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Unnecessary injections and paralytic poliomyelitis in India

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Abstract

The effect of prior injections on the pattern and severity of paralytic poliomyelitis has been examined by a retrospective analysis of case notes from an outpatient pediatric clinic in South India. Of 262 children with acute polio, 176 had received unnecessary injections <48 h before paralysis and 12 had received diphtheria-pertussis-tetanus or provocative injections. Two children injected in the right arm had paralysis in that limb only. Children with no injections (controls) had an equal chance of paralysis (0·73) in each left and right leg. Children with injections in the right or left gluteus or in both had a 19% greater chance of paralysis in the injected leg(s), whereas uninjected legs had a 31% lower chance of paralysis. Injected leg muscles were weaker than those of control children. Legs of control children were stronger than those with one leg injected and much stronger than those with both injected. More than 96% of the children had at least one leg paralysed. Age and vaccine status did not affect the results of injections. After injections there was greater likelihood of death or lack of recovery of muscle strength. About three-quarters of the children had received unnecessary injections; of these 60% had more severe paralysis and a non-paralytic attack became paralytic in 40%. If oral medicines for fevers and diarrhoea replaced unnecessary injections, the prevalence and severity of paralytic polio would be reduced.

Introduction

Poliomyelitis is endemic in India. Probably 200 000 children are paralysed each year by polio. Indian doctors have noted that paralysis of a limb often followed an injection in that limb <48 h previously: e.g., 11% of children in 1954–1956 (Athavale, 1960), 27% in the 1970s (Gujral *et al.*, 1977), 66% at Pondicherry in 1968–1987 (Mahadevan *et al.*, 1989). Similar observations have been made for Afghan children (Greetham, 1991). Very young children with fever or diarrhoea are often given an injection; their symptoms may be caused by a poliovirus infection. Although injections can increase the risk of paralysis by up to 25-fold, called provocation (Wyatt, 1981, 1985), the association may still be coincident and not causal. Controls should be sick, not healthy children (Wyatt, 1989). Prospective studies would be unethical as children could not be deprived of vaccine.

Provocation is defined as paralytic polio occurring 7–21 d after an intramuscular injection of inflammatory material (see Wyatt, 1981). Paralysis in a few children <7 d after an injection of, e.g., penicillin was considered coincident (e.g., see Greenberg & Abramson, 1952). Although in babies incubation may be <7 d (Wyatt, 1990), less than 2 d would be too short for provocation. Paralysis following injections by <48 h is, therefore, either coincident or a new phenomenon similar to paralysis immediately after physical activity. If coincident, the pattern and severity of the paralysis should be unchanged. If causal, the injection might modify the paralysis.

We have compared limb and muscle involvement and muscle strengths in 262 children with acute paralytic poliomyelitis, of whom 191 had received injections and 71 had not. We have separated 12 with provocation from 176 who received injections 48 h before paralysis, including 2 with injections in an arm. Three cases, each with an abscess and injections, will be presented elsewhere.

Materials and Methods

The clinical records at the Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER) were searched for every fifth case of acute paralytic poliomyelitis from the Pondicherry area admitted from February 1987 to July 1990. We examined the doctor's initial notes and those made later by the physiotherapists: the latter were usually fuller. Clinical judgements were made by S.M. Cases with incomplete notes, or muscle tests later than one week after paralysis, or 'IM?' (about 10% of cases) were discarded. Details of leg paralysis were noted for 227 admitted acute cases in the JIPMER Polio Register, 26 August 1987 to 14 May 1988. With very ill babies and children in a crowded ward, complete muscle examination is not possible. Muscle chartings were often incomplete with only the gluteus maximus and quadriceps marked, and the toes and hallux unrecorded. Limb involvement is compared in children but average muscle strength may be compared either by child or by paralysed limb: for those with injections in both legs, there is little difference.

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Results

The 262 children were compared in 5 groups: controls without injections (71), injections in left (36), right (29) or both (40) gluteus muscles, and those injected but with the site not recorded (69). Within each of the groups, the cases were compared by age, under and over 1·5 years, sex and oral poliovaccine (OPV) status—none or 1 dose and 2 or more doses of OPV. There were small but not consistent differences within these subdivisions. The median ages were comparable although, as expected, children receiving 2 or more doses of OPV were slightly older than those receiving 0 or 1.

Limb paralysis

The pattern of paralysis differed in the controls and those injected <48 h before paralysis (Table 1).

(i) In controls, paralysis of legs, 73%, was equal in right and left legs, but in those with injections, injected legs had a greater chance, 93%, although uninjected legs had a smaller chance, 42%, of paralysis.

(ii) Overall paralysis (all 4 limbs) was less in those with one leg injected than in controls, but one-third greater in those with both legs injected (1·67 and 2·26).

(iii) In all groups left leg paralysis was less frequent than right.

(iv) Children with both legs injected and those with injections but site unknown had a greater chance of arm paralysis ($P<0·01$).

In children who had not received an injection, paralysis ranged from minor paresis of only one quadriceps muscle to total (flail) in all 4 limbs.

Muscle paralysis in the legs

Within the groups, the gluteus, quadriceps and ankle muscles were equally affected, but in individual children different muscles were affected: e.g., gluteus spared in one, the quadriceps in another. Fewer toes than other muscles were affected: e.g., in 65 injected left or right legs the proportion of gluteus, quadriceps and ankle

Table 1. Proportions of limbs with paralysis or paresis in children with acute poliomyelitis[a]

	Injections: None (controls)	Left gluteus	Right gluteus	Left + right gluteus	Site not recorded
Number	71	36	29	40	69
Leg					
Left	0·70	0·95	0·38	0·83	0·84
Right	0·75	0·45	1·00	0·95	0·81
Arm					
Left	0·14	0·08	0·10	0·25	0·22
Right	0·08	0·08	0·07	0·23	0·22
Leg + arm					
Left	0·84	1·03	0·48	1·08	1·06
Right	0·83	0·53	1·07	1·18	1·03
All 4 limbs	1·67	1·56	1·55	2·26	2·09

[a]Notes.

(i) Proportion of legs paralysed in controls (no injections) was 0·73, in injected legs (36+29+40+40)=0·92 and in uninjected legs of those given injections (36+29)=0·42.

(ii) The probability that there is no difference in the proportion of paralysed legs in controls (104/142 legs) and injected legs (134/145) is $\chi^2=17{\cdot}9$, $P<0{\cdot}0005$; difference in limbs paralysed is 19% (95 confidence limit 10%–28%). [χ^2 with Yates's correction.]

(iii) The probability that there is no difference in the proportion of paralysed legs in controls (104/142 legs) and uninjected legs (27/65) in children with one leg injected is $\chi^2=17{\cdot}5$, $P<0{\cdot}0005$; difference in limbs paralysed is 31% (95% confidence limit 17%–45%). [χ^2 with Yates's correction.]

Table 2. Average muscle strengths in injected and uninjected legs

Injection status	No. of legs	Muscle strengths in legs[a]: Not injected: Gluteus	Quadriceps	Ankle	Injected: Gluteus	Quadriceps	Ankle	Injected+uninjected: Gluteus	Quadriceps	Ankle	Total 2 legs Gluteus only
Controls	142	2·0	1·9	2·4	–	–	–	–	–	–	2+2 =4·0
Left or right	130	3·0	3·0	3·2	0·8	0·5	1·1	–	–	–	3+0·8=3·8
Left+right	80	–	–	–	1·2	1·2	1·5	–	–	–	1·2×2 =2·4
Site not recorded	138	–	–	–	–	–	–	1·5	1·2	1·7	1·5×2 =3·0
Provocation[b]	24	(5·0)	(5·0)	(5·0)	1·5	1·2	1·8	1·3	1·2	2·2	–

[a]Muscle strength measured by the MRC scale: 0=flail, 5=normal. The lower the score, the greater the paralysis. The values 0 to 5 are arbitrary, therefore the averages are only indicative. The scale reflects functional tests, not destruction of neurones: a muscle will test as strength 5 even with a loss of 60% of the relevant neurones (SHARRARD, 1956).

[b]The number of legs in each group was small: 2 not injected, 8 injected and 14 with at least 7 legs injected.

muscle involvement was 0·95 for each but 0·80 for the toes.

Paralysis is usually expressed as the number or proportion of limbs or muscles affected: the higher the number the greater the paralysis. However, remaining muscle strength is assessed by the Medical Research Council (MRC) scale where 0 is complete paralysis and 5 is normal: the lower the number, the greater the paralysis. The scale is arbitrary, as loss of up to 60% of the motor neurones does not affect muscle strength (SHARRARD, 1956); average muscle scores are, therefore, only indicative.

Ankle muscles were the strongest (Table 2) and the quadriceps were weaker than the glutei even when the latter had been injected. Injected legs had less strength than those not injected. Children receiving injections had more severe paralysis than controls (Table 2, last column).

The average muscle strength of all legs includes those with no paralysis, but the degree of disability may be better judged by considering only those legs with paralysis (Table 3). Paralysed legs of controls and the uninjected legs of those receiving injections had similar muscle strengths. Injected legs had more severe paralysis. The high proportion with paralysis of both legs suggests that 'IM+' was often used instead of 'both legs injected'.

Table 3. Average strengths of muscles in legs with paralysis

	No. of legs	Average strengths of muscles[a]: Gluteus	Quadriceps	Ankle
Controls				
Paralysed legs only	104	0·9	0·7	1·5
Injected				
Uninjected leg	27	1·0	0·9	1·5
Injected leg	134	0·7	0·5	1·0

[a]Excluding legs without paralysis. Muscle strength measured by the MRC scale: 0=flail, 5=normal; see footnote to Table 2.

Trunk and arm paralysis

Of 21 children with trunk paralysis, 4 were controls and 8 had received injections in both legs. Only 2 children had been injected in the arm and both had paralysis only in the injected (right) arm. Seven other children, 5 with injections in the legs, had paralysis of only one arm. Involvement of the arms was not increased by injection in one leg (Table 1) but was doubled by injections in both legs ($P<0{\cdot}01$). Of the 42 children with arm and leg paralysis (16% of the total), 10 had both legs and 1 arm paralysed and 29 were paralysed in all 4 limbs. Twelve per cent of arms were affected.

Death in the acute illness

Only one control child died. Of the 13 deaths of children receiving injections, 2 had single injections, 4 had at least 2 injections with a fifth having massage as well, one had 3 injections and 2 each had 7 injections. Deaths are over-represented as the histories were more complete.

Provocation, and diphtheria-pertussis-tetanus vaccine injections

Twelve children (5%) had received injections 3–25 days before paralysis which were assessed as provocation (see Tables 2 and 4). Four had received diphtheria-pertussis-tetanus vaccine (DPT) and 3 more had received DPT <48 h before paralysis. DPT was involved in at least 3% of the cases, and in one case there was also a subsequent injection.

Table 4. Provocation and aggravation compared[a]

	Provocation	Aggravation
Incubation (d)	7 (?5)–21 (median *c.* 12)	1–2
Stage of infection	Very early	Very late
Virus	None in CNS	Already in CNS
Increased risk of paralysis (population)	Up to ×25	Only those incubating non-paralytic polio
First paralysis	Injected limb, 85%	Not known
Increased risk (individual)	All limbs	Only injected/exercised limbs except with multiple injections
Average severity of paralysis after one injection	Increased	Decreased
Cause	Intramuscular injection, muscle damage (e.g. by bone fracture, parasites)	Intramuscular injection, physical activity
Agents	Inflammation in muscle	Increased vascular flow in CNS?
No. of children affected in the 'third world'	Very few, as only DPT is given to healthy babies	Many; intramuscular injections frequently given for fever and/or diarrhoea, often the symptoms of poliovirus infection

[a]See WYATT (1976, 1981, 1990).

Recovery

Most children left the hospital after a few days and fewer than half returned for physiotherapy. While in hospital, 7 controls recovered from zero strength to 3 or 5, and from 2 or 3 to 5: these recoveries came 7–14 d after the acute illness. Few with injections in the legs made such good progress but, where the site of injection was not recorded, several had recovery from zero to 3 or 4 in one leg only. In 4 children with strengths 0 to 3 in both arms, both arms recovered completely: 3 of these children had had injections in the legs. We think that injected limbs do not recover as rapidly or as much as uninjected limbs.

Injections

Few parents knew what had been injected. Identified drugs included antihistamines, neostigmine, gentamicin, tetracycline and probably penicillin. One child was given injections of one vial each of Decadron® and ampicillin every 6 h for 3 d. Others received 6 or 4 injections in a single day. Another received 6 injections in one day and the next day an injection of vitamin B complex in an already paralysed right gluteus 'for strength'. Most of the injections were given for fever but an aminoglycoside was given for a cough and rhinorrhoea.

Prevalence of left and right leg paralysis

The JIPMER Polio Register showed an excess of single left legs with paralysis, 76 against 48 right, a ratio of 1:0·63 (n=227; 45% with both legs paralysed). In our sample, children over 18 months old were more likely to be injected in the left (10) than the right gluteus (3).

Sex

The sex ratio was 1·32 boys:1 girl, with small differences within the groups. More girls (26) had arm involvement than boys (23) and more deaths, 8 girls vs 6 boys.

Discussion

Without injections, there was equal chance of paralysis in right and left limbs, but this pattern and the severity of paralysis were different in children who had received injections. Paralysis following <48 h after injections is therefore a new phenomenon, not coincident as previously assumed (e.g., by GREENBERG & ABRAMSON, 1952). When paralysis follows 48 h after physical activity (RUSSELL, 1949; WYATT, 1990) or injections, poliovirus must already have been in the central nervous system (CNS); we term this aggravation. [See note on p. 549.]

By definition, provocation occurs after 7–21 d. In our cases, aggravation was manifest in <3 d or not at all (Table 4). Moreover, provocation by single injection increased paralysis (KORNS *et al.*, 1952) whereas in aggravation total paralysis is reduced. Some substances may be more aggravating than others and, in India, syringes, needles and the substance injected are seldom sterile (WYATT, 1984). In aggravation, uninjected limbs were not affected (Table 3). However, children with both legs injected were more likely to have paralysis of all 4 limbs and to die. As we do not know how many children were given injections or what was injected, the increased risk of paralytic polio cannot be calculated.

Two important and apparently anomalous findings can be explained. Some injected limbs suffered no paralysis: there may have been too little virus in the CNS to produce paralysis, the substance injected (saline?) was not inflammatory, or—though unlikely—the parents were mistaken about the limb injected. Secondly, the chance of paralysis in uninjected legs of children given injections was less, 42%, than in controls, 73% (Table 1). We suggest that children who received injections included not only those already incubating paralysis but also some incubating non-paralytic polio. None of these latter children would have paralysis in the uninjected leg, whereas those incubating paralytic polio would have a 73% chance of paralysis, as in the controls. The ratio of children who received injections while incubating paralytic and non-paralytic polio will determine the chance of paralysis (between zero and 73%) in uninjected legs.

About 75% of children received injections and, using this proportion, we can explain the 42% paralysis. Of every hundred children, if 75 received injections of whom 44 were incubating paralytic and 31 incubating non-paralytic polio, then 42% of uninjected legs would be paralysed (see WYATT, 1992). The model can be tested with data where the proportions of children given injections are different.

Although the coincidence of injections and paralysis has been noted by many authors, there seems to be no report of action to limit injections. Few studies have mentioned children with multiple injections, or injections in both legs, or that the site was unknown, or whether some children had had an injection. Two consecutive studies analysed paralysis in 58 children without OPV and in 80 given 3 doses of OPV (SEN *et al.*, 1985, 1989). Of those not receiving OPV, only 10% had received injections and 71% suffered severe paralysis. Of those with 3 doses of OPV, 67% had received injections and only 37% had severe paralysis. Severity was measured by the average muscle score of the paralysed limbs, but no detail of limbs and muscles were given. In our study, 36% of 181 children given injections and 31% of 67 children without injections had received 2 or more doses of OPV: we found no effect of age or OPV status.

In our sample, few if any of the injections and little of what was injected seem indicated by the symptoms: indeed, the injections were unnecessary and dangerous (see also PRAKASH *et al.*, 1989; WYATT, 1984). If medication was necessary, oral medicines should have been given.

Few cases resulted from injected DPT (see also WYATT, 1986), although greater care in postponing DPT for children with fevers would help.

Many children incubating non-paralytic polio may receive an injection which increases loss of neurones up to 60% without ensuing paralysis. The increased paralysis due to injections may be the visible sign of hidden damage: the tip of an iceberg. More and earlier immunization with polio vaccine is essential: for many babies, immunization comes too late. Fewer unnecessary injections would lead to fewer cases of paralysis. Only vaccines and life-saving injections help babies and small children.

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Note added in proof

At the third symposium of the European Association against Poliomyelitis, held in Zurich 1955, one session was entitled 'The role of aggravating factors in poliomyelitis' (see *Reports and Contributions* [duplicated, no page numbers, no address]; Bruxelles, 1955). Physical activity was discussed by Behrend as a factor '*favorisant*' paralysis and Mattia, Angela and Nola discussed '*fatigue comme facteur d'aggravation*'. Mollaret discussed lumbar puncture among '*facteurs aggravants*'. These are the only previous uses of the term aggravation that I have discovered.

H. V. Wyatt

Announcement

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