maintain body weight the reduction in saturated fat must be countered by another source of calories. An increase in carbohydrates might itself increase the risk of coronary artery disease by increasing production in the liver of triglyceride-rich lipoproteins[9] of very low density. This can be avoided by substituting polyunsaturated for saturated fat in the diet. To facilitate such dietary change the Committee of the New Zealand Heart Foundation[4] advocated that the composition of foodstuffs should be widely publicized and that those which contain polyunsaturated oils should have no restrictions placed on their availability. S. Dayton and colleagues[10] reported that the incidence of carcinoma was increased in a group of people on a diet high in polyunsaturated fat, but this observation does not appear to have been substantiated in other studies.[11] Certainly the New Zealand committee saw no reason for restricting the consumption of polyunsaturated fats even though it did not consider there was any particular need to promote their use in the whole population.

While it would seem sensible to endorse these recommendations there is clearly not enough evidence to justify a full-scale campaign aimed at changing the dietary habits of the nation.[12] But the accumulating evidence is impressive, and it seems likely that if it is clearly presented many people will wish to modify their diet. Though cigarette sales have not fallen precipitously, it is now clear that many other sensible people besides doctors have given up the smoking habit. To such people the fat on their bacon could become just as unnecessary as the smoke from their cigarettes.

1 Rifkind, B. M., *British Journal of Hospital Medicine*, 1970, **4**, 683.
2 Kannel, W. B., Castelli, W. P., Gordon, T., and McNamara, P. M., *Annals of Internal Medicine*, 1971, **74**, 1.
3 Carlson, L. A., and Böttiger, L. E., *Lancet*, 1972, **1**, 865.
4 National Heart Foundation of New Zealand, *Coronary Heart Disease —A New Zealand Report*. Dunedin. John McIndoe Ltd., 1971.
5 Keys, A., *Circulation*, 1970, **41**, **42**, Supplement 1.
6 Morris, J. N., and Gardner, M. J., *American Journal of Medicine*, 1969, **46**, 674.
7 Atherosclerosis Study Group, *Circulation*, 1970, **42**, A-55.
8 National Heart Foundation of Australia, *Medical Journal of Australia*, 1971, **1**, 1155.
9 Fredrickson, D. S., Levy, R. I., and Lees. R. S., *New England Journal of Medicine*, 1967, **276**, 34.
10 Dayston, S., *et. al.*, *Lancet*, 1968, **2**, 1060.
11 Ederer, F., Leren, P. Turpeinen, O., and Frantz, I. D., *Lancet*, 1971, **2**, 203.
12 Fredrickson, D. S., *British Medical Journal*, 1971, **2**, 187.

Presymptomatic Detection of Huntington's Chorea

Huntington's chorea is inherited in an autosomal dominant fashion. Symptoms usually begin after the age of 30, which means that people who develop the disease usually have already conceived their offspring by the time it first appears. The child of an affected parent who has seen the gradual progression of choreo-athetoid movements and mental deterioration to a totally crippled state and death is all too well aware that he himself has a 50% chance of developing the disease. Suicidal depression is not unusual in this group of people. If some effective method were available for detecting the gene for Huntington's chorea before the development of signs and symptoms, it would at least be possible to reassure half of these patients who are at risk.

There are indications that such a test may now be possible. Two groups of workers have recently reported on the use of levodopa in the investigation of people genetically at risk of developing the disease.[1-3] The basis of the test is that patients with Parkinson's disease who are treated with levodopa in high dosage frequently develop dyskinesias, including choreo-athetoid movements very similar to those seen in Huntington's chorea. It is possible that Huntington's chorea is due to an abnormal reaction to dopamine. It is therefore also posible that such movements may be induced by levodopa in asymptomatic persons who are later to develop the disease. In a recent report[3] patients and controls received levodopa in gradually increasing doses to a maximum of 2·5 g daily for a total of 10 weeks. In a second part of the study levodopa at a dose of 800 mg/day was given in combination with a peripheral dopa decarboxylase inhibitor. The age range studied was from 17 to 33 years. None of the 24 controls developed dyskinetic movements on either regimen. However, about a third of the people genetically at risk of developing Huntington's chorea did develop such dyskinetic movements.

Many things need to be elucidated before the levodopa test can be accepted as an effective method for the detection of presymptomatic Huntington's chorea. Though false positive reactions appear to be unlikely, a larger series of normal persons will be required to make certain that an occasional normal person may not develop dyskinetic movements during this test. Moreover, it still remains to be proved that the people who develop dyskinetic movements will in fact go on to the full development of Huntington's chorea. Though they seem likely to do so, a long follow-up of these positive reactors is awaited with interest. Finally, a negative response in a person genetically at risk of developing the disease cannot be regarded as proof of the absence of the gene for it. Again a long follow-up will be required to find out the proportion of false negative responses and at what period in the life of the patient a false negative response can be expected to occur.

Until these questions have been answered it will be difficult to know exactly what to tell the patient. In fact it has been discussed whether it is ethical even to carry out such investigations until an effective treatment for Huntington's chorea is available.[4] At present the only reasonable way in which the results of the test may be applied is in advising individuals on the risk of transmitting the disease to children. Many people seek advice on whether there is any sign of their having the disease before they embark on a family of their own. If the reaction to levodopa is positive, it is probably reasonable to explain that there is a possibility that the disease might be passed on to the children even though there is no certainty that the individual himself may develop it. This is the sort of advice that many of them are seeking.

1 Klawans, H. L., Paulson, G. W., and Barbeau, A., *Lancet*, 1970, **2**, 1185.
2 Cawein, M., and Turney, F., *New England Journal of Medicine*, 1971, **284**, 504.
3 Klawans, H. L., Paulson, G. W., Ringel, S. P., and Barbeau, A., *New England Journal of Medicine*, 1972, **286**, 1332.
4 Gaylin, W., *New England Journal of Medicine*, 1972, **286**, 1361.

Papovaviruses and Human Disease

The papovaviruses are small icosahedral (20-sided) viruses which have until recently seemed to be of only limited interest in clinical medicine. The group includes the various papilloma or wart viruses of man and animals, polyoma

virus (a mouse tumour virus), and the simian virus SV_{40}, which is found in monkey kidney tissue and which causes tumours on inoculation into hamsters.

Human wart virus, the first and so far the only known human tumour virus, was recognized many years ago,[1 2] but there is increasing evidence that there are other members of the group which can also be pathogenic for man. The disease with which they are mainly associated is progressive multifocal leucoencephalopathy—a rare neurological complication of debilitating diseases such as leukaemia and reticulosis[3-5] or of renal transplantation.[6] Clinically, progressive multifocal leucoencephalopathy shows a variety of neurological signs. Among the commonest are hemiparesis, dementia, impaired vision often with homonymous hemianopia, dysphasia, and hemianaesthesia. The cerebrospinal fluid is normal or shows only minimal changes. The disease is always fatal—usually within three to four months. Histologically, there are scattered foci of demyelination, mainly in the cerebral hemispheres, but the brain stem, cerebellum, or basal ganglia may also be affected. A characteristic feature of the lesions is the presence of oligodendrocytes with swollen nuclei containing intranuclear inclusions—a useful sign that a virus is probably involved. This observation was soon followed by the electron-microscopic detection of virus particles in affected cells, and it was noticed at an early stage that the particles were identical with those of the papovaviruses.[7-9]

The first report of successful culture of a virus from progressive multifocal leucoencephalopathy appeared last year when B. L. Padgett and his co-workers in Wisconsin isolated in cultures of human fetal glial tissue a papovavirus from brain extract from a case of the disease.[10] The virus was not serologically related to human papilloma, polyoma, or SV_{40} viruses and therefore appeared to be a new member of the papovavirus group. At the same time, Sylvia D. Gardner and her colleagues in London described the isolation of a papovavirus from the urine of a patient on immunosuppressive drugs after renal transplantation.[11] This patient did not have any neurological signs, but he had ureteric obstruction to which the infection with the virus probably contributed, since the ureteric cells were heavily infected with virus. Both the patient and his donor brother had antibody to the virus before operation, though the patient developed a considerable antibody rise postoperatively. This suggests that the patient's infection was the result of reactivation of virus infection which he had acquired at some earlier date. This papovavirus also proved to be different from papilloma, polyoma, and SV_{40} viruses, though it did have some minor antigenic relationship with SV_{40}. It is not known if these two new papovaviruses are related serologically, but they differed in certain biological characteristics, which suggests that they may be two different viruses.

In February this year the isolation of yet another papovavirus from two cases of progressive multifocal leucoencephalopathy was reported by L. P. Weiner and his co-workers in the United States.[12] But in this instance the virus appeared to be SV_{40} virus. It was isolated by a complicated technique which involved the fusion of cultured brain cells with kidney cells from the African green monkey; in one case the isolation was also made without fusion. The fused cells were then passaged into fresh cultures of the same monkey kidney cells. The choice of monkey kidney cells for these cultures was unfortunate, since they are notoriously liable to be contaminated with SV_{40}, though this is less likely with tissue from African green monkeys than with that from either rhesus or cynomolgus monkeys.[13] The authors, however, set up careful controls to eliminate the possibility that they had merely isolated a contaminant virus, and it seems probable that the isolates did indeed derive from the brains of the two patients. The fact that one patient developed antibody to the virus is further proof of this. Both isolates differed from the two new papovaviruses described last year but showed serological identity with SV_{40} virus.

This and the two earlier reports raise some important questions. For example, what is the source of these viruses? There is really no evidence about this except that both brothers involved in the kidney transplantation had been infected previously. It would be of great interest to know if antibody to this virus is present to any extent in the general population. The source of the SV_{40} virus in the case of the two patients with progressive multifocal leucoencephalopathy is also unknown. Many people in the United States were infected with SV_{40} in the late 1950s and early 1960s owing to the contamination of early batches of poliovaccine with the virus. However, though vaccination histories are not always reliable, neither of these patients seemed to have had poliovaccine. It is of some interest that antibody to SV_{40} virus has been found in sera from people who have never had poliovaccine,[14] so that there may be some as yet unknown way of acquiring infection with the virus. An alternative explanation is that there may be a naturally occurring human virus which is antigenically similar to SV_{40} virus of monkeys.

A second question concerns the role of these papovaviruses in human disease. It seems clear that at least one of the newly described papovaviruses as well as SV_{40} can cause progressive multifocal leucoencephalopathy. Possibly these papovaviruses are opportunistic in the sense that disease is produced only when the host defences are lowered by some pre-existing disease. Progressive multifocal leucoencephalopathy, for example, is almost always associated with some debilitating condition. Another papovavirus—namely, human wart virus—can certainly be opportunistic, since a surprisingly high rate of recurrence of warts has been observed in patients after renal transplantation.[15] In the case of the patient with the transplant who became infected with the new papovavirus, this virus too may have been opportunistic, since it seems to have been reactivated after transplantation, probably as a result of immunosuppressive therapy. Possibly the most interesting feature of these reports is the indication that there are at least two and perhaps three different papovaviruses involved. Clearly much remains to be learned about the ecology and interrelationships of these papovaviruses together with their role in human disease. Clinical virologists will doubtless be turning increasing attention to this hitherto somewhat neglected group of viruses.

[1] Strauss, M. J., Shaw, E. W., Bunting, H., and Melnick, J. L., *Proceedings of the Society for Experimental Biology and Medicine*, 1949, 72, 46.
[2] Strauss, M. J., Bunting, H., and Melnick, J. L., *Journal of Investigative Dermatology*, 1950, 15, 433.
[3] Ström, K.-E., Mancall, E. L., and Richardson, E. P., *Brain*, 1958, 81, 93.
[4] Cavanagh, J. B., Greenbaum, D., Marshall, A. H. E., and Rubinstein, L. J., *Lancet*, 1959, 2, 524.
[5] Richardson, E. P., *New England Journal of Medicine*, 1961, 265, 815.
[6] Manz, H. J., Dinsdale, H. B., and Morrin, P. A. F., *Annals of Internal Medicine*, 1971, 75, 77.
[7] Zu Rhein, G. M., and Chou, S.-M., *Science*, 1965, 148, 1477.
[8] Howatson, A. F., Nagai, M., and Zu Rhein, G. M., *Journal of the Canadian Medical Association*, 1965, 93, 379.
[9] Silverman, L., and Rubinstein, L. J., *Acta Neuropathologica*, 1965, 5, 215.
[10] Padgett, B. L., Walker, D. L., Zu Rhein, G. M., Eckroade, R. J., and Dessel, B. H., *Lancet*, 1971, 1, 1257.
[11] Gardner, S. D., Field, A. M., Coleman, D. V., and Hulme, B., *Lancet*, 1971, 1, 1253.

[12] Weiner, L. P., *et al.*, *New England Journal of Medicine*, 1972, **286**, 385.
[13] Sweet, B. H., and Hilleman, M. R., *Proceedings of the Society for Experimental Biology and Medicine*, 1960, **105**, 420.
[14] Shah, K. V., Ozer, H. L., Pond, H. S., Palma, L. D., and Murphy, G. P., *Nature*, 1971, **231**, 448.
[15] Spencer, E. S., and Andersen, H. K., *British Medical Journal*, 1970, **3**, 251.

Urinary Tract Infection in Newborn

Infection of the urinary tract in infancy and childhood is a dangerous condition. In about half the cases radiological investigation shows an abnormality such as pyelonephritic scarring or vesicoureteric reflux.[1 2] It may be associated with progressive renal damage unless the infection is controlled.

The peak incidence is during the first 4 weeks of life,[3] and at this age mortality is high during the acute stage of the illness. But despite the possibility of reliable diagnosis from examination of the urine and effective treatment with antibiotics cases probably still remain undetected. The problem is that at this age the symptoms are varied and most of them are nonspecific.

In a recent review[4] of 66 infants with urinary tract infection in the first month of life J. M. Littlewood found that the commonest features were low weight, pyrexia, lethargy, and gastrointestinal symptoms such as anorexia, vomiting, and loose stools. Though the kidneys were palpable in more than half the patients, in only some were they thought to be enlarged. In no case did a macroscopic abormality of the urine or an observed disorder of micturition draw attention to the diagnosis. The more serious symptoms such as dehydration, irritability, and convulsions were found in only a minority of patients, probably as a result of early diagnosis in this series. Jaundice, which occurred in 11% of the cases, has been reported before as a result of renal tract infection,[5] but could be a trap for the unwary. Boys were more often affected than girls, and predisposing factors were an abnormal mode of delivery, perinatal anoxia, and low or high birth weight.

It is not easy to obtain uncontaminated urine from infants, and quantitive culture[6] is especially useful in this age group. However, obvious bacteriuria on simple microscopy of fresh uncentrifuged urine correlates well with a count of more than 100,000 organisms per ml on culture. The problem of contamination can be overcome by obtaining urine by suprapubic puncture, and provided conditions are suitable this is a safe techniques in infants.[7] Littlewood also confirmed the well-known facts that neither the absence of proteinuria nor the absence of pyuria excludes the diagnosis of infection.

The severity of the illness in newborn babies in contrast to adult patients was emphasized by the finding of a positive blood culture in 30% and a blood urea higher than 50 mg/100 ml in over half of the patients. The overall mortality was 11%. Two of the deaths occurred in infants with major congenital abnormalities of the urinary tract incompatible with survival, while the other five were of patients treated some years ago by means (alkalis and sulphonamides) which would be considered inadequate now. No deaths occurred in the latter part of the series, when ampicillin was the drug of choice and streptomycin or chloramphenicol were used for the more severely ill infants. Pyelonephritis in infancy can cause acute renal failure, which may be completely reversible and peritoneal dialysis has been used successfully in this situation.[8]

The clinical features of neonatal urinary infection may be classed in four groups: firstly, a severe systemic illness, often with septicaemia, and with clinical evidence of pyelonephritis; secondly, infection secondary to a major congenital abnormality of the urinary tract; thirdly, mild nonspecific symptoms with no signs to incriminate the renal tract; and, fourthly, asymptomatic infants in whom infection of the urine is an incidental finding. The clinical spectrum is so wide that urinary tract infection should be suspected in any newborn baby whose progress is in any way abnormal, and examination of the urine should be carried out as a routine.

[1] Smellie, J. M., Hodson, C. J. Edwards, D., and Normand, I. C. S., *British Medical Journal*, 1964, **2**, 1222.
[2] Rolleston, G. L., Shannon, F. T., and Utley, W. L. F., *British Medical Journal*, 1970, **1**, 460.
[3] Stansfeld, J. M., *British Medical Journal*, 1966, **1**, 631.
[4] Littlewood, J. M., *Archives of Disease in Childhood*, 1972, **47**, 218.
[5] Arthur, A. B., and Wilson, B. D. R., *British Medical Journal*, 1967, **1**, 539.
[6] Kass, E. H., *Transactions of the Association of American Physicians*, 1956, **69**, 56.
[7] Pryles, C. V., *Pediatrics*, 1965, **36**, 128.
[8] Meadow, S. R., Cameron, J. S., Ogg, C. S., and Saxton, H. M., *Archives of Disease in Childhood*, 1971, **46**, 221.

International Cancer Research

The permanent building of the International Agency for Research on Cancer (I.A.R.C.), a gift of the French, was formally opened in Lyons during June 1972. To mark the event the Agency's annual report for 1971[1] includes comments on general developments since it moved to its temporary quarters five years ago. From the outset the study of the role of environmental factors in the aetiology of human cancers has been central to the Agency's activities. Studies in cancer diagnosis and control remained the province of the cancer unit of the World Health Organization, with which a close liaison was established early on.

Organizing research on an international basis is expensive. Language barriers and politics are apt to add to the intrinsic problems of the research itself. But the research in the I.A.R.C.'s programme is essentially international. It was sensible for the Agency, therefore, to concentrate on cancer epidemiology, because the time was ripe for studies of cancer incidence in remote communities and on migrants from one country to another. The appropriate methods based on the use of computers had been developed, and there remain parts of the world still relatively unaffected by such features of modern Western life as motor cars, air pollution, and prepacked and processed foods.

The Agency has five units based in Lyons: epidemiology and biostatistics, environmental carcinogenesis, biological carcinogenesis, chemical carcinogenesis, and research training. In addition it helps to support regional centres in Nairobi, Singapore, and Jamaica. The fact that information reaches Lyons from cancer registries all over the world has enabled the I.A.R.C. to suggest improvements in the international classification of diseases. At the same time the Agency has been able to draw attention to cancer problems peculiar to particular communities or geographical areas—for example, the high incidence of laryngeal and hypopharyngeal cancers in Thailand among smokers of "keeyo," a mixture of tobacco and other substances. The publication[2] of the proceedings of a symposium on cancer and other chronic diseases in