Oxygen can be introduced into the blood stream by this method, and the extrapulmonary addition is of benefit to dogs made anoxic by a reduction of oxygen in the inspired air. The site of return of artificially arterialized blood is of great importance, and should be either into a central vein or into an artery close to the heart.

For these reasons it is felt that the heart-lung machine is now ready for clinical trials in selected cases of extreme cardio-respiratory dysfunction. In those patients in whom derangement of pulmonary function is the chief symptom, it may be advantageous to return the arterialized blood into a central vein, thus greatly simplifying the cannulation and making the surgical intervention a relatively minor one. Though no shunting of blood around the heart would occur in this technique, it is possible that the improved oxygenation would reduce the demands on the heart, and secondarily reduce its work.

Where the myocardium is primarily involved it is suggested that continuous venesection with return of arterialized blood into the arterial circulation will relieve the heart of part of its burden.

APPENDIX I

The oxygenator and connecting-blocks were chemically sterilized with "roccal" detergent and 3% formalin, being steeped in the solution for twelve hours. The tubing and cannulae, which we used only once, were autoclaved. After assembly the apparatus was washed with at least 40 litres of sterile distilled water to which had been added enough sodium chloride to provide approximate isotonicity. Frequent checks for the presence of formalin provided an indication of the efficiency of the washing process. When two checks were negative the wash-outs were discontinued and the apparatus was charged with donor blood or dextran solution. After circulation through the by-pass tube to ensure that no air bubbles remained in the arterial line, the machine was ready for use.

APPENDIX II

1. The arterial and venous blood oxygen were measured by the method of Van Slyke and Neill (1924).
2. The red-cell, platelet, leucocyte, differential, and Arneith counts were made, and haematocrit values found by standard methods (Dacie, 1950).
3. The plasma haemoglobin was estimated as oxyhaemoglobin on a Spekker absorptiometer modified to accept 1 by 6 in. (2.5 by 15 cm.) test-tube cuvettes. A standard oxyhaemoglobin curve was prepared for each estimation in the following manner: 3-ml. aliquots of plasma were placed in each of five cuvettes; to the first was added 8 ml. of dilute ammonia reagent (5 ml. concentrated NH_3 per litre), and this served as a plasma blank; to the remainder was added 0.02, 0.04, 0.06, and 0.08 ml. of whole blood diluted 1 in 2 with normal saline; these were then diluted with 8 ml. of ammonia reagent and read against the plasma blank. 3 ml. of plasma obtained from samples taken during the experiment was similarly treated and compared with the standard curve.
4. The plasma sodium and plasma potassium were determined by means of an internal standard flame photometer similar to that described by Berry, Chappell, and Barnes (1946).
5. The plasma chloride, plasma CO_2 combining power, blood sugar, and blood urea were estimated by standard methods (King, 1951).
6. The pH was measured by a Muirhead pH meter type D-303-b.

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POST-INOCULATION POLIOMYELITIS

BY

JAMES GRANT, M.D., D.P.H.

Medical Officer of Health, Gateshead, and Medical
Superintendent, Sheriff Hill Hospital

The successful prophylaxis of diphtheria through the mass immunization of very young children with diphtheria toxoid was associated with few mishaps of importance. When given subcutaneously, the alum-precipitated toxoid commonly gave rise to a painless nodule which was gradually absorbed, but occasionally there was an inflammatory swelling and very rarely a sterile abscess. These rare reactions to the toxoid were minimized by intramuscular administration, a route which was necessary for the injection of the pertussis vaccine introduced in 1946 and of combined diphtheria toxoid and pertussis vaccine made available in 1947. Since then the latter product has been increasingly used to immunize children simultaneously against diphtheria and whooping-cough by one series of injections.

In 1948 Martin (1950) observed flaccid paralysis of the arm in two children, each of whom had received an inoculation of a prophylactic in the paralysed limb within the preceding three weeks. Having traced and studied 15 other patients who had developed limb paralysis following injections of antigens in 1944-9, he concluded that all of these had really suffered from poliomyelitis. Gale (1950) was able to add 56 cases of limb paralysis following the inoculation of prophylactics, and then, independently and simultaneously, McCloskey (1950) and Geffen (1950) published their findings during two epidemics of poliomyelitis in 1949. In Melbourne, McCloskey found that 35 out of 340 patients with poliomyelitis had been inoculated against diphtheria or whooping-cough within three months before the onset of the illness, and that the paralysis affected the inoculated limb in 24 out of 31 patients about whom full information was obtained. Geffen reported that out of 182 poliomyelitis patients under 5 years of age in London, 37 had been recently inoculated and about 30 of these suffered from paralysis, affecting particularly the limb recently injected. Investigating a small group of the London children, MacCallum (1950) was able to isolate the poliomyelitis virus from the stools of two children with paralysis of a recently inoculated limb and from three other inoculated children suffering from poliomyelitis without paralysis. Hill and Knowelden (1950) carried out a statistical inquiry, covering 33 areas, into the incidence of paralysis as a sequel to recent inoculation in 1949, and concluded that this misfortune occurred more frequently within a period of one month after the inoculation than could be attributed to chance.

On the other hand, Culley (1951) could find only nine recently inoculated persons among the 380 Welsh

patients with poliomyelitis in 1950 and only four of the nine with paralysis in the inoculated limb. In Scotland, Sutherland (1952), studying 43 cases of poliomyelitis following inoculation in 1950, could not show that inoculation increased the risk of a child developing poliomyelitis, although he found that the paralysis was suggestively but not significantly associated with the limb most recently injected. From both the academic and the practical point of view, the present position is best summarized in the advice of the Chief Medical Officer of the Ministry of Health (1952), that in any area in which poliomyelitis is exceptionally prevalent inoculation of diphtheria and pertussis antigens should be suspended for a time.

Poliomyelitis on South Tyneside

In the spring of 1952 a local epidemic of poliomyelitis began on Tyneside, centred mainly on the south side of the river. This outbreak witnessed the resumption of the classical age distribution of the disease, for two-thirds of the patients were under the age of 5 years. The districts chiefly involved were Gateshead (population 115,000), and the

contiguous districts of Felling (population 25,286) and Whickham (population 23,116). Poliomyelitis was confirmed in 91 patients from Gateshead, 28 from Felling, and 13 from Whickham. All these districts are normally served by Sheriff Hill Isolation Hospital, in which 112 of the patients were treated along with six cases from other areas.

In the last week of March and during April, four children were admitted to hospital at intervals for investigation of an illness which was at first diagnosed as "viral encephalitis" but later revised to polio-encephalitis in the light of further developments. The first patient with unmistakable poliomyelitis became ill with a sore throat on May 2, 1952, and was admitted to hospital on May 6 with flaccid paralysis of both legs. During May, 8 non-paralytic and 2 paralytic cases of poliomyelitis were later admitted from the three districts, to make a total of 15, of whom three were paralysed. Two of the three paralytic children had recently been inoculated. Intramuscular inoculations were therefore stopped in the Gateshead clinics, and local practitioners were advised on June 3 to restrict immunization to the subcutaneous use of A.P.T. and P.T.A.P. Confirmed cases of poliomyelitis in June numbered 38, and it was evident that the infection was widespread throughout the area. In July,

Poliomyelitis Following Inoculations—South Tyneside, 1948–52

Year	Patient and Area	Age in Years	Inoculation			Poliomyelitis		
			Antigen	Date of Injection	Site	Onset	Clinical Summary	Last Assessment
1952	H.S. (G)	11/12	D & P 0.5 ml.	24/4/52 (second)	Left arm	10/5/52	Fever, complete loss of power left shoulder-girdle and arm. Slight movement of fingers. C.S.F., 2 polymorphs per c.mm.	22/9/52: paralysis of left shoulder, extensors of elbow, and flexors of wrists and fingers
	R.H. (G)	12/12	D & P 0.5 ml.	16/5/52 (first)	Left buttock	1/6/52	Off feet; drowsy; paresis left quadriceps. C.S.F., pleocytosis and increased protein	2/7/52: complete recovery
	M.J. (G)	110/12	D & P 0.5 ml.	20/5/52 (second)	Left arm	4/6/52	Restless; vomiting and retention of urine followed by neck stiffness with paralysis left shoulder and arm, except fingers. C.S.F., increased cells and protein	19/9/52: paralysis and wasting left shoulder muscles, biceps, and triceps
	E.S. (G)	14/12	D & P 0.5 ml.	20/5/52 (third)	Right arm	17/7/52	Pyrexia, irritability, neck stiffness with paralysis right shoulder and upper arm. C.S.F., pleocytosis and increased protein	22/9/52: paralysis of right shoulder, biceps, and triceps
	M.B. (G)	4	D 0.5 ml.	17/6/52 (booster)	Right buttock	20/6/52	Headache, fever, neck stiffness, off feet, loss of tendon reflexes right leg but no paralysis. C.S.F., increased cell count only	5/7/52: perfect recovery
	P.H. (W)	5	D 0.5 ml.	5/5/52 (booster)	Left arm	23/5/52	Headache, fever, neck stiffness, pain in left calf, proceeding in 5 days to paresis both arms and left leg. C.S.F., increased cells	9/10/52: normal range of joint movement, but left deltoid muscle very weak
	V.C. (F)	2	D 0.5 ml.	26/6/52 (first)	" "	1/7/52	Vomiting, irritable, listless, paralysis of left external and right internal rectus muscles, with spasm of right neck muscles. C.S.F., increased cells	1/8/52: complete recovery
	A.B. (F)	9	D 0.5 ml.	29/5/52 (booster)	" "	14/7/52	Headache, weakness of legs, and vomiting, frequency of micturition. 17/7/52: paralysis extensors right ankle. C.S.F., pleocytosis and increased protein	12/9/52: slight right foot drop; otherwise walking well
1950	J.L. (G)	15/12	D & P 0.5 ml.	31/5/50 (second)	" "	10/6/50	Diarrhoea with paralysis left arm on 16/6/50. Out-patient treatment only	13/9/52: wasting and paresis of left deltoid, biceps, and triceps
	A.P. (Wn)	11/12	D 0.5 ml.	6/7/50 (first)	" "	19/7/50	Earache followed by diarrhoea. 29/7/50: paralysis of both arms with neck stiffness. C.S.F., increased cells and protein	18/9/52: paresis both deltoids, with wasting more marked on left side; slight wasting left thigh and eversion of left foot and slight drag in gait
	A.D. (G)	10/12	D & P 0.5 ml.	31/7/50 (first)	Left thigh	31/7/50	Feverish on 31/7/50, drowsiness, vomiting. 5/8/50: neck stiffness, paresis of left facial muscles, and internal squint of right eye. C.S.F., pleocytosis and increased protein	5/9/50: complete recovery maintained until 1952
	J.T. (G)	11/12	D & P 0.5 ml.	26/6/50 (first)	Left arm	14/8/50	Feverish and vomiting. 16/8/50: paralysis left arm and shoulder. C.S.F., 1.2 polymorphs and 6 lymphocytes per c.mm.	15/9/52: no loss of movement shoulder or elbow, but paresis and wasting left deltoid, biceps, and triceps
1948	K.M. (G)	2	P 1 ml.	25/10/48 (third)	" "	7/11/48	Paralysis left arm and shoulder with irritability and stupor: spread to right arm except fingers on 15/11/48. C.S.F., 2 polymorphs and 3 lymphocytes per c.mm.	17/11/52: no movement of either shoulder-joint—left arm completely paralysed, including all fingers; right arm limited movement of elbow-, wrist-, and finger-joints; severe wasting of paralysed muscles. In special school

Areas: G = Gateshead; F = Felling U.D.; W = Whickham U.D.; Wn = Washington U.D.

Antigens: D = Diphtheria; P = Pertussis.

August, and September confirmed cases numbered 50, 19, and 14 respectively, and thereafter only sporadic cases occurred.

In spite of the precautions, eight of the South Tyneside patients with poliomyelitis had previously been injected intramuscularly with an immunizing antigen not more than two months before the onset of the illness. All these were admitted before July 17, when the number of cases was 94.

The relevant details of the inoculated children are summarized in the Table on the previous page along with similar data relating to five examples of post-inoculation poliomyelitis in 1950 and 1948. Four were recorded among the 27 confirmed poliomyelitis cases on South Tyneside in 1950, while the fifth was a solitary patient who came to hospital two months after the notification of the last case in 1948.

After the end of May, 1952, 101 children were inoculated subcutaneously with A.P.T. and P.T.A.P., but none of these suffered an attack of poliomyelitis.

Comparative Incidence of Poliomyelitis in Recently Inoculated and Other Children in Gateshead in 1952

The total number of children aged 6 months to 2 years in the borough in mid-year, 1952, has been calculated from the births less deaths to be 3,097, among whom there were 17 cases of poliomyelitis, a ratio of 1 in 182. Of the 17 children, 13 presented some degree of muscular paralysis.

In April and May, 1952, 249 children, aged between 6 months and 2 years, received intramuscular arm injections in the Gateshead local authority clinics, and 105 others within the same ages received intramuscular inoculations from local practitioners in April, May, and early June—that is, a total of 354. Of this number, three aged from 11 to 22 months developed poliomyelitis in the paralytic form before the end of June.

Deducting the 354 inoculated children from the total, children of the same age not recently inoculated number 2,743, of whom 9 developed poliomyelitis in May and June, 6 being affected by muscular paralysis. The attack rate in recently inoculated children was therefore 1 in 118, as compared with 1 in 305 in non-inoculated children. During July another case of paralytic poliomyelitis occurred in a recently inoculated child and 3 cases in the control group, of whom two were paralysed. The comparative incidence in May, June, and July was therefore 1 in 88 for the recently inoculated and 1 in 228 for the control group. As an additional paralytic case occurred in the control group in August, the respective attack rate over the four months May to August remained 1 in 87 among the recently inoculated and increased to 1 in 211 in the controls.

Two of the children, E.S. and N.S., who developed a limb paralysis following an injection of antigen in April were previously inoculated in March, both in the left arm. Although these March injections were given one week before the first case of poliomyelitis in 1952, and E.S. was paralysed in the right arm, it seems advisable to recalculate the incidence of the disease in children inoculated in the months March to June.

In March, 53 children of the age group under study received intramuscular inoculations at the clinics and 43 others received similar injections from the general practitioners. Out of 450 children inoculated in the months of March, April, May, and June, 3 developed poliomyelitis in May and June, giving a ratio of 1 in 150. Of 2,647 children of the same age who had not been recently inoculated 9 developed poliomyelitis in these months, a ratio of 1 in 294. When this comparison is extended to include July there were 4 cases in the inoculated, or 1 in 112, and 12 cases among the others, or 1 in 221. Including the August case among the controls, the respective incidence rates for May to August were 1 in 112 for the inoculated and 1 in 204 for the others. As no other child of these ages contracted poliomyelitis, the last-mentioned attack rates cover the whole epidemic. The 13 children in the control group who contracted poliomyelitis were aged from 6 months to 1 year and 10 months. Only two of them had in fact ever been inoculated, the prophylactic injections having been given

in the autumn of 1951. In spite of the smallness of these numbers, I feel that they are reasonable in assessing the risk of a child developing poliomyelitis as being at least doubled as a result of intramuscular immunization during an epidemic.

In the 4 recently inoculated Gateshead children the paralysis was limited to the injected arm in three instances and the injected leg in one. In contrast, the 9 patients with paralytic poliomyelitis among the control group of Gateshead children suffered paralysis affecting the trunk and all the limbs in two cases (one of whom died), the right arm, leg, and facial muscles in the third, the left face, eye, and leg in a fourth, one leg only in four instances, and the left external rectus muscle of the eyeball in the ninth.

Poliomyelitis in Recently Inoculated Persons

Analysis of the form of the disease in the 138 South Tyneside cases, so as to compare the recently inoculated patients with the remainder, gives this result:

Form of disease	Recently Inoculated	Others
Non-paralytic	1	70
Paralytic:		
Cranial nerves only	1	15
One arm only	3	3
One leg only	2	17
Both legs	—	7
Arms and legs	1	3
Trunk and limbs	—	6 (2 died)
Cranial nerves and limbs	—	5
Cranial nerves, trunk, and limbs	—	4 (1 died)
	8	130

Among the recently inoculated patients, paralysis affected solely the inoculated arm in 3 patients, the inoculated leg in one, and extended from the inoculated arm of a fifth patient so as to involve the opposite arm and a leg. In two patients paralysis was localized to the ocular muscles and to the right leg respectively, although the injection had been given in the left arm. Only 60 of the 130 patients not recently inoculated suffered a paralysis, and this much more often affected the legs than the arms.

Health of Contacts

As it is well known that poliomyelitis becomes manifest in only a small proportion of the individuals who have been infected, it is common to find that familial contacts of patients suffer from illnesses which are presumably abortive attacks of poliomyelitis. It is rare, however, in urban areas to find two cases of undoubted poliomyelitis from the same family.

Among the 8 families of children with post-inoculation poliomyelitis two, those of E.S. and P.H., are notable for associated illnesses.

Family of E.S.—E.S., aged 1 year, was inoculated in the left arm on February 12 and March 11, 1952, and in the right arm on May 20, with combined antigen. She became ill on July 17 with paralysis of the right shoulder and upper arm. She was admitted to hospital on July 18 along with a brother Eric S., aged 6 years, who complained of headache and vomiting on July 17. On admission he presented an inflammatory exudate on the tonsils, a temperature of 100.6° F. (38.1° C.), but the cerebrospinal fluid was normal. He was considered to be a possible atypical case of poliomyelitis. Two weeks before, an older brother, H.S., aged 11 years, was ill with a high temperature lasting for 24 hours.

Family of P.H.—P.H., aged 5 years, inoculated in the left deltoid on May 5, 1952, with a "booster" dose of A.P.T., became ill on May 23 and was admitted to hospital on the 25th with pyrexia, marked signs of meningeal irritation, and an abnormal cerebrospinal fluid. She developed paresis of both arms and the left leg on May 28, the left arm being the more severely affected. Her sister, M.H., aged 2 years, became ill on May 22, with pyrexia, neck stiffness, and irritability, which persisted until the 28th, when she also was admitted to hospital, making a very rapid recovery in the following three days. In her case the cerebrospinal fluid showed a raised protein content only. Still another child in this house, aged 6 years, complained of pyrexia, headache, and neck stiffness, beginning on May 22, but she was convalescent when her sisters were removed to hospital.

On examining the family histories of the remaining 129 poliomyelitis patients who had not been inoculated recently

there was only one example of two siblings with frank poliomyelitis and one family with a possible double infection.

Family of Sw.—T. Sw., aged 2 years, became ill on July 9, 1952, with drowsiness and irritability accompanied by vomiting. On admission to hospital on July 16 he presented neck and spinal rigidity and loss of the tendon reflexes of the left leg, but he was able to move all his limbs. The cerebrospinal fluid showed an increased cell count and a raised protein content. On July 20 the patient showed a definite weakness of the muscles of the left ankle joint. A sister, G. Sw., aged 4 years, became ill on July 11, with vomiting, fever, and fretfulness, and complained of headache and backache. When admitted to hospital on July 19 there were signs of meningeal irritation but no paralysis. The cerebrospinal fluid showed a pleocytosis of polymorphs and lymphocytes and a raised protein content. This child was fully convalescent on July 27.

Family of M.—The patient D.M., aged 1 year, became fretful and off-colour on August 2, 1952, and was admitted to hospital on August 6, when he presented neck stiffness, minimal pyrexia, and weakness of the right hip muscles, together with a slight increase of cells in the cerebrospinal fluid. This child was not definitely paralysed, but the muscles governing the movement of the joint were all weak. Two weeks previously a sister, aged 3 years, was very restless and had a bout of vomiting, and was thought to have been an abortive case.

Among the 8 households of the recently inoculated patients one can find two with multiple illnesses in the family. In these, the two recently inoculated children suffered paralysis of the injected arm. To find two other instances of multiple illness one has to review the background of the other 129 patients. In these the paralysis affected the lower limb in two children and was slight. It seems probable that all three of the children in each of the households of E.S. and P.H. had been infected with the poliomyelitis virus, and that it was the recent inoculation which determined the appearance and the site of the paralysis.

Intervals between Inoculation and Onset of Poliomyelitis

In 5 of the 8 recently inoculated patients of 1952, paralysis was definitely related to the site of the preceding injection, whereas there was no paralysis in one, and paralysis remote from the inoculation in two. The intervals between the injection and the onset of symptoms in the former patients were 15, 16, 16, 18, and 58 days respectively. In contrast, the respective intervals were 3, 5, and 46 days in the latter three cases. Turning to the 5 patients of 1948 and 1950, the relevant intervals were 10, 13, 13, and 18 days in the cases with paralysis involving an inoculated limb, and in the exceptional case the onset of polio-encephalitis coincided with the inoculation. This divergent finding raises a strong probability that the relationship between the preceding inoculation and the subsequent localized paralysis was one of cause and effect in the group of 8 patients showing intervals of 10 to 18 days between the inoculation and the onset of symptoms, whereas the association was purely a coincidence in the 3 patients in whom the respective intervals between the inoculation and the onset of illness were 5 days or less.

There remain two patients with lengthy intervals between inoculation and illness. In one of these the relationship between inoculation and paralysis may also have been causal.

Site of Injection

In the 1952 group of 8 recently inoculated patients, the upper-arm paralysis following injection tended to be fairly severe and lasting, whereas the paresis of the leg following previous injection of antigen in the buttock was very transient. Studying all the 13 cases of poliomyelitis following recent inoculation, it is notable that antigen given intramuscularly in the arm on 10 occasions was followed by severe paralysis limited to the arm in 5 patients and by more extensive paralysis involving both arms in 3 others. All these 8 patients have or are likely to have some degree of permanent disability. On the other hand, in 3 patients inoculated in the buttock or thigh only one showed paralysis of the injected limb, which was transient. All the 5 post-inoculation cases of paralysis limited to the injected arm

were of a severity and permanence not observed in the three single-arm palsies among the 129 patients not recently inoculated, in whom the affected muscles showed a transient loss of power without any residual disability. In the 3 cases of more extensive paralysis following the injection of an arm, paralysis started and was most severe in the injected limb, whence it spread to the opposite arm and thence to other muscles. Although the issue here is clouded by the time relation between inoculation and subsequent illness, the relative severity and persistence of the damage to muscles of the arms in post-inoculation poliomyelitis were impressive.

Prophylactics Used

In the 13 cases of post-inoculation poliomyelitis, paralysis followed the use of diphtheria alum-precipitated toxoid, pertussis alum-precipitated vaccine, and combined diphtheria toxoid and pertussis vaccine.

The dose injected was taken from multiple-dose containers of 5 ml. and 10 ml. Two patients, E.S. and M.J., probably received antigen from the same container, but otherwise each patient was the sole poliomyelitis case associated with a multiple-dose container. The worst case was K.M., to whom the largest dose of antigen, 1 ml., had been given, with a severe local reaction.

During the summer of 1952 many intramuscular injections of penicillin, streptomycin, and other medicaments must have been given to Gateshead patients, both children and adults, in hospital wards and departments and at home, for the treatment of various conditions. In only one instance was there a suspicion that intramuscular injection of a substance other than a prophylactic antigen might have precipitated paralytic poliomyelitis. In this instance, a child of 6 months admitted to hospital with pneumonia on May 30, 1952, was given penicillin by injection into the buttocks alternately before June 5. In convalescence a flaccid paralysis of the right leg was first noticed on June 14, and the cerebrospinal fluid taken on July 21 showed an increase of cells and a slightly raised protein.

Discussion

The Gateshead experience must be added to the London and Melbourne evidence against intramuscular inoculation with diphtheria and whooping-cough antigen as a causal factor in the development of paralytic poliomyelitis affecting particularly the limb previously injected. In Gateshead as in London, the upper limbs were much more frequently affected in the recently inoculated than the legs, and the left arm more often than the right—features quite contrary to the usual distribution of paralysis of poliomyelitis. This can be accounted for only by the traditional use of the left arm for all the immunization procedures.

That the patients with whom we are concerned in Gateshead were in fact cases of poliomyelitis cannot be doubted. They were all diagnosed as such on clinical grounds, for they showed an involvement of the motor neurones and a complete absence of sensory disturbance, together with the changes of the cerebrospinal fluid and many of the common symptoms and signs of this disease. They occurred at a time when poliomyelitis was prevalent, and their numbers were proportionate to the intensity of prevalence. I have, too, been able to cite the simultaneous occurrence of non-paralytic and post-inoculation paralytic poliomyelitis in the same household.

Although mass immunization against diphtheria started in Gateshead in 1941, there were no recorded cases of post-inoculation paralysis among the thousands of children inoculated. This seems to be largely true of the millions of children in the country who were immunized before and after 1941.

The indications are that these mishaps became so numerous as to attract general attention in 1949, a year when poliomyelitis was prevalent in England. Yet in 1947, also a year of high prevalence of this disease, cases of post-inoculation paralysis were very few, if in fact they occurred. It seems that the change in frequency of the misfortune of

post-inoculation paralysis may have been associated with the increasingly popular use of the pertussis vaccine, alone or combined with diphtheria toxoid. It is worthy of note that these antigens were given by the intramuscular route.

Although there is ample room for speculation and research regarding the pathology of post-inoculation paralytic poliomyelitis, the convenient explanation is that muscle trauma due to inoculation enables the virus already present in a patient to attack the motor cells in the spinal cord which innervate the muscles that have been damaged. This would mean that, as a sequel to previous inoculation during the outbreak of poliomyelitis, a number of non-paralytic, atypical, or symptomless cases of infection with the virus would be transformed into frank cases of paralytic poliomyelitis. There would then be an actual increase of the number of cases of paralytic poliomyelitis as a result of the common inoculation procedures. Statistical proof of this increased incidence has not been forthcoming in two national surveys, but this is understandable when one recalls that poliomyelitis seldom shows a national prevalence, and information has to be gathered second- or third-hand about a disease notorious for errors of diagnosis. In a local epidemic it is difficult to get adequate numbers to offset the vagaries of chance.

Difficulties will also arise as a result of the recommended advice to suspend intramuscular inoculation during an epidemic, and there is, too, the further consideration that children who have been recently inoculated may acquire poliomyelitis during an epidemic without this being related at all to previous immunizing procedures. If one could disregard the element of chance in the Gateshead experience of poliomyelitis in 1952, the risk of contracting the disease was doubled, if not trebled, for a child in the age group usually selected for primary immunization. If so, one-third to one-half of all the recorded cases of poliomyelitis following recent inoculation would present the disease as it might have occurred naturally, and the remainder would present the special feature of the localized paralysis in the limb injected. This, in fact, is what did happen to something like the proportions expected, a point which seems to justify the statistical comparison.

In Gateshead, patients developing poliomyelitis less than six days after inoculation were clinically similar to those with the naturally occurring disease, but in those who were inoculated more than 10 days and less than 18 days before the onset of symptoms the inoculated limbs showed the paralysis of the disease. This is in accord with the findings of McCloskey. In two patients with respective intervals of six and eight weeks, the findings were equivocal, but it seems that the effect of the muscle trauma may extend much longer than a period of three weeks.

The practical aspects of this problem require some attention. The advice of the Ministry of Health to suspend intramuscular immunization was acted upon fairly early in the Gateshead epidemic, but it could have been given three weeks before. Then 6 of the 8 cases of post-inoculation poliomyelitis would not have been recorded as such, and at least three cases of post-inoculation paralysis would not have occurred. Now that poliomyelitis has become the most important acute infectious disease, intramuscular immunization should normally be suspended at once on the appearance of the first case of paralytic poliomyelitis in any year, in order to allow an assessment of the trend of prevalence of the disease. The earlier in the year the first case occurs, the more important it is to follow this course, for poliomyelitis in the spring presages a severe visitation.

Manufacturers of prophylactics differ in their advice regarding intramuscular injection. One firm recommends deep intramuscular injection above the insertion of the deltoid; another recommends that this should be given on the outer side of the thigh; and a third leaves it to the physician to choose the site. Certain considerations suggest that all intramuscular inoculations of prophylactic antigens should be given in the buttock or thigh, as is the custom in hospital. It seems that the amount of trauma in the muscle may exer-

cise an effect on the severity and extent of post-inoculation paralysis. The smaller the muscle the greater the proportion of the whole muscle damaged by the injection of an irritant antigen. Local trauma will probably be more severe when an irritant antigen is injected into the deltoid muscle of an infant than when the same amount is injected into the gluteal or vastus muscles.

A further point concerns the observed tendency of the damage in the cord to spread locally so as to affect other muscles in the vicinity, to cross the mid-line so as to affect muscles innervated by the same segment of the cord and even to spread further. Now the fifth and sixth cervical segments of the spinal cord innervating the arms are continuous above with the segments supplying the diaphragm and below with those innervating the intercostal muscles. Thus respiratory paralysis in poliomyelitis is usually coupled with an arm paralysis. There is therefore at least a theoretical possibility that the possible spread of post-inoculation paralysis of the arm may involve the muscles of respiration, and that this has actually occurred seems to be demonstrated by three if not four of the cases reported by Geffen. Thirdly, it seems that the disability inflicted by an arm paralysis must be compared with that produced by paralysis of a corresponding degree and extent in the leg. Although there is room for controversy, it is felt that in modern conditions a paralysis of leg muscles which can be neutralized by modern orthopaedic appliances is to be preferred to a corresponding paralysis in the arm which cannot at present be compensated by appliances. These arguments indicate the election of the lower limb as the site for intramuscular injections.

It would, of course, be better still if all the prophylactic antigens were issued for use only after they had proved acceptable to the subcutaneous tissues, for proper subcutaneous administration would seem to avoid all the risk of inducing a subsequent paralysis. In the prophylactics incriminated in the matter under discussion, the presence of alum seems to emerge as the common factor. If immunizing antigens cannot be made suitable for subcutaneous administration, manufacturers would also be well advised to try to reduce the quantity of material to be injected, in order to minimize the amount of muscle trauma.

There is an obvious medico-legal aspect of the problem of post-inoculation poliomyelitis which concerns all who administer prophylactic antigens. In the interest of both patients and practitioners, it is particularly important that confirmed cases of poliomyelitis should be promptly notified in order that the medical officer of health may at once apprise and advise the practitioners of his area.

Summary

A number of cases of post-inoculation poliomyelitis personally encountered in Gateshead and district have been studied. It is concluded that there was no doubt of the increased risk to a child of developing a paralytic attack of poliomyelitis as a result of intramuscular immunizing injections at a time when poliomyelitis was prevalent.

A close look-out must now be maintained in every area for the appearance of poliomyelitis. Immediately the first confirmed case has been detected intramuscular immunization procedures should be halted for a short period so as to take stock of the situation.

Manufacturers of prophylactics should aim at the production of antigens which will be satisfactory in every way when given by subcutaneous injection.

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