TABLE IV.—*Clinical Progress of the Two Groups During Follow-up Period*

	Worse on Discharge	Trial Group					Control Group				
		Better or Unchanged	Slightly Worse	Much Worse	Steady Deterioration	New Episodes	Better or Unchanged	Slightly Worse	Much Worse	Steady Deterioration	New Episodes
1		X				1			X		4
2	X			X	X	10		X	(X)	X	5
3				X		2		X			2
4			X	X		2			X		3
5	X			X		4	X				5
6			X			3		X	X	X	3
7	X			(X)	X	3			X		1
8				X		7	X	X		X	3
9	X			X		1		X			1
10				X		3		X		X	1
11			X	X	X	1					1
12				X		1		X			1
13	X			X	X	1		X			1
14				X		2		X			1
15	X		X	X	X	1		X	X		3
16			X			1	X				1
17			X			1			X		1
18		X				1					1
19						3	X				1
20	X			(X)	X	3	X				1

(X) Died.

TABLE V.—*Comparison of Follow-up Results*

	Trial Cases	Control Cases
Better or unchanged	2	5
Slightly worse	6	6
Much worse (including deaths)	12	9
Deaths	2	1
Continuous deterioration	6	3
New episodes	52	31
No sign of activity of the disease	1	3

directly related to the closeness of medical supervision, and if the 12 episodes observed in the trial group while in hospital after the P.P.D. treatment are subtracted the numbers are more comparable in the two groups. However, the same 12 episodes so soon after the P.P.D. led us to stop the trial in September, 1959.

No significant difference in the clinical progress was observed in two subgroups: (1) *B.C.G. cases* (Nos. 13, 14, 15, and 19 in the trial group, and Nos. 11 and 14 in the control group). (2) Cases with a maximal *C.S.F. protein of more than 500 mg./100 ml.* (Cases 7, 19, and 20), of whom two had died and one was unchanged at the end of the follow-up period.

We were struck by the great variability in the individual C.S.F. reactions in our cases. This seemed to differ from two previous studies. Smith *et al.* (1957), who tended to use larger doses of P.P.D., emphasized a single pattern of response with relatively high protein levels and apparent absence of an early polymorphonuclear reaction. Marshall and O'Grady (1959) described two patterns of response of either a slow rise in protein and cells or of an early peak followed by a later and smaller rise in protein and cells; these patterns were also observed in motor neurone disease, Parkinsonism, and Huntington's chorea.

The significance of the changes in the protein fractions on electrophoresis of the serum and C.S.F. has been discussed elsewhere (Gavrilescu *et al.*, 1961).

Finally, we can unfortunately claim success only for our choice of cases with measurable activity of their disease; our series must not be taken as representative of disseminated sclerosis; as seen generally, this is a much more benign disorder.

Summary and Conclusions

A trial of intrathecal tuberculin (P.P.D.) was made on 20 patients with disseminated sclerosis in whom the disease seemed active and in whom new episodes of demyelination or deterioration were anticipated.

On comparing their fate with a group of 20 carefully matched control cases we conclude that intrathecal tuberculin in disseminated sclerosis is a form of treatment which confers no benefit on the patient, despite the unpleasantness of the reaction and the length of the stay in hospital. Indeed, we are not satisfied that it may not lead to reactivation of the condition during the month after the treatment.

We hope that trials like ours and the similar results of Miller *et al.* (1961) will prevent the use of P.P.D. as a placebo in a condition where there is great pressure for some active form of treatment. Other untested and potentially harmful methods such as intravenous "pyrifer," or arsenic and bismuth, should similarly be abandoned for truly harmless placebos.

We thank the patients who agreed to participate in this trial and the other members of the staff of Maida Vale Hospital who allowed us to follow the progress of the control cases. We are obliged to Dr. Honor Smith for her kind advice on the technique of the P.P.D. course during the planning of this trial; to Miss Marjorie Durward for the psychometric tests; to Dr. H. Townsend for analysis of the many E.E.G. tracings; and to Dr. M. H. Russell for his help in the follow-up of control case No. 17.

REFERENCES

- Brit. med. J.*, 1958, 2, 1025.
Gavrilescu, K., Jellinek, E. H., and McMenemey, W. H. (1961). *Wild Neurol.* In press.
Marshall, J., and O'Grady, F. (1959). *J. Neurol. Neurosurg. Psychiat.*, 22, 277.
Miller, H., Ridley, A., Newell, D. J., and Schapira, K. (1961). *Ibid.* In press.
Smith, H. V., Espir, M. L. E., Whitty, C. W. M., and Russell W. R. (1957). *Ibid.*, 20, 1.

FAECAL EXCRETION OF ADENOVIRUS IN A CLOSED COMMUNITY

BY

P. S. GARDNER,* M.D., Dip.Bact.

A. E. WRIGHT, M.D., D.P.H., Dip.Bact.

AND

J. H. HALE, O.B.E., M.D., M.R.C.P.

Regional Public Health Laboratory, General Hospital,
Newcastle upon Tyne

The adenoviruses are a large group of viruses possessing a common soluble antigen but divisible into no fewer than 23 serological types, of which 18 are of human and five are of simian origin. Since the observation of a spontaneous degenerating agent in human tonsils growing in tissue culture (Rowe *et al.*, 1953), many family and institutional outbreaks of adenovirus infections have been described among civilians (Munro-Ashman *et al.*, 1958). Serological evidence suggests that infection is widespread and probably occurs in children (Huebner *et al.*, 1954), although the exact role of these agents in causing clinical symptoms is not yet clear. Some types, such as 3, 4, and 7, are associated with acute respiratory disease (Berge *et al.*, 1955), type 8 (Jawetz *et al.*, 1955, 1956) is associated with epidemic keratoconjunctivitis. Others, such as 1 and 2, are more often found in human adenoids and tonsils removed at operation. Maternal antibodies to many of these agents are

*Now at the Joint Department of Bacteriology, Royal Victoria Infirmary, and the Medical School, King's College, Newcastle upon Tyne.

found in babies (Morrison *et al.*, 1957); these disappear by 6 months of age and reappear when stimulated to do so by natural infection. These antibodies are not confined to the so-called epidemic strains but may be antibodies to any members of the group. Thus it appears that antibodies are produced against some viruses which cause no clinical signs of infection.

This communication presents the results of a year's study of the excretion of adenoviruses in the stools of children living in a residential nursery, together with an account of the general health of the community throughout the period.

Plan of Investigation

The home was situated in a large country-house which was controlled by a matron and a number of staff, some of whom were qualified nurses, and others who were in training. The domestic staff were recruited locally and lived at home, in contrast to the nursing staff, who were resident. The children were admitted usually to convalesce after some illness or because of domestic difficulties; some children remained for only a few weeks, though the stay was more often measured in months. The children, about 25 in number, lived in two main groups. The first, under 1 year of age, lived in their own nursery; the second, aged from 1 to 6 years, mixed with greater freedom among themselves. There was little contact between these groups, although the attempt to keep them separate usually failed owing to staff shortages at nights and at holiday periods.

Faecal specimens from staff and children were examined at fortnightly intervals for viruses. Ten per cent. suspensions of faeces in distilled water were centrifuged at 10,000 g for 30 minutes, and 0.2 ml. of the supernatant was used for inoculating HeLa-cell cultures. Monkey-kidney and amnion-cell cultures were also used when available. Any agents isolated were identified by neutralization with specific antisera.

No attempt was made to examine sera for antibody to viruses as it was thought that periodic bleeding might lead to a loss of co-operation between the children and staff, and, in any case, the primary interest was the spread of viruses in the community. Blood for serology was, however, obtained when a child became ill.

The home was visited at regular intervals in order to compile records of illnesses and to correlate these so far as possible with any virus excretion.

Results

Many types of adenovirus were found to be excreted by the occupants of the home but no seasonal variation was noted, and with the exception of one incident none were related to clinical illness.

Adenovirus types 1, 2, 3, 4, 5, 6, and 7 were all encountered, but type 5 was isolated with far greater frequency (Table I).

TABLE I.—Total Adenovirus Excretion in the Nursery

Adenovirus No. of Isolations	5	1	6	7	4	2	3
..	88	17	9	5	3	2	1

Table II shows the incidence of adenovirus excretion in the babies, the toddlers, and the adults; it can be seen that excretors are more frequent in the young.

Duration of Excretion.—Five children excreted adenovirus type 5 for prolonged periods (three to six

TABLE II.—Age Incidence of Adenovirus Infection

Age	No.	Infection with One Type Only During the Investigation	Infection with Two or More Types During the Investigation
<1 year	34	20	7
1-6 years	34	13	5
Adults	21	6	2

months); in fact, one child aged 1 year had excreted this virus in her faeces for nine months when this investigation ceased, so it was conceivable that the period of excretion was much longer. Four of the five children were 1 year of age or under and the fifth was 4 years old. During the period of type 5 excretion one child excreted type 4 and another type 6.

Correlation of Virus Excretion with Clinical Disease.

—With one curious exception adenovirus appeared to circulate in the community without being associated with or giving rise to respiratory illness, although accepted pathogenic adenovirus types 4 and 7 were isolated on different occasions. In December four children became ill with an infection of the upper respiratory tract which subsequently became an acute bronchiolitis severe enough to necessitate their admission to Newcastle General Hospital. All four children were taken ill within a few days, and the only laboratory finding was the faecal excretion of adenovirus type 5 after the beginning of the illness. In three cases this excretion ceased very shortly after the illness, while the fourth child continued excretion for a further eight weeks. Serological investigations and throat swabs were negative, a not uncommon finding in this condition (Gardiner *et al.*, 1960b).

Discussion

Several features became apparent during this investigation. We were rather surprised by the ease with which the adenovirus could be isolated from faeces, although to detect virus by our method there must have been at least 50 TCD₅₀/g. (Gardner *et al.*, 1960a). This suggested to us that, although these viruses are regarded as respiratory viruses, they must also have multiplied somewhere in the region of the alimentary tract, probably in the lymphatic tissue, as we did not believe faecal isolations resulted from faeces being contaminated by material swallowed from the upper respiratory tract. If this is accepted then it also follows that the site of multiplication could be the same as that favoured by the poliovirus. This immediately raises the question of whether such an adenovirus infection could result in interferon production (Isaacs and Lindenmann, 1957; Pereira, 1960) possibly, for example, interfering with poliovirus infection. In such cases the children who showed prolonged adenovirus excretion might have exhibited a non-specific resistance to other viruses, such as the poliovirus (Hale, 1961). Another surprising feature was the long-continued excretion of adenovirus, particularly type 5. It is possible that carriage of adenovirus is permanent or semi-permanent, its detection varying with the waxing and waning of an interferon-like substance in the bowel (Wagner, 1960). More studies are required into the length of virus excretion in different populations.

Adenoviruses were not mutually exclusive; simultaneous double type infection was found; on other occasions two children showed adenovirus type 5 excretion, but at a later date type 7 and type 6 were isolated

respectively, to be followed by adenovirus type 5 again. This must have been simultaneous double infection, and the laboratory result merely reflected that type 5 was normally dominant but occasionally the other types predominated. In a recent trial a similar picture was found when children were fed three types of poliovirus simultaneously (Hale *et al.*, 1961). One or two viruses would be isolated in the faeces, then the third would appear; this was followed by the irregular reappearance of all types.

In spite of the frequency of isolation of adenovirus the general health of the community remained high. Mild coryzas were common, but never seemed to be related to the appearance of any adenovirus in the stools of those affected. Adenovirus type 7, an organism usually regarded as an epidemic strain, did not spread or produce clinical disease. This virus was introduced by a nurse in November, appeared in a toddler in December, and, after being excreted by a baby a month later, disappeared.

Adenovirus type 5 was isolated from no less than 50% of the children in the home, but never seemed to be responsible for any clinical illness with the possible exception of the outbreak of bronchiolitis described above. There are a number of hypotheses which might account for this outbreak. A new type 5 strain of virus may have been introduced during December which, when encountered by the very young and not the older children, caused respiratory illness; alternatively, perhaps conditions at the time might have been such that if type 5 virus infection took place illness resulted. On the other hand, the bronchiolitis at this period might have been due to an agent undetectable by available methods, or to this agent in combination with adenovirus type 5 (Gardner *et al.*, 1960b). These cases, however, emphasize the difficulty in deciding the aetiology of a disease which may be due to a virological agent that can be carried by a large number of normal individuals showing no sign of disease.

As a result of a constant influx of new children and prolonged excretion by some residents, conditions for endemicity are established. Communities of this type, in which viruses are epidemic, may act as foci of infection for the general population.

Summary

A residential nursery has been studied over a period of a year for the excretion of adenovirus. Types 1-7 were found in stools, and in a number of children adenovirus type 5 was excreted for many months. Many children were capable of carrying more than one adenovirus, and the significance of this is discussed. The relationship of adenovirus excretion to the general health of the community is discussed, with special reference to an outbreak of bronchiolitis which occurred during the period of study.

We are indebted to Dr. C. Cooper, consultant paediatrician, the matron, and the staff for their co-operation.

REFERENCES

- Berge, T. O., England, B., Mauris, C., Shuey, H. E., and Lennette, E. H. (1955). *Amer. J. Hyg.*, **62**, 283.
 Gardner, P. S., McGregor, C. B., and Dick, K. (1960a). *Brit. med. J.*, **1**, 91.
 — Stanfield, J. P., Wright, A. E., Court, S. D. M., and Green, C. A. (1960b). *Ibid.*, **1**, 1077.
 Hale, J. H. (1961). *Advances in Immunology*. In press.
 — Lee, L. A., Gardner, P. S., and Lim, K. A. (1961). To be published.

- Huebner, R. J., Rowe, W. P., Ward, T. G., Parrott, R. H., and Bell, J. A. (1954). *New Engl. J. Med.*, **251**, 1077.
 Isaacs, A., and Lindenmann, J. (1957). *Proc. roy. Soc. B*, **147**, 258.
 Jawetz, E., Kimura, S. J., Hanna, L., Coleman, V. R., Thygeson, P., and Nicholas, A. (1955). *Amer. J. Ophthal.*, **40**, No. 5, pt. 2, p. 200.
 — Thygeson, P., Hanna, L., Nicholas, A., and Kimura, S. J. (1956). *Proc. Soc. exp. Biol. (N.Y.)*, **92**, 91.
 Morrison, B., Bass, D., Davis, J. A., Hobson, D., Madsen, T. I., and Masters, P. L. (1957). *Lancet*, **2**, 1077.
 Munro-Ashman, D., Gardner, P. S., Taylor, C. E. D., and McDonald, J. C. (1958). *Ibid.*, **2**, 121.
 Pereira, H. G. (1960). *Virology*, **11**, 590.
 Rowe, W. P., Huebner, R. J., Gilmore, L. K., Parrott, R. H., and Ward, T. G. (1953). *Proc. Soc. exp. Biol. (N.Y.)*, **84**, 570.
 Wagner, R. R. (1960). *Bact. Rev.*, **24**, 151.

TABETIC GASTRIC CRISIS WITH FLUID LEVELS AND VISIBLE PERISTALSIS

BY

R. D. CATTERALL, M.R.C.P.Ed.

A. J. C. LATCHMORE, M.B.E., M.S., F.R.C.S.

AND

E. E. SHERWOOD-CUNDALL, M.B., Ch.B.

From St. James's Hospital, Leeds, and the
General Infirmary at Leeds

Gastric crises are recurrent paroxysmal attacks of severe abdominal pain, with or without vomiting, occurring in patients suffering from tabes dorsalis. Their onset is usually sudden, and an attack may last hours, days, or weeks, and usually subsides rapidly and completely. The incidence of these attacks has declined during recent years with the decrease in cases of tabes dorsalis. However, the condition is still seen from time to time in different branches of medical practice, and the importance of considering the possible diagnosis of gastric crisis in patients complaining of severe abdominal pain cannot be stressed too frequently. Unnecessary surgical interventions in such patients occur so often that the presence of abdominal operation scars with pain has been alluded to by Tilney as one of the diagnostic signs of this syndrome.

The incidence of gastric crises in cases of tabes dorsalis appears to be about 12%. Bonar (1901), at Columbia University, found 36 cases of gastric crises among 286 cases of tabes dorsalis. Nuzum (1916) reviewed 1,000 cases of tabes and found that gastric crises were the initial symptom in 17%. The Cooperative Clinical Group in the United States (O'Leary *et al.*, 1938) studied 985 patients with tabes dorsalis, gastric crises occurring in 118.

The cause of gastric crises remains undetermined. Some authors regard the attacks to be of sympathetic origin. Others believe that they result from recurrent posterior ganglionitis in the lower dorsal segment of the cord. Others regard involvement of the vagus as responsible for the symptoms. Gowers (1900) showed that in cases of tabes with gastric crises there were marked lesions in the upper cervical segments of the cord. Eppinger and Hess (1917) regarded visceral crises as the outcome of irritation and later of paralysis of the autonomic nervous system. The only factors known to induce attacks are acute infection, emotional tension, and severe fatigue, but the majority occur