only a temporary effect on the positive swabs from the washbasin and sinks.

Table of the actual disease in a patient has varied from the use of Phenoxetol one per cent as a local application to a skin lesion or to a discharging ear, to streptomycin by intramuscular injections alone (dosage 20-40

### Table 3

<table>
<thead>
<tr>
<th>Ps. pyocyanea</th>
<th>Water</th>
<th>Broth</th>
<th>25% Blood</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hibitane (Chlorhexidine)</td>
<td>80,000</td>
<td>20,000</td>
<td>2,000</td>
</tr>
<tr>
<td>Domiphen bromide (Bradosol)</td>
<td>48,000</td>
<td>2,000</td>
<td>400</td>
</tr>
<tr>
<td>Phenooctide</td>
<td>10,000</td>
<td>400</td>
<td>100</td>
</tr>
<tr>
<td>p-Chlor-m-xylol</td>
<td>3,330</td>
<td>312</td>
<td>104</td>
</tr>
<tr>
<td>4.8% solution</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cetavlon (Cetrimide)</td>
<td>8,000</td>
<td>1,000</td>
<td>400</td>
</tr>
<tr>
<td>Benzalkonium chloride (Roccoll)</td>
<td>32,000</td>
<td>1,500</td>
<td>500</td>
</tr>
<tr>
<td>Sodium Hypochlorite</td>
<td>10,000</td>
<td>200</td>
<td></td>
</tr>
</tbody>
</table>

The figure show the final dilution of antiseptic in terms of the active ingredient.

### Table 4

<table>
<thead>
<tr>
<th>Ps.pyocyanea</th>
<th>25%</th>
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</thead>
<tbody>
<tr>
<td>Hibitane 2%</td>
<td>Water 1/40</td>
</tr>
<tr>
<td>Domiphen bromide 5%</td>
<td>1/100</td>
</tr>
<tr>
<td>p-Chlor-m-xylol</td>
<td>1/25</td>
</tr>
<tr>
<td>4.8% solution</td>
<td></td>
</tr>
<tr>
<td>Cetavlon 1%</td>
<td>1/10</td>
</tr>
<tr>
<td>Benzalkonium chloride</td>
<td>1/10-1/20</td>
</tr>
<tr>
<td>Sodium hypochlorite 1%</td>
<td>1/20</td>
</tr>
</tbody>
</table>

### Table 5

<table>
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<th>Prevention</th>
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<tbody>
<tr>
<td>1. Review of all chemical antiseptic procedures</td>
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<tr>
<td>2. Review use of antibiotics</td>
</tr>
<tr>
<td>3. Review water-borne carriage of disease (also airborne)</td>
</tr>
<tr>
<td>4. Bacteriological supervision of staff, patients</td>
</tr>
<tr>
<td>5. Isolation of cases</td>
</tr>
<tr>
<td>6. Adequate treatment</td>
</tr>
<tr>
<td>7. Closure of unit</td>
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</tbody>
</table>
mg./kg./day) or with polymyxin B. Colistin has been used in the majority and thiosporin in about three cases. Of the nine deaths in the premature group, three were virtually dead before treatment was started (as were the two cases in the chest unit), two more were treated early in the experience of polymyxin, the remaining four being two with colistin and two with thiosporin.

The experience of finding infants apparently having respiratory distress with positive swabs for *P. pyocyanea* is becoming increasingly common (personal communications—other units). There is now a tendency to treat any episode of pyrexia changing to hypothermia of odd ileus or skin rash or sudden anorexia in the premature babies, by giving one of the polymyxin series.

The polymyxin preparations used have been polymyxin B. sulphate, sulphomethylpolymyxin (both in dosages of 2,000 units/kg. 4 hourly), colistin sulphate and colistin methanesulphonate (both in dosages of 50-100,000 units/kg. 6-8 hourly). It would seem that the first and third are virtually the same as the second and fourth preparations. No evidence of toxicity has been seen in the dosage used.

No more than impressions of the value of therapy can be given, for the disease does seem to vary from the patient living in symbiosis with the organism, to a severe septicemia with rapid death. To evaluate any agent, the stage of the disease at which diagnosis is made and treatment started has to be judged. Using one of the polymyxins, certainly patients with generalised oedema and cyanotic attacks have been seen to recover.

No toxic reactions to polymyxin B in the form of renal damage (other than that due to the disease) or fever were seen (the other described effects of dizziness, ataxia, peripheral neuritis, parasthesiae, especially itching and facial flushing, not being recognised). With colistin no fever, apparent pain at site of injection or nausea was seen, nor leucopenia or azotaemia.

The other infants in the series (meningo-myeloeceles), were treated by intramuscular, intravenous and intraventricular colistin and seven died, so that only two with meningitis tended to recover from the disease whilst the other three seemed to confine their disease to the local area with little generalised spread.

The leukaemia patients had negative swabs after the use of colomycin. The children with fibrocystic disease did not get disseminated disease when given colomycin, although becoming intermittently positive. The other cases responded to systemic colomycin; Zynotracin powder (xanthocillin, zinc bacitracin, hydrocortisone) was used locally on the umbilicus.

An attempt was made to isolate each case as it developed and “prevention of cross infection” techniques carried out.

**Summary**

A total of 73 cases of pyocyanea infection have occurred, in 49 premature infants, 16 with congenital abnormalities, two with leukaemia, two with fibrocystic disease and four other children with infection.

The available means of treating the infection and endeavouring to prevent further cases have been described.

**REFERENCES**


The Investigation of an Outbreak of Pseudomonas Pyocyanea Infection in a Paediatric Unit

J. Jacobs

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