Preliminary Communications

Enteral Infection with *Pasteurella Pseudotuberculosis*

Isolation of the Organism from Human Faeces

Until 1954 human infections with *Pasteurella pseudotuberculosis* were thought to be rare. Masshoff (1953) described an abscess-forming reticulocytic ileocaecal lymphadenitis. The causative organism was identified by Knapp (1954) as *P. pseudotuberculosis*. Since then reports of some 200 cases have been published. The first cases in Great Britain were described by Mair *et al.* (1960). For further information about these infections see the extensive study by Knapp (1959).

From the beginning it was thought that the pathological changes found were the result of an enteric infection, arising in the last portion of the ileum and resulting in an infection of the ileocaecal lymph nodes. This point of view was supported by Graber and Knapp (1955), who found, under a small mucosal ulcer in the ileum of one of their patients, an identical reticulocytic infiltration breaking through the muscular coat. They could trace this characteristic picture along the lymph pathways to the regional lymph nodes. A similar case was seen by Flamm and Kovac (1958). For further support of the enteral infection theory they fed cultures of *P. pseudotuberculosis* to laboratory mice. This gave rise to pathological changes in the mesenteric lymph nodes similar to those found in their patient.

The isolation of *P. pseudotuberculosis* from faeces of patients suffering from this form of ileocaecal lymphadenitis would in my opinion almost prove the enteric character of this infection. No mention of this isolation from human faeces could be found.

EXPERIMENTS AND METHOD

In preliminary studies mixtures of faeces and known quantities of *P. pseudotuberculosis* were cultivated on different media. The best results were obtained on desoxycholate-citrate-agar plates. Enrichment broth of different kinds gave no improvements. Accordingly the following method was adopted. A small amount of faeces is suspended in some 0.85% NaCl and inoculated on desoxycholate-citrate-agar plates (Difco B 274), which are incubated at 22° C. for five days. As the medium is not selective for *P. pseudotuberculosis*, all suspected colonies have to be tested in the usual way.

RESULTS

With this method we investigated the faeces of 23 guinea-pigs known to be suffering from a spontaneous infection with *P. pseudotuberculosis*; in nine the micro-organism was recovered from the faeces—six times type I and three times type II. Up to the time of writing we had examined faecal specimens of five patients known to be infected with *P. pseudotuberculosis*. From the faeces of one patient *P. pseudotuberculosis* type Ia was isolated on the fifth and sixth post-operative days. All specimens of later date were negative. This patient, a 25-year-old man, was operated on for suspected appendicitis. The appendix proved to be normal, but the last portion of the ileum was thickened, oedematous, and fiercely reddened. In the ileocaecal angle many swollen infected lymph nodes were noted. Ileitis regionalis was suspected. The pathological changes in

a lymph-node biopsy were those usually found around the focus of a lymphadenitis of Masshoff; there were no micro-abscesses. The serum taken on the day of operation agglutinated *P. pseudotuberculosis* type I strongly (titre 1:2,560). This micro-organism was also found in the excreta of a canary owned by the patient. It proved to be of the same type Ia.

CONCLUSION AND SUMMARY

Faeces in five patients known to be suffering from the lymphadenitis ileocaecalis of Masshoff were examined for *Pasteurella pseudotuberculosis* by means of inoculation on desoxycholate-citrate-agar plates (incubation for five days at 22° C.). *P. pseudotuberculosis* type Ia was isolated from one patient. Of 23 guinea-pigs with positive cultures from liver abscesses, the faeces were also positive in nine.

This seems to be the first time that *P. pseudotuberculosis* has been cultured from human faeces. It strongly supports the theory that the mode of infection is by the enteral route. This isolation may also be of importance for epidemiological studies.

I gratefully acknowledge the encouragement and advice given by Professor A. Ch. Ruys. I am indebted to the Central Bacteriological Laboratory and the Laboratory for Public Health in Rotterdam for their hospitality and technical assistance. Thanks are expressed to Dr. W. J. H. Schmidt, head of the surgical department, for permission to publish case-notes concerning the patient.

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Medical Memoranda

Anencephaly in a Mono-amniotic Twin

It is generally agreed that mono-amniotic twins are extremely rare, although it is possible that some cases are being missed (Wilson, 1955). In the case reported below the patient was delivered of mono-amniotic twins, one of which was normal and the other anencephalic. Two detailed reports of similar cases were found in the literature (Litt and Strauss, 1935; Wilson, 1955), and Dumoulin and Gordon (1959) have reported di-amniotic mono-chorionic twins, one of which was anencephalic.

CASE REPORT

A primigravida aged 23 first attended the Belfast City Hospital antenatal clinic on June 26, 1959, in the 10th week of pregnancy. She was a normal healthy woman and careful inquiry failed to reveal any history of congenital abnormality or familial disease among her own or her husband's relatives. Her mother was a twin. The husband was a healthy tradesman aged 22.

Pregnancy progressed normally, and the patient did not suffer any virus disease at any stage. At 30 weeks twins were suspected, and an x-ray examination showed that one twin was anencephalic while the other appeared to be normal. There was no hydramnios, and pre-eclampsia did not develop.

Labour began spontaneously during the 41st week, and after six hours the membranes ruptured and meconium-stained liquor drained. Four hours later the first twin was delivered with forceps because of poor progress in the second stage. Immediate vaginal examination revealed that the face of the anencephalic second twin had entered the pelvis. The expected second sac of membranes was not present. The infant was delivered by traction with the finger in the mouth aided by a little fundal pressure during a uterine contraction.

Examination of the placenta revealed a single sac surrounded by the chorion and amnion. The two cords were attached eccentrically to the foetal surface and were only $\frac{1}{2}$ in. (1.3 cm.) apart. There was no trace of any

Details of Blood-grouping

	ABO	Rh Phenotype	Probable Genotype	MN	K	Fy ^a	S	Le ^a
Father	B	CCDee	CDe/CDe	M	—	—	Not tested for these factors	—
Mother	A ₁	—	cde/cde	M	—	+	+	—
Twin I	A ₁	CeDee	CDe/cde	M	—	+	+	—
„ II	A ₁	CeDee	CDe/cde	M	—	+	+	—

septum of membranes between the cords, and it was clear that there had been a single amniotic sac containing both twins.

The anencephalic twin was a freshly stillborn female weighing 5 lb. 12 oz. (2,610 g.). Post-mortem examination did not reveal any other deformities. The normal twin, also a female, weighed 6 lb. 7 oz. (2,920 g.) at birth and was healthy.

Blood-grouping of parents and infants was carried out and the findings are shown in the Table.

COMMENT

It is interesting that severe congenital deformity was found in as many as 9.2% of infants in the combined series of 142 mono-amniotic twin pregnancies collected and reported by Quigley (1935) and by Wilson (1955). This type of twinning is undoubtedly uniovular, and abnormality of one twin of a pair cannot be convincingly explained on a basis of direct hereditary genetic factors or on generalized intrauterine environmental conditions which, presumably, affect both twins equally.

Streeter (1930) suggested that local congenital abnormalities are due to disparity in the vitality of different tissues in the embryo. It is believed (Corner, 1955) that mono-amniotic twins must separate later than diamniotic twins, because their separation must occur after a single embryonic disk has formed, thereby inducing the formation of a *single* amniotic cavity—that is, between the seventh and the fourteenth day. It is possible that separation at this later and more highly developed stage might disturb the growth or diminish the vitality of localized embryonic tissues, thereby increasing the incidence of localized congenital abnormalities, such as anencephaly, in mono-amniotic twins. Incomplete separation will, of course, give rise to a double monster, and it is well known that abnormalities of any of the component parts of double monsters are relatively common.

There is a very high foetal loss associated with mono-amniotic twinning, and this is mostly ascribed to inter-twinning of the umbilical cords *in utero*. Quigley (1935) reported a loss of 68% in his collected cases.

My thanks are due to Mr. J. A. Price for permission to publish this case, which was admitted under his care.

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Megaloblastic Anaemia during Combined Phensuximide and Phenobarbitone Therapy

Megaloblastic anaemia is a rare complication of anticonvulsant therapy and has been described during the administration of phenytoin sodium and primidone (Badenoch, 1954; Gordin, 1958) and in patients receiving large doses of barbiturate (Hobson *et al.*, 1956; Calvert *et al.*, 1958; Chanarin *et al.*, 1960). Details are given below of an epileptic patient who developed megaloblastic anaemia while under treatment with phensuximide (N-methyl- α -phenylsuccinimide; "milontin") and phenobarbitone, a combination of drugs not previously associated with the development of megaloblastic anaemia.

CASE REPORT

A 33-year-old unmarried woman had suffered from epilepsy from the age of 3 years. Anticonvulsant therapy was initiated with phenobarbitone in 1933; between 1946 and 1954 she received phenobarbitone 2 gr. (0.13 g.) daily and sodium phenytoin 3 gr. (0.2 g.) daily, and during the last three months of 1954 also had primidone 750 mg. daily. On December 21, 1954, she was admitted to another hospital with a severe degree of anaemia; she was transfused with 3 pints (1.7 litres) of blood and given folic acid, cyanocobalamin, and ferrous sulphate. Within three months her blood findings had returned to normal, and after seven months all haematinics had been discontinued. The epilepsy, however, was poorly controlled on phenobarbitone alone, and two and a half years later (August, 1957) she was admitted to the neurological unit of the Northern General Hospital, where investigations showed an epileptogenic focus in the right temporal lobe on E.E.G. but a normal cerebrospinal fluid and air encephalogram.

In considering further anticonvulsant therapy it was decided to avoid primidone and phenytoin because of the uncertain nature of the type of anaemia which had developed during previous treatment with these drugs. Phensuximide was chosen for trial, since there were no reports of this drug's administration having been associated with haematological disturbances. On August 6, 1957, treatment was started with phensuximide, 0.5 g. six times daily, and the dose of phenobarbitone was reduced to 2 gr. (0.13 g.) daily. Ten weeks later, on a routine out-patient visit, her epilepsy was controlled but she complained of the recent onset of exertional dyspnoea. The haemoglobin, which had been 12.9 g./100 ml. two weeks previously, had fallen to 6.4 g./100 ml. She was readmitted for further investigation.

The mucous membranes were pale but no other abnormalities were found on physical examination; the dietary history was satisfactory and there were no alimentary symptoms. Blood examination showed normochromic red cells with anisocytosis, poikilocytosis, and some macrocytosis. The sternal marrow was frankly megaloblastic and aspirated gastric juice contained hydrochloric acid. Serum vitamin B₁₂ level (*Lactobacillus leichmannii* assay method without added cyanide) was 140 μ g./ml. (normal range, 120–810 μ g./ml., Girdwood, 1960) and the absorption of labelled vitamin B₁₂ (methods of Heinle *et al.*, 1952; Schilling *et al.*, 1955) was normal, the faecal and urinary recoveries of radioactivity being respectively 16% and 19% of that contained in the 0.5 μ g. oral dose. A folic acid absorption test (Girdwood, 1960) also gave normal results;