

patients in whom a nipple was made there was continence of faeces and only three of these had an occasional leakage of flatus; none required an ileostomy appliance.

Other surgeons are now reporting their experience with the operation. Cameron⁴ has treated six patients; one died in hospital from unconnected causes and in one the operation had been performed only recently, but of the four remaining three were continent (catheterizing the stoma two to four times daily) and one incontinent. Beahrs and his colleagues⁵ from the Mayo clinic have created an ileal reservoir in 20 patients. There was no surgical mortality. One patient developed intestinal obstruction just proximal to the pouch during the postoperative period, which made it necessary to remove the pouch and establish a conventional ileostomy. During the follow up period of up to two years, three more patients required re-exploration. One of these had recurrent inflammatory disease of the ileum and two more had intestinal obstruction requiring division of adhesions. About half of patients have experienced some difficulty in inserting the catheter for evacuation and one has preferred not to intubate the reservoir at all but to permit it to overflow into a conventional appliance. Among 14 patients in whom a nipple was not created nine usually wear an appliance because of incontinence, though spillage may amount to only 10 to 50 ml per day. Six of these patients are not continent for flatus. In the five patients in whom a nipple was created as a valve three are continent of both gas and fluid and do not require an appliance.

The reservoir operation can be performed either at the time of colectomy or on patients who already have an established conventional ileostomy. Clearly this technique still requires evaluation, since results improve with greater experience of the procedure. Selected patients who abhor an incontinent ileostomy may be offered the operation, but they must accept the fact that continence cannot be guaranteed and that there is inevitably a morbidity from the procedure.

¹ Brooke, B. N., *Lancet*, 1952, 2, 102.

² Kock, N. G., *Archives of Surgery*, 1969, 99, 223.

³ Kock, N. G., *Progress in Surgery*, 1973, 12, 180.

⁴ Cameron, A., *British Journal of Surgery*, 1973, 60, 785.

⁵ Beahrs, O. H., *et al.*, *Annals of Surgery*, 1974, 179, 634.

Cytomegalovirus Again

Intrauterine cytomegalovirus infection has been estimated¹ to be responsible for damage to the central nervous system manifested as mental retardation in over 400 children born in England and Wales each year. In many other children there may be subtler changes, particularly deafness and minor degrees of intellectual impairment. The virus is also known to cause in adults an acute febrile illness resembling infectious mononucleosis,² a few cases of hepatitis,³ and what was once called the post-perfusion syndrome.⁵ This is a serious illness, sometimes fatal, in patients who have had several units of blood, usually after cardiac surgery or renal transplantation, and is in effect a Paul-Bunnell-negative mononucleosis. Though infection with cytomegalovirus is widespread it is seldom manifest as serious illness except in the fetus and in those naturally immunodeficient or artificially immunosuppressed. Symptomless infection occurs, with prolonged excretion of the virus in the urine, particularly in children and in pregnant

women. In pregnancy there is a considerable rate of excretion via the cervix, especially in some races.⁶ The prevention of the effects of the virus depends on protecting from chronic excretors those at risk—the unborn fetus (through the person of its mother), patients undergoing major surgery, and the immunodeprived. Since most chronic excretors go unrecognized this means, in effect, the maintenance of that ill-defined thing general hygiene. That such a measure is effective is borne out by the fact that the incidence of cytomegalovirus infection rises as socioeconomic status, with its concomitant poor standards of housing, sanitation, and personal hygiene, falls. Further support comes from the 50% incidence of infection in institutionalized children,⁸ a figure reminiscent of the carriage of Australia antigen in institutions.⁹ Also reminiscent of hepatitis B is the tendency for infections in childhood, rather than those in adult life, to be symptomless.

One of the difficulties in the study of cytomegalovirus has been simply the lack of accurate, well-attested information about what is going on—largely because few laboratories have been equipped, qualitatively or quantitatively, to glean information about the virus rather than because of any intrinsic difficulty in techniques. A recent survey by Deibel *et al.*¹⁰ based on three years' experience of the virus in the population of the State of New York as a whole (excluding New York City) is therefore of interest and importance as a large-scale study of a definite population. The total number of patients from whom specimens were submitted for diagnostic virology was 1,171. The congenital infections formed the biggest single group, with postoperative infections next, and then immunodeficiencies (natural or induced). After this came fever of uncertain origin and an assortment of miscellaneous conditions. The authors concluded that a diagnosis of cytomegalovirus should be considered in cases of otherwise unexplained fever in patients with splenomegaly, hepatitis, mononucleosis, or lymphadenopathy. It was possible to isolate the virus in just over 14% of suspected cases and, perhaps disappointingly, to make a serological diagnosis by complement fixation in rather less. Thirty patients with positive laboratory findings were followed for periods up to three years. Of these, 13 excreted virus for 10-12 months, and five for 1-3 years.

In addition, a serological study of 4,721 healthy individuals showed that over 90% of the population acquired infection during their lifetime, but that this might be delayed until quite late in life. At the age of 25 only a third of the healthy adults had evidence of present or past infection with cytomegalovirus. This means that two-thirds or more of women in New York State enter pregnancy susceptible to the virus. The comparable figures in England and Wales¹¹ are about 40-45%—no doubt a consequence of the freedom from infection in childhood in these women, but it raises the question of the need for a vaccine. Ultimate protection depends in large measure on vaccination of those at risk, and since the virus can be grown in cells in culture relatively easily it is not surprising that vaccination is being attempted and preliminary results with a potential vaccine have recently been reported. Elek and Stern¹² gave a live-tissue-culture-adapted strain of cytomegalovirus to volunteers taken from medical students and laboratory staff. Increasing doses were given to successive individuals, subcutaneously, and there were no important side effects apart from some enlargement of axillary lymph nodes. The objection has been voiced that the virus may have oncogenic potential.¹³ This is in fact true of several members of the herpesvirus group, but it is also true of several viruses of other groups used for vaccination in man. In any case, as Elek and Stern¹⁴ say in their reply to this criticism, "... one is compelled to weigh the

real advantages of preventing a common disease, with its tragic and long-lasting effects on entire family units, against the still theoretical possibilities of a cancer hazard."

Cytomegalovirus is a virus of paradoxes. It is a potential killer, but most of the time it appears to be innocuous. Infection is frequent, laboratory techniques not difficult, but interpretation of serological results far from easy. Indeed, it is one of the few virus infections where it has been suggested¹⁰ that serological diagnosis on a single titre or even a four-fold fall in titre may be allowable. Its spread is permitted by poor hygiene, but improved hygiene means a greater risk of primary infection at child-bearing age. Isolation of the agent from the urine is fairly easy, but it may also be sequestered in the circulating leucocytes, and hence be relatively inaccessible to culture. Medical advances in other fields (cardiac surgery, renal dialysis and transplantation, massive blood transfusion, immunosuppression) mean greater opportunities for spread, and more susceptibles created and exposed.

The control of infection by cytomegalovirus must be based on the same principles as the control of any other infection: detection of the sources, breaking the chain of infection, and the creation of a population of immunes by vaccination. The risks of oncogenesis by cytomegalovirus (never absent, in theory, from any virus) have probably been exaggerated, and in any case they rest on extrapolation of incomplete data from similar viruses. Certainly the prevention each year of 400 cases of gross mental retardation (let alone lesser degrees of impairment) in Britain alone would be a great prize.

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- ³ Lamb, S. G., and Stern, H., *Lancet*, 1966, 2, 1003.
- ⁴ Carter, A. R., *British Medical Journal*, 1968, 3, 786.
- ⁵ Kääriäinen, L., Klemola, E., and Paloheimo, J., *British Medical Journal*, 1966, 1, 1270.
- ⁶ Montgomery, R., Youngblood, L., and Medearis, D. N., *Pediatrics*, 1972, 49, 524.
- ⁷ Numazaki, Y., et al., *American Journal of Epidemiology*, 1970, 91, 410.
- ⁸ Diosi, P., et al., *Pathologica Microbiologica*, 1966, 29, 513.
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- ¹⁰ Diebel, R., et al., *New York State Journal of Medicine*, 1974, 74, 785.
- ¹¹ Walker, G. H., and Tobin, J. O'H., *Archives of Disease in Childhood*, 1970, 45, 513.
- ¹² Elek, S. D., and Stern, H., *Lancet*, 1974, 1, 1.
- ¹³ McDougall, J. K., and Harnden, D. G., *Lancet*, 1974, 1, 135.
- ¹⁴ Elek, S. D., and Stern, H., *Lancet*, 1974, 1, 171.

Smoking and the Common Cold

Smokers are well-known to be prone to chronic bronchitis, but not all of them develop the airways obstruction which can lead to disability and death.¹ A number of other factors have been invoked to account for this selective appearance of airways obstruction in smokers: these have included atmospheric pollution, development of emphysema and plasma α_1 -antitrypsin activity, bronchial reactivity, and lung infection. Bronchial infection was at one time thought to play an important role in producing and promoting airways obstruction, but there is now good evidence to conclude that the progress of airways obstruction associated with chronic bronchitis is unaffected by recurrent chest infections.²

Against this background a recent study³ of airways function during mild viral respiratory illnesses took a fresh look at the problem. Firstly, it studied healthy young subjects, looking in particular at function of small peripheral airways. Secondly, it was a prospective study largely of rhinovirus infections; 52

healthy subjects were selected for investigation, and those 22 who developed an upper respiratory illness were repeatedly studied until recovery had occurred. Though several organisms were identified, rhinovirus was the causative agent in 16 cases.

By studying healthy young subjects the authors were able to detect subtle abnormalities in lung function, and they used some of the newer techniques which purport to study small airway function.⁴⁻⁶ Of the tests available to do this the most promising at present are measurements of closing volume and maximal expiratory flow volume curves.⁷ Using these tests, smokers have been shown to be prone to develop small airways obstruction in the presence of normal FEV₁ (forced expiratory volume in one second) and vital capacity.⁵ In this recent study the authors found no change in lung volumes but were able to show a rise in closing volume and a fall in maximal expiratory flow rate at low lung volumes when the subjects were breathing a helium-oxygen gas mixture. These functional changes are consistent with obstruction in small peripheral airways and were seen only in the smokers and lasted between 10 and 60 days with a mean of about 30 days; this was less than the duration of symptoms, which on average lasted 36 days. Non-smokers showed no abnormality in lung function, and their symptoms averaged 17 days.

These findings suggest another harmful effect of smoking cigarettes. In addition to covert obstruction in peripheral airways, healthy smokers also appear to be more vulnerable to the effects of common chest colds than non-smokers; but the mechanism for the appearance or worsening of small airways obstruction is not clear. Abnormalities of tracheobronchial clearance have been shown following rhinovirus infection in smokers and non-smokers,⁸ and smokers have also been shown to clear particles more slowly from the bronchial tree than non-smokers.⁹ The viral interference with tracheobronchial clearance lasts for about 30 days, and it is possible that the functional changes are related.

What do the results of this latest study signify? At a purely practical level they draw attention to a factor that needs to be borne in mind if these newer tests of small airway function are to be used to screen for early airways obstruction.¹⁰ Smokers suffering from chest colds should not be screened until free from symptoms. Having distilled this practical conclusion, what is left? It is difficult to do more than speculate at this stage, in view of the evidence which shows the progress of advanced airways obstruction to be little influenced by the frequency and severity of bronchial infections. These changes in small airway function were reversible, but it can be argued that some residual damage may have been produced in the small airways; and later in the disease these small airways are known to be mainly concerned in the development of crippling airways obstruction.¹¹ Whether or not this chain of events is substantiated the conclusion is obvious; it is more practical to stop smoking than avoid chest colds.

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