the organized emboli produced experimentally in the pulmonary arteries of animals.[16-19] The lesions that result from encrustation differ, therefore, from both "atheroma" in human arteries, which is rich in lipid, and spontaneous atherosclerosis in animals, in which encrustation does not occur.[20]

The relatively non-sclerotic "fatty streak" in the human aorta has a different anatomical site and histological appearance[21] from fibrous and fatty atherosclerotic plaques. Likewise, these fatty streaks are common in the South African Bantu,[22] who develop only minor degrees of atherosclerosis. But the early fatty and non-sclerotic lesions, produced by feeding animals with a diet rich in cholesterol or triglyceride, develop eventually into fibro-fatty plaques resembling those seen in human atherosclerosis.[23-26] Cholesterol is in fact potent in producing sclerosis,[27] and will excite an inflammatory response just as severe as that which occurs when encrustations on the intima become organized. From these observations it can only be concluded that the lesions of atherosclerosis are as diverse as the pathogenic mechanisms that lead to their formation, and it may therefore be premature to regard any one of these atherogenic mechanisms as the sole factor that leads on to arterial occlusion.

Colds and Their Viruses

We can no longer talk about the "common cold virus," because many viruses which can cause colds are now known.[1,2] But to know that a virus exists and that it can cause a cold or other upper respiratory infection is only the beginning. Fortunately, many different groups of workers are now studying the problem, and from their results we are learning what varieties of disease some of the "new" respiratory viruses cause and also something of their prevalence and epidemiology.

For example, the parainfluenza virus type 2 was discovered in cases of severe infection of the lower respiratory tract—namely, croup or acute laryngotracheobronchitis of small children, a disease with which it seems to be causally connected.[3] Later it was found in the throats of adults suffering from relatively mild disease.[4] Then at the Common Cold Research Unit, Salisbury, the third clause of Koch's postulates was fulfilled by cultivating the virus *in vitro* and causing disease on giving it back to man. A mild cold-like disease with relatively little coryza was produced in eight out of twenty-eight volunteers.[5] Also during last year a careful study of a small epidemic of parainfluenza virus type 2 infection has been reported.[6] The outbreak occurred in a children's home, and two results were of special importance. One was that a correlation was found between the presence of the virus in the throat and the occurrence of a febrile illness—two-thirds of 15 infected children were ill. The other was that the illness observed was "croup" in only one case; in the remaining nine it was upper respiratory illness or fever only, and there were two cases of otitis media.

This was an isolated epidemic and the conditions were quite unlike general practice, but Drs. J. E. Banatvala, T. B. Anderson, and B. B. Reiss in this issue of the *B.M.J.* describe (page 537) the importance of parainfluenza viruses in the "run-of-the-mill" respiratory infections seen so frequently by the general practitioner. They attempted both to isolate parainfluenza viruses and to detect infection by serological tests. However, they studied only febrile cases, and many patients in their practice may have had milder diseases which they never reported to the doctor. They found parainfluenza type 1 was the commonest virus and type 3 was less so, but 2 of 21 parainfluenza viruses isolated from children belonged to type 2. By serological tests they also recognized fourteen cases of infection with parainfluenza viruses in adults. There appeared to be an epidemic wave of infections with the type 1 virus. The illness often seemed to spread to other members of the family, children rather than adults being affected, and on a few occasions infection with the same virus in both patients was diagnosed by laboratory tests. The illness was marked by cough and a hoarse voice; barely half of the children had a running nose or sore throat.

Various other viruses related to the enteroviruses have been isolated from patients with colds. They have been named ECHO 28 virus, Salisbury strains, entero-like or enteroviruses, coryzaviruses, and muriviruses. It is now known that all these viruses may be distinguished from enteroviruses in the laboratory because they are unstable in acid solution (*p*H 3 to 5)[7,8] and it has been agreed to call them all rhinoviruses,[9] and to combine them with enteroviruses into the larger group of the *picorna* viruses—that is, small (*pico*) viruses containing R.N.A. as their nucleic acid. The rhinoviruses are called M strains if they affect monkey cells as well as human cells *in vitro* and H if they attack human cells only.

There are numerous serotypes of rhinoviruses, but they all seem to cause colds when given to human volunteers, a disease which is generally afebrile and milder than that described by Dr. Banatvala and his colleagues. Several groups of workers are now studying the distribution of these viruses in various populations. D. Hamre and J. J. Procknow,[10] found six parainfluenza viruses and nearly a hundred rhinoviruses in 406 cases of common colds in medical students. They showed that certain individuals who had repeated colds had repeated infections with rhinoviruses as well as infections with parainfluenza viruses. They rarely recovered viruses from subjects without colds. An investigation at an American military base also showed an association in adults between colds and infection with rhinoviruses, while a wave of M rhinovirus infections was found to be distinct from a wave of H rhinovirus infections. Rhinoviruses were recovered from children less frequently than from adults.[11] The illnesses in adults were typical mild colds which could not be distinguished clinically from colds due to Coxsackie A21 virus (Coe virus), though a group of illnesses produced

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by adenoviruses was on the average more severe and characterized by inflammation of the throat.[12]

In a recent study in Great Britain a rhinovirus was recovered from almost a quarter of 104 men who were found to have colds when they reached an R.A.F. camp from various parts of the country.[13] The viruses isolated fell into more than five different serotypes. The only other virus infections detected were one of influenza C and one of respiratory syncytial virus, and these may not have been the cause of the clinical symptoms. The work suggested that rhinoviruses were the main identifiable cause of colds in this population group. Two of the H rhinoviruses isolated have been further studied by inoculation to volunteers as described by Drs. D. Taylor-Robinson and M. L. Bynoe in this issue of the *B.M.J.* (page 540). They produced typical colds, but in addition interesting data were obtained on the antibody responses. Though virus was recovered from all the 19 volunteers who developed colds barely half of them developed antibody. The presence of a low titre of antibody prevented the volunteer from getting a cold, but the presence of antibody of higher titre did not prevent some volunteers from becoming infected and developing more antibody. These results differ in some respects from those obtained with M rhinovirus. Moreover it has been found that antibody responses to M. rhinoviruses are better than to H rhinoviruses.[14] The latter are therefore specially likely to induce repeated colds. A similar study in the U.S.A.[15] gave rather similar results.

Finally, the connexion between infections by the "new" respiratory viruses and relapses of chronic bronchitis is now being explored. Patients with this disease often seem to be especially susceptible to acute infection of the respiratory tract, and exacerbations of their chronic illness are often said to arise from a common cold. In a nine-month study of thirty cases and ten controls in the U.S.A. a non-bacterial infection was detected by means of specimens collected from twenty-four out of forty-six cases of acute respiratory illness and not in control specimens. Eight infections were by respiratory syncytial virus, four by influenza A2, four by *Mycoplasma pneumoniae* (Eaton's agent),[16] and others were by adenovirus, parainfluenza, psittacosis, and *Rickettsia burneti* (Q fever).[17] Rhinoviruses were not detected though they were sought in some of the cases. In Great Britain infection by respiratory syncytial virus has been noted in association with chronic bronchitis in relapse and pneumonia among adults[18] and with acute bronchiolitis and pneumonia in infants.[19 20] We are still a long way from understanding thoroughly the viruses which cause colds and their complications, but we have every reason to be pleased with recent progress in this field.

Liver and Lung Transplantation

Transplantation of the liver is a formidable operation technically and at present the source of material for clinical transplantation must of necessity be the cadaver. In the last few years reports of experimental liver transplants in dogs have appeared.[1-5] The liver can be transplanted to the normal hepatic bed or alternatively to some other site. The first procedure entails removing the recipient's own liver before the donor liver can be transplanted, which adds considerably to the hazard. But to transplant a liver to another part of the body raises problems in forming the portal circulation and the biliary drainage and in accommodating the bulky friable organ at its new site.

The liver is exceedingly sensitive to ischaemic damage, more so even than the kidney, and since the operation is technically more difficult to perform than renal transplantation the risk of damage to the liver during the surgical transplantation is high. In the technically successful experimental studies the livers have been shown to function moderately well for a few days and then to be rejected in a similar manner to kidneys, with a cellular infiltration of the liver parenchyma and liver-cell necrosis. No long-term survivors have been reported experimentally.

Experience in transplantation of the liver in man has recently been published by T. E. Starzl and colleagues from Denver.[4-6] The diseases from which the recipients suffered were congenital biliary atresia, Laennec's cirrhosis with a primary hepatoma, and intrahepatic duct-cell carcinoma. The livers were obtained from the cadavers of patients of the same major blood group as the recipients.

The first donor died during an operation for removal of a brain tumour, the second from an astrocytoma, and the third from a cerebral haemorrhage. Immediately after death the femoral artery and vein were catheterized, the catheters being inserted into the abdominal aorta and vena cava respectively. The cadaver was then perfused with 5% dextrose at 15° C. To the perfusate were added procaine hydrochloride, penicillin, heparin, and in one case prednisone as well. The livers of both donor and recipient were removed simultaneously. The operation on two of the three recipients was done in stages. The first stage consisted in preparation of the recipient for hepatectomy by dissection of the structures subsequently to be anastomosed to the homograft. The second stage was the transplantation. As soon as the inferior vena cava was clamped the return of blood to the heart from the lower part of the body was effected by an external by-pass from the inferior vena cava via the femoral vein to a jugular vein. In one patient biliary drainage was provided by a cholecystojejunostomy and in the other two patients by choledochodochostomy, the common duct being drained with a T-tube. Drugs to inhibit the immune response were given; in addition the spleen was removed from the first two patients and the thymus also from the first.

The first patient bled to death on the operating-table four hours after transplantation. The second and third patients lived 22 and 7½ days respectively, both dying from multiple pulmonary emboli. The time intervals from the death of the donor to revascularization of the homograft in the recipient were 465, 152, and 192 minutes.

During the operation abnormal bleeding occurred in all patients, owing apparently to an explosive increase in plasma fibrinolytic activity soon after removal of the liver. Postoperatively a state of hypercoagulability developed, which probably contributed to inducing the pulmonary emboli. Hepatic functions were deranged immediately after operation, but in the two patients who survived for some days liver function progressively improved and no evidence of homo-

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