campaign should also target teenagers and emphasise that smoking is an important cause. Tobacco advertising should be banned.

Secondly, a short course of teaching by oral surgeons should be introduced into the curriculums of all medical schools so that doctors, who are responsible for referring 40% of patients with oral cancer, are educated in examination and diseases of the mouth at the beginning of their careers. Finally, the free dental check up should be reintroduced, as recommended by the House of Commons Select Committee on Health,²² so that casual patients with oral ulcers have no financial disincentives to attending a dentist for diagnosis.

The treatment of advanced oral cancer entails long, costly surgical operations and prolonged courses of radiotherapy and chemotherapy. The disease puts an immense emotional and physical strain on patients and their families. Now is the time for the government and the Department of Health to institute the measures outlined above in a nationally co-ordinated campaign to reduce the burden of this crippling disease.

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Asymptomatic infection with hepatitis C virus

Screening of blood donors is detecting people with unsuspected, but dangerous infection

The history of infectious hepatitis illustrates the ever-challenging battle between humans, micro-organisms, and disease. In the 1970s the organisms causing viral hepatitis types A and B were identified, allowing more accurate diagnosis and treatment, and the battle seemed to be on the way to being won. But nature persisted, and the term non-A non-B hepatitis was coined for the viral liver disease not due to hepatitis A or B virus, cytomegalovirus, or Epstein-Barr virus. Without specific assays the diagnosis of non-A non-B hepatitis was based on exclusion. The disorder accounted for 75-90% of cases of post-transfusion hepatitis, but it also included enterically transmitted, sporadic, endemic, and community acquired disease.¹ In developed countries this type of hepatitis is second only to alcohol as a cause of chronic liver disease, cirrhosis, and hepatocellular carcinoma, but its treatment remains problematic.²

Most non-A non-B hepatitis is due to a single virus, hepatitis C virus, and with cloning of its virion, a positive single stranded RNA molecule,³ the diagnosis of liver disease became more reliable. Further precision came with assays for specific antibodies to hepatitis C⁴ and, more recently with identification of hepatitis C virus RNA in the serum by reverse transcriptase polymerase chain reaction—a marker for viraemia and the infectious state.⁵

Three papers in this issue (p 695, 696, 697) present some of the important current issues in relation to an even more difficult problem—that of asymptomatic hepatitis C.⁶⁻⁸ Ryan *et al* found that many asymptomatic “healthy” people with antibodies to hepatitis C virus are detected during screening of blood donors (obligatory since 1991), screening of relatives of patients with known hepatitis C, and screening by health clinics. Some people with antibodies to hepatitis C virus who

seem healthy may, in fact, have raised serum transaminase activities—as do patients with chronic hepatitis C.

Serum markers for liver disease may be normal in healthy people whose serum contains antibodies to hepatitis C virus, but evidence is growing that most of these “healthy” people have histologically abnormal livers. Irving *et al* found that all but two out of 52 “healthy” blood donors infected with hepatitis C virus had abnormal liver biopsy tissue.⁸ The abnormalities ranged from fatty change, chronic persistent hepatitis, chronic active hepatitis to cirrhosis. These were more severe in men and correlated with peak circulating alanine aminotransferase activities, suggesting the people with repeatedly positive results on hepatitis C virus testing must have their liver pathology assessed by biopsy. Follow up of such people is essential if morbidity and mortality from liver disease is to be averted.

Several issues must now be addressed. Should further screening programmes be planned to pick up more of these “healthy” people in the community, since they may be at risk of future liver disease by a synergistic effect with other agents such as alcohol and drugs (paracetamol, aspirin)? Established chronic hepatitis C is an insidious disease, and its progress is usually monitored by repeated measurement of transaminase activities and hepatitis C virus RNA.⁹ It is difficult to recognise because it has a mild or subclinical course, clinical signs are often absent, and the transition from the acute to the chronic stage is silent.^{6,7} Once the condition has been diagnosed in someone who seems healthy, with or without abnormal results of liver enzyme tests, a liver biopsy seems essential. Subjects with an abnormal liver may progress to cirrhosis or hepatocellular carcinoma¹⁰ and so may warrant treatment.

Both Ryan *et al* and Bruno *et al* rightly suggest that it is timely to screen more widely for these asymptomatic "healthy" people who will need further investigation and possibly treatment. In the general population the prevalence seems to be around 1 in 1400. Screening for hepatitis C virus could well be more cost effective than current mass (non-targeted) screening for high serum cholesterol concentrations since the papers in this issue show that a positive test result indicates problems both for the person and for the community. Furthermore, prevention of the spread of hepatitis C virus infection must at present rely on effective screening programmes.

What should be done about a positive test result for hepatitis C virus? Counselling is essential, and Ryan *et al* have shown it to be effective on a limited scale. More studies of asymptomatic people will be needed to determine the precise risk of progression to chronic liver disease and the effects of treatment, when appropriate. At present the only results we have are of treatment of patients with hepatitis C. Up to half go on to have some form of chronic hepatitis and if untreated, up to a fifth of them may progress to cirrhosis.¹¹ Patients with community acquired hepatitis C may have a lower risk of cirrhosis; meta-analysis suggests that the disease progresses in one fifth of such patients and that two thirds of those develop chronic hepatitis.¹² Furthermore, Irving *et al* suggest that a substantial proportion of donors with repeatedly positive results on hepatitis C virus testing should have liver biopsies to assess any liver pathology.

What treatment is available for patients who are found to be positive for the hepatitis C virus? Interferon alfa at low to moderate doses for 6-12 months is the only effective treatment. This will return the transaminase activities to normal in 80% of patients¹³ and induce complete (25%) or temporary (50%) remission, at least during treatment.¹⁴ Interferon alfa is currently licensed for use in patients with hepatitis C virus and abnormal transaminase activities in a few European countries but not yet in Britain. Trials are needed of interferon alfa in the "healthy" asymptomatic people who are positive for hepatitis C virus and have histologically abnormal

liver tissue. But when this treatment is stopped, relapse rates are high in patients with chronic hepatitis C. In addition, repeated liver biopsy (necessary to assess the hepatic response to treatment) may not be acceptable to people who feel well. Measurement of the serum hepatitis C virus RNA excludes viraemia but tells us nothing about the liver.

The issues highlighted by the papers in this issue have clear implications for the nation's health and preventive medicine. A nationwide policy is needed—with the appropriate resources—for identifying, following up, and treating asymptomatic people with hepatitis C virus infection to prevent cirrhosis in those people and the spread of hepatitis C in the population. Many of the crucial questions about treating this disease remain unanswered.

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Reactive arthritis

Large, multicentre prospective trials are needed to establish the best treatment

Reactive arthritis is an aseptic arthritis that develops after an infection elsewhere in the body. The triad of arthritis, urethritis, and conjunctivitis—Reiter's syndrome—is one distinct variety of reactive arthritis.

Many micro-organisms may induce reactive arthritis, and new agents are continuously being added to the list, suggesting a pathogenic mechanism that is not antigen specific. The condition is associated most commonly with urogenital or enteric infections with *Chlamydia trachomatis*, *Yersinia enterocolitica*, salmonella, shigella, and campylobacter.^{1,2} Less common or more recently identified agents include *Clostridium difficile*, *Vibrio parahaemolyticus*, *Borrelia burgdorferi*, *Chl pneumoniae*, and ureaplasma. A type of reactive arthritis not associated with HLA-B27 may occur after infections with β haemolytic streptococci and neisseria. In about one quarter of all cases the triggering organism remains unknown.¹

Between 60% and 90% of patients with postvenereal or postenteric reactive arthritis are positive for HLA-B27.^{1,2} The arthritis usually develops within four weeks of the primary infection; it is typically oligoarticular and asymmetric. Painful

joints and muscle and tendon insertions are common. Extra-articular manifestations occur in 10-50% of cases and include mucocutaneous symptoms, ocular inflammation, urethritis, nephritis, and carditis.^{1,2} The average duration of the arthritis is four to five months, but two thirds of patients have mild joint or tendon symptoms for more than a year, and 15-30% develop chronic arthritis or sacroiliitis.¹ The presence of HLA-B27 predicts prolonged and more severe disease.

Recent research has increased our understanding of the relation between host and microbial factors. High and persistent plasma concentrations of antibodies, mainly IgA, directed against lipopolysaccharides and also outer membrane proteins, have been found in serum from patients with reactive arthritis triggered by yersinia and salmonella, indicating chronic stimulation by bacterial antigens of lymphatic tissue associated with the gut.³⁻⁵ Recently, arthritic patients with persistently raised IgA antibodies to yersinia were found to harbour the bacteria in lymph nodes and intestinal biopsy specimens.⁴

Both lipopolysaccharide antigens from salmonella, shigella,