- ³ Salmon, P. R., Brown, P., Htut, T., and Read, A. E., *Gut*, 1972, 13, 170.
- ⁴ Cotton, P. B., Rosenberg, M. T., Waldram, R., and Axon, A. T. *British Medical Journal*. In press.
- ⁵ Cotton, P. B., Price, A. B., Tights, J. R., and Beales, J. S. M. In preparation.
- ⁶ Cotton, P. B. *et al.*, *British Journal of Surgery*. In press.
- ⁷ Belber, J. P., *Gastroenterology*, 1971, 61, 55.
- ⁸ Classen, M., Koch, H., and Demling, L., *Gastrointestinal Endoscopy*, 1971, 18, 78.
- ⁹ Morrissey, J. F., *Gastroenterology*, 1972, 62, 1241.
- ¹⁰ Taylor, P. A., Cotton, P. B., Towey, R. M., and Gent, A. E., *British Medical Journal*, 1972, 1, 666.
- ¹¹ Prout, B. J., and Metreweli, C., *British Medical Journal*, 1972, 4, 269.
- ¹² Schiller, K. F. R., Cotton, P. B., and Salmon, P. R., *Second European Congress for Digestive Endoscopy, Paris*, 1972.
- ¹³ Ansell, G., *Investigative Radiology*, 1970, 5, 374.
- ¹⁴ Zamcheck, N., and Klausenstock, O., *New England Journal of Medicine*, 1953, 249, 1062.
- ¹⁵ Cooley, R. N., *American Journal of the Medical Sciences*, 1961, 242, 628.
- ¹⁶ Koch, H., personal communication, 1972.
- ¹⁷ Brummer, P., and Hakkinen, I., *Acta Medica Scandinavica*, 1959, 165, 329.
- ¹⁸ Barfred, A., *Proceedings of the World Congress on Gastroenterology*. Baltimore, Williams and Wilkins, 1959.
- ¹⁹ Krag, E., *Acta Medica Scandinavica*, 1965, 178, 713.
- ²⁰ Gregory, D. W., Davies, G. T., Evans, K. T., and Rhodes, J., *British Medical Journal*, 1972, 4, 519.
- ²¹ Comfort, M. W., *et al.*, *Surgery, Gynecology and Obstetrics*, 1947, 105, 435.
- ²² Klotz, A. P., Kirsner, J. B., and Palmer, W. L., *Gastroenterology*, 1954, 27, 221.
- ²³ Templeton, F. E., *Gastroenterology*, 1955, 28, 378.
- ²⁴ Dvorsky, A., *Endoscopy*, 1969, 1, 54.
- ²⁵ Demling, L., Classen, M., and Koch, H., *Urgent Endoscopy of Digestive Abdominal Diseases*, p. 261. Basel, Karger, 1972.
- ²⁶ Kasugai, T., Kuno, N., Aoki, I., Kisu, M., and Kobayashi, S., *Gastrointestinal Endoscopy*, 1971, 18, 9.
- ²⁷ Classen, M., *Archives Françaises des Maladies de l'Appareil Digestif*, 1972, 61, 321.
- ²⁸ Davis, R. H., and Williams, J. E., *British Medical Journal*, 1968, 1, 502.
- ²⁹ Kasugai, T., *Gastroenterology*, 1970, 58, 429.
- ³⁰ Brown, P., Salmon, P. R., Thien-Htut, and Read, A. E., *British Medical Journal*, 1972, 3, 661.
- ³¹ Gear, M. W. L., Truelove, S. C., Williams, D. G., Massarella, G. R., and Boddington, M. M., *British Journal of Surgery*, 1969, 56, 739.
- ³² Sakita, T. *et al.*, *Gastroenterology*, 1971, 60, 835.
- ³³ Runyeon, W. K., and Hoerr, S. O., *Gastroenterology*, 1957, 32, 415.
- ³⁴ Wychulis, A. R., Priestley, J. T., and Foulk, W. T., *Surgery, Gynecology and Obstetrics*, 1966, 122, 89.
- ³⁵ Hirschowitz, B. I., in *Progress in Gastroenterology*. New York, Grune and Stratton, 1970.
- ³⁶ *Lancet*, 1971, 2, 415.
- ³⁷ Palmer, E. D., *Journal of the American Medical Association*, 1969, 207, 1477.
- ³⁸ Paul, F., Seifert, E., and Otto, P., *Urgent Endoscopy of Digestive and Abdominal Diseases*, p. 64. Basel, Karger, 1972.
- ³⁹ Solanke, T. F., Kumakura, K., Maruyama, M., and Someya, N., *Gut*, 1969, 10, 436.
- ⁴⁰ Scott-Harden, W. G., *Gut*, 1972, 13, 850.
- ⁴¹ Williams, C., and Muto, T., *British Medical Journal*, 1972, 3, 278.
- ⁴² Cotton, P. B., *Gut*, 1972, 13, 1014.

Hospital Topics

Outbreak in Bristol of Conjunctivitis Caused by Adenovirus Type 8, and its Epidemiology and Control

D. L. BARNARD, J. C. DEAN HART, V. J. MARMION, S. K. R. CLARKE

British Medical Journal, 1973, 2, 165-169

Summary

In an investigation of an outbreak of adenovirus type 8 infection involving over 40 people it was found that the infection spread initially within the eye hospital, but subsequently involved several family contacts and two local hospitals for mentally subnormal patients. Presumptive diagnosis should be possible before subepithelial opacities have developed provided an adequate history is taken, and had that been done in this outbreak it is reasonable to suppose that many cases could have been prevented.

Introduction

In Western countries epidemic keratoconjunctivitis caused by

adenovirus type 8 is usually spread by medical personnel. Such outbreaks are preventable but continue to occur.¹⁻⁵ In 1971 three outbreaks occurred in the United Kingdom, the first starting in the Clyde valley in May and involving over 100 people, the second in the Bristol area starting in July and involving over 40 people, and the third in London involving fewer people.⁶

Adenovirus type 8 infection often causes a painful and distressing keratitis with severe photophobia, and corneal opacities may impair vision for over two years. Patients will often be unable to work during the early stages of the infection. Unfortunately, the effects of an outbreak are not limited to infected patients but also have direct and serious consequences on other patients because tonometry is usually drastically curtailed (since tonometers, which are known to spread the infection, are notoriously difficult to disinfect adequately) and because elective surgery is often stopped during outbreaks.

In this report the virology and epidemiology of the Bristol outbreak is presented, and methods of prevention and control are discussed.

Patients and Methods

From August, when the outbreak was recognized, until September, when the hospital epidemic stopped, all patients seen in the hospital with a recent onset of follicular conjunctivitis were referred to a special clinic to isolate them from other patients and to follow them clinically, epidemiologically, and

Department of Pathology, Bristol Royal Infirmary, Bristol BS2 8HW
D. L. BARNARD, B.M., M.R.C.P., Registrar. Present address: Department of Pathology, Western General Hospital, Edinburgh, 4.

Bristol Eye Hospital, Bristol BS1 2LX

J. C. DEAN HART, B.SC., F.R.C.S., Consultant Senior Lecturer
V. J. MARMION, M.R.C.P., F.R.C.S., Consultant Ophthalmic Surgeon

Public Health Laboratory, Bristol BS2 8EL

S. K. R. CLARKE, M.D., F.R.C.PATH., Consultant Virologist

virologically. In addition to these patients a few presenting both before and after this period were included in the study as they were suspected, on clinical or epidemiological grounds, of having an adenovirus type 8 infection. A total of 87 patients were referred to the clinic, but six persistently failed to attend and were excluded from the study.

All 81 patients in the study were classified clinically (by J.C.D.H.) and epidemiologically (by D.L.B.) before the results of the virological studies were revealed. The clinical findings have been described elsewhere.⁷

The ages of the 81 patients studied ranged from 6 to 87 years.

VIRUS ISOLATION

Conjunctival swabs taken within 21 days of clinical onset were sent to the laboratory in milk saline transport medium. Adenoviruses were isolated in human embryo kidney, HeLa cell, or human embryo fibroblast tissue culture, and identified by neutralization. The TRIC agent was isolated in irradiated McCoy cells.⁸

SEROLOGY

Haemagglutination-inhibiting (HAI) antibodies to adenovirus type 8 were measured by the microtitre technique of Bell *et al.*⁹ with human group 0 red cells.

Results

SEROLOGY

Convalescent serum—that is, collected three weeks or more after clinical onset—was obtained from all 81 patients. In addition, early serum—that is, collected within seven days of clinical onset—was obtained in 32 of these patients. HAI antibody titres to adenovirus 8 were measured in these sera and in 64 control sera matched for age and sex taken from blood donors and patients undergoing serological examination for Australia antigen, and the results are shown in table I.

No control serum had an HAI titre of more than 8 and this is in keeping with most experience in the Western hemisphere,¹⁰ where infection is rare and significant titres are found in only about 5% of the population. Raised titres may be taken to imply previous infection with adenovirus type 8.

A total of 35 patients had a convalescent HAI titre below 8 and this makes a recent or past infection improbable. In none

TABLE I—Convalescent HAI Antibody Titres to Adenovirus Type 8 and Interpretation

Convalescent HAI Antibody Titre	No. of Control Sera	No. of Patients						Total
		Convalescent Serum Only		Paired Sera Showing No Rise		Paired Sera with 4-Fold Rise		
		Culture Negative or No Swab	Culture Positive	Culture Negative or No Swab	Culture Positive	No Swab	Culture Positive	
<8	63	24 (-)	0	11 (-)	0	0	0	35
8	1	1 (?)	0	3 (?)	0	0	0	4
>8	0	20 (?+)	5 (+)	2 (?)	0	2 (+)	13 (+)	42

+ = Definitely recent infection (20 patients).
 ?+ = Probably recent infection (20 patients).
 ? = Doubtful (6 patients).
 - = Probably no infection (35 patients).

of these patients was adenovirus type 8 isolated. Altogether, 42 patients had a convalescent HAI titre above 8, implying a re-

cent or past infection. Of these, 15 showed a four-fold rise, which definitely implies a recent infection, and in all 13 of these from whom conjunctival swabs were taken adenovirus type 8 was isolated. Adenovirus type 8 was isolated from five other patients with convalescent HAI titres above 8, definitely implying a recent infection. In the other 20 patients with convalescent HAI titres above 8 but no available early sera, clinical and epidemiological grounds make it likely that their adenovirus type 8 infections were of recent origin.

Six patients remain in whom the interpretation of the laboratory findings is doubtful; in three of these the clinical and epidemiological findings suggested a recent adenovirus type 8 infection.

In summary, of the 81 patients, 20 had definite, 20 probable, 6 doubtful, and 35 no evidence of recent infection. Adenovirus type 8 HAI antibody levels sometimes rose quite late, and in some patients antibody was not detectable 14 days after clinical onset.

ISOLATIONS

Adenovirus Type 8.—Eighteen out of 20 of the patients who had positive serological findings for adenovirus type 8 and who were swabbed within 14 days of clinical onset yielded adenovirus type 8; isolation attempted in two such patients at 17 and 18 days was not successful. No adenovirus type 8 was grown from patients with no convalescent adenovirus type 8 HAI antibodies.

Other Virus Isolations.—One patient yielded an adenovirus type 3 and one a TRIC agent, the latter having been suspected on clinical grounds. Neither of these two patients developed adenovirus type 8 HAI antibodies.

EPIDEMIOLOGICAL FINDINGS

All the patients were classified into three groups: those acquiring the infection at the eye hospital; contacts of these patients; and those for whom no possible source of infection could be found. The correlation of these groups with the virological findings is shown in table II. The sources of infection were found in all 40 patients with definite or probable adenovirus type 8 infection and in three of the patients with doubtful infection. Possible sources of infection were found in only three of the 35 patients with no laboratory evidence of adenovirus type 8 infection.

TABLE II—Correlation of Source of Infection with Laboratory Findings

Possible Source of Infection	No. of Patients			Total No. of Patients
	Definite or Probable Recent Adenovirus 8 Infection	Adenovirus 8 Infection Doubtful	No Evidence of Adenovirus 8 Infection	
Eye Hospital	27	2	1	30
Contacts	13	1	2	16
Unknown	0	3	32	35
Total	40	6	35	81

EPIDEMIOLOGY OF ADENOVIRUS TYPE 8 INFECTION

The 45 patients in the outbreak thought to have had a recent adenovirus type 8 infection included the 43 patients just mentioned, a patient with convalescent antibody to adenovirus type 8 but with inadequate clinical information to justify earlier inclusion, and a 6-year-old boy who developed sub-epithelial opacities and who was the only known source of infection for his father, whose infection was established virologically.

None of these patients had any connexion with metallurgical industries and none had any discoverable connexion with outbreaks elsewhere in the country. Unfortunately, the patient who first brought the virus to the Bristol Eye Hospital was not discovered, but this is not unduly surprising as it is quite possible that this patient, having acquired the infection from Clydebank, the Orient, or elsewhere, had presented at the hospital with an unremarkable mild follicular conjunctivitis, been examined, and not been seen subsequently.

The source of infection for all 45 patients was successfully determined and is shown chronologically and geographically in the chart. The patients fell into three groups which will be considered separately: those acquiring the infection at the Bristol Eye Hospital (three house doctors and 27 patients); family contacts (seven patients); and those acquiring the infection in two local hospitals for mentally subnormal patients (one nurse and seven patients). It is clear from the chart that the epidemic involved the eye hospital first and spread by at least two (and possibly four) patients attending the eye hospital to the two local hospitals for mentally subnormal patients where they reside.

Eye Hospital Group.—The probable dates of acquisition of the infections of the 30 patients was found to extend thinly from the first patient, 22 June 1971 (arrow A in chart), and with gathering momentum to the last, 19 August. Concerted measures to control the infection were introduced at that time and the first special clinic was held on 21 August (arrow D, in chart). No cases of infection were acquired at the hospital after this, although, of course, those patients who had previously acquired their infection continued to appear with follicular conjunctivitis during the next two weeks. The reasons for the initial attendance at the eye hospital are enumerated in table III. Attention is drawn to the fact that of the 45 infected patients described in this whole outbreak, only 15 had had tonometry. The three doctors may well have acquired the

infection by transferring (on their finger-tips) the ocular secretions of infective patients into their own eyes. Probably even before they developed the signs of infection themselves they were also spreading these secretions directly into the eyes of other patients that they examined. Spread ceased when the outbreak was recognized and attention focused on all staff thoroughly washing their hands immediately after examining all patients.

Family Contacts.—The seven family contacts consisted of three wives (one of a house doctor), two fathers, one daughter, and one close friend. It is remarkable that all but one had been involved in administering eye drops to the relations from whom they acquired the infection. The seventh wears contact lenses and had been in close contact with her husband when his eyes were lacrimating profusely.

Hospitals for Mentally Subnormal.—The patients at the two local hospitals for mentally subnormal patients lead a communal and unusually close life together, tending to fondle each other, share towels and clothes, and so on. Furthermore, weekly social evenings are held jointly between the two hospitals so that opportunities for spread of infection abound. It is apparent from the long gap between cases shown in the chart that a number of patients at these hospitals were infected but did not come under our surveillance. In the circumstances it is not surprising that the infection smouldered on in one of these hospitals for several weeks after the outbreak had been stopped at the eye hospital.

INITIAL RECOGNITION OF THE OUTBREAK

Adenovirus type 8 infection in this outbreak was first diagnosed when a patient was seen on 22 July 1971 (arrow C in chart) with subepithelial corneal opacities. Unfortunately, he was thought to be an isolated case and no general measures were taken. In fact he had probably acquired his infection when refrigeration fluid was washed out of his eye at the casualty department on 22 June (arrow A in chart), and had returned with follicular conjunctivitis on 3 July (arrow B in chart) when the significance of his history was not fully appreciated. It is to be noticed that 30 days elapsed between his acquiring the infection and its clinical recognition. During this time a further 15 patients had acquired the infection.

Had effective control measures been introduced immediately this apparently isolated case had been diagnosed, 29 of the 45 cases would not have become infected. In fact measures were introduced one month later (arrow D in chart) when several members of the staff had seen and discussed patients with

TABLE III—Underlying Disorder in Infections Acquired from the Eye Hospital

Reason for Attendance at Bristol Eye Hospital	No of Cases	No. with Tonometry at Time of Acquisition of Infection
Glaucoma or investigation for same	13	13
Conjunctivitis	6	2
Foreign bodies	5	0
Uveitis	1	0
Optic atrophy	1	0
Swollen eyelids	1	0
House doctors with infection . .	3	0
Total	30	15

subepithelial opacities, and subsequently no new cases were acquired from the eye hospital.

CONTROL MEASURES ADOPTED

The measures introduced included vigorous hand-washing by staff after examining all patients, referral of all patients with follicular conjunctivitis to a separate clinic, and severe limitation of tonometry.

Discussion

An adenovirus type 8 infection is rare but a potential calamity to any eye hospital and this outbreak has been described to discuss current methods of prevention and control.

PREVENTION

Most adenovirus type 8 infections in this outbreak (as in some others for example, Dawson *et al.*⁴) were probably spread by the hands of the medical attendants; a minority were spread by tonometers and possibly other instruments. The virus is hardy and survived for at least nine days at room temperature on a tonometer.⁵

On epidemiological grounds it appears that if the medical attendants' hands are washed only briefly in soap and water the infection might continue to be transmitted, but if washing is thorough the spread of epidemics is stopped.^{5,11} We have shown that while thorough hand-washing reduced the amount of adenovirus on a finger 3,000-fold, it did not remove the virus completely.¹² Clearly, disposable gloves could eliminate this mode of infection.

Experiments on disinfection of applanation tonometers and gonioscopes were done and have been reported in detail elsewhere.¹² $10^{3.3}$ TCD₅₀ of adenovirus type 8 were unaffected either by five minutes under ultraviolet light as used in the eye hospital or by 1:32,000 phenyl mercuric borate (recommended by tonometer manufacturers). However, $10^{4.5}$ TCD₅₀ of adenovirus type 8 were inactivated after 15 minutes in 0.6% chloramine, or after two minutes in a waterbath at 60°C or after 30 seconds at 75°C. While neither instruments were affected by immersion in chloramine for seven days, the gonioscope contact lens did not withstand five minutes in water at 75°C, and the applanation tonometer head let in water after seven days (but not after three days) at this temperature. Svartz-Malmberg and Germanis³ immersed the heads in 5% chloramine for 10 minutes and found this satisfactory on epidemiological grounds.

For the Schiøtz tonometer a tonofilm is available.¹³ Alternatively, the instrument may routinely be disinfected by immersion in a waterbath (with an anti-rust preparation) at 75°C or more for five minutes, which would kill vegetative bacteria as well. Svartz-Malmberg and Germanis³ used a special instrument heating to over 240°C. As virus may get lodged above the plunger, chemical disinfection or flaming the plunger in alcohol is not satisfactory,¹³ especially as the latter method is easy to skip.

CONTROL OF OUTBREAKS

It is usually found that, once an outbreak is recognized, the tightening of aseptic techniques rapidly brings the outbreak to a halt, and this was our experience. The real problem of control of outbreaks is one of early suspicion, early diagnosis, and early institution of control measures.

Early diagnosis implies diagnosis in the infective stage of the illness (which lasts from the onset of follicular conjunctivitis until about 14 days later). Unfortunately, definitive diagnosis is not usually possible until the end of this stage, when subepithelial opacities may be seen, when adenovirus type 8 HAI antibodies may have appeared, and when the virus growing from earlier conjunctival swabs may be identified. By the time that a definitive diagnosis was possible in the first patient of this outbreak, a further 15 patients had acquired the infection.

However, a strong presumptive diagnosis is possible at the onset of follicular conjunctivitis, provided that an adequate history is taken. While follicular conjunctivitis is a non-specific finding, table II shows that in all 40 established cases of adenovirus type 8 infection a possible source of infection was found, whereas in only three of 35 cases of recent onset of follicular conjunctivitis not due to adenovirus type 8 infection was a "false" possible source of infection found.

Clearly, anyone with a recent onset of follicular conjunctivitis and a possible source of adenovirus type 8 infection—that is, an ophthalmological examination or contact five to 19 days before onset—should be regarded as having an adenovirus type 8 infection until proved otherwise, and appropriate measures should be taken. Had this approach been adopted in this epidemic, 43 of the 45 cases could probably have been prevented.

SUGGESTED MEASURES

This list is intended as a guide to be modified in the light of future experience.

Methods of Prevention.—(1) Aseptic technique in ambulance rooms, ophthalmological offices, and eye hospitals, with attention either to the wearing of disposable gloves or to thorough hand-washing immediately after examining patients. (2) The use of individual bottles for eye-drops and ointments, and careful disposal of applicators (for fluorescein studies). (3) The use of tonofilm with Schiøtz tonometers, or disinfection of the tonometers and their blocks by heat (see above). (4) Disinfection of applanation tonometer heads and contact lenses for electroretinography and gonioscopy by immersion in fresh 5% chloramine in a disposable container for 10 minutes. (5) Cleaning of slit lamp heads by soap and water after use on a suspect. (6) The prevention of eye injury—for example, by wearing of glasses or goggles in some metal-working occupations.

Additional Measures in Control of an Outbreak.—(1) Early suspicion and presumptive diagnosis (see above). (2) Investigation to determine source and to stop spread. (3) Isolation of suspected patients and particularly medical staff by stopping work until 14 days after the onset or until the conjunctivitis has subsided. (4) Segregation of such patients to a separate clinic if continued surveillance is thought to be necessary. (5) Patients should be informed about the mode of spread and advised to administer their own drops (if any are needed) where possible, to use disposable tissue rather than handkerchiefs, and to use individual towels, face-flannels, and pillowcases (which can be disinfected by boiling). (6) Whether or not elective eye operations, tonometry, and gonioscopy are stopped will depend on whether aseptic techniques can be adequately maintained.

We would like to thank the clinicians of the Bristol Eye Hospital for allowing us to examine patients under their care, Messrs. E. O. Caul, N. J. Bishop, P. C. Roberts, G. W. Smyth, and Mrs. S. J. Hobbs for technical help, and Dr. D. C. E. Speller for valuable advice.

Requests for reprints should be sent to S.K.R.C. Public Health Laboratory, Myrtle Rd., Bristol, BS2 8EL.

References

- ¹ Dawson, C. R., and Darrell, R., *New England Journal of Medicine*, 1963, 268, 1031.
- ² Berg, R., and Ringström, C., *Scandinavian Journal of Infectious Diseases*, 1969, 1, 153.
- ³ Svartz-Malmberg, G., and Germanis, M., *Scandinavian Journal of Infectious Diseases*, 1969, 1, 161.
- ⁴ Dawson, C. R., Hanna, L., Wood, T. R., and Despain, R., *American Journal of Ophthalmology*, 1970, 69, 473.
- ⁵ Wegman, D. H., Guinee, V. F., and Millian, S. J., *American Journal of Public Health*, 1970, 60, 1230.
- ⁶ *British Medical Journal*, 1972, 1, 60.
- ⁷ Dean Hart, J. C., Barnard, D. L., Clarke, S. K. R., and Marmion, V. J., *Transactions of the Ophthalmological Society of the United Kingdom*, 1972, 92, 795.
- ⁸ Gordon, F. B., et al., *Journal of Infectious Diseases*, 1969, 120, 451.
- ⁹ Bell, E. J., Martin, K. W., and Ross, C. A. C., *Journal of Medical Microbiology*, 1969, 2, 125.
- ¹⁰ Jawetz, E., Thygeson, P., Hanna, L., Nicholas, A., and Kimura, S., *Proceedings of the Society of Experimental Biology and Medicine*, 1956, 92, 91.
- ¹¹ Thygeson, P., *American Journal of Ophthalmology*, 1957, 43, No. 4, part 2, p. 98.
- ¹² Clarke, S. K. R., Dean Hart, J. C., and Barnard, D. L., *Transactions of the Ophthalmological Society of the United Kingdom*, 1972, 92, 613.
- ¹³ Wood, R. M., *Archives of Ophthalmology*, 1962, 68, 202.

A New Look at Infectious Diseases

Enterovirus Infections

E. H. BROWN

British Medical Journal, 1972, 2, 169-171

The enteroviruses belong to the picorna group and comprise the following:—(a) Poliovirus types I, II, and III; (b) Coxsackie group A types 1-23; (c) Coxsackie group B types 1-6; (d) ECHO types 1-30.

Poliomyelitis was first recognized as a clinical entity by Heine in 1840 and transmission of the virus demonstrated by Landsteiner in 1908. Recognition of the other enteroviruses, however, awaited the advent of tissue culture in 1948 and over the subsequent years more and more types were identified and knowledge of the various diseases attributed to them has emerged. The name Coxsackie was derived from a village in New York State where the first of these viruses was isolated. ECHO stands for enteric cytopathogenic human orphan, as these viruses were not at first known to cause any disease in animals or man and, though we now know this is no longer the case, the name has persisted.

Normally the enteroviruses inhabit the intestinal tract of man, but they can invade the body and may show special affinities for some tissues and organs. They have no definite geographical preferences; in temperate climates illnesses caused by them are most often seen in the late summer and autumn months, whereas in the tropics they tend to occur throughout the year. Subclinical and inapparent infections far outnumber those manifesting as clinical illnesses. These viruses are highly infectious, transmission being predominantly by the faecal-oral route, and, though able to cause disease in any age group, most frequently affect children and young adults.

The polioviruses, Coxsackie group B, and ECHO viruses grow readily in a variety of tissue cultures but Coxsackie group A viruses (except A9) do not unless specially adapted after primary isolation in suckling mice. The enteroviruses can be isolated from throat swabs in the early stages of the illness and from the faeces for rather longer. With improved techniques they can now be isolated from the cerebrospinal fluid in an increasing proportion of cases presenting as virus meningitis and can then be assumed to be the cause of the

meningitis. In all other cases, however, the illness cannot be attributed to the virus isolated unless paired sera taken at 10-14 day intervals show a significant rise (four-fold or greater) of specific neutralizing or complement fixing antibody.

Clinical Manifestations

When they invade the body the polioviruses affect only the nervous system and are best considered separately. The ECHO and Coxsackie viruses, however, are responsible for a wide variety of clinical syndromes though many of these are due only to certain types. The incidence of the various enteroviruses varies from one year to the next—for example, in 1971 the strains most frequently isolated were Coxsackie A9, Coxsackie B1-5, and ECHO 4; whereas in 1972 they were Coxsackie A9, Coxsackie B4 and 5, and ECHO 4 and 11. The incubation period probably varies according to the type of clinical illness resulting and is difficult to define as the time of infection is rarely known. It is probable that in the majority of cases it falls within the range of 7-12 days.

POLIOVIRUSES

Although poliomyelitis is predominantly a disease of childhood, its age incidence depends on the standards of hygiene and ease of faecal transfer. Epidemics occurred in Great Britain from 1947 to 1956 mainly due to type I, and about one-third of the paralytic cases were over the age of 15 years. With the advent of poliomyelitis immunization (first with killed virus vaccine and then with oral attenuated virus) poliomyelitis has become an uncommon disease and in recent years virtually absent. In the underdeveloped countries, however, where immunization has barely begun, it remains an important disease. It has been variously estimated that the ratio of inapparent to paralytic infections is between 100 and 850 : 1, and it is now thought that the virus reaches the nervous system via the blood stream rather than via peripheral nerves from the pharynx or intestinal tract.

Abortive Cases

A small proportion of cases (24-5%) present as a