(figure). Maximum individual gall bladder contraction during infusion (79 (SEM 5)%) was significantly greater ($p<0.05$) than that after bolus injection (58 (5)%). Furthermore, when the variability of gall bladder volumes at the time of mean maximum contraction (that is, 20 minutes after bolus injection and at 60 minutes during infusion) was analysed gall bladder contraction after bolus injection ranged from 5% to 71% compared with 57% to 89% during infusion. Peak increments in plasma cholecystokinin during infusion (10.7 (SEM 0.7) pmol/l; 42 (2.7) ng/l), however, were significantly smaller ($p<0.0001$) than those after bolus injection (275 (25) pmol/l; 1.1 (0.1) μ g/l). Plasma cholecystokinin concentrations during infusion were significantly raised above basal value in all samples obtained during the 60 minute infusion period ($0.0001<p<0.05$), whereas after bolus injection plasma cholecystokinin concentrations were significantly raised for only 25 minutes ($0.0001<p<0.05$) (figure). After bolus injection of cholecystokinin all subjects experienced transient abdominal discomfort, cramps, nausea, and a feeling of facial flushing, whereas no side effects were reported during infusion of the hormone.

Effects of one minute bolus injection (●) and 60 minute infusion of cholecystokinin (○) on gall bladder volumes (top) and plasma cholecystokinin concentrations (bottom).

*Significant difference between bolus injection and infusion of cholecystokinin (see text).

Conversion: SI to traditional units—Cholecystokinin: 1 pmol/l $\approx$ 3.9 ng/l.

Comment

This study shows that a 60 minute infusion of cholecystokinin is a more efficient stimulus of gall bladder contraction than a bolus injection of the same dose. Gall bladder contraction during infusion of cholecystokinin was not only stronger but also more consistent and longer lasting than that after bolus injection. Hence this procedure may facilitate the visualisation of biliary tract abnormalities and is an important technique for the diagnosis of impaired gall bladder contraction. Furthermore, that maximum gall bladder contraction during cholecystokinin infusion is maintained for at least 30 minutes makes the exact timing of gall bladder imaging less critical.

Our finding that a 60 minute infusion of cholecystokinin is a more efficient stimulus than a bolus injection of the same dose is the more

interesting because peak plasma concentrations of cholecystokinin were substantially lower during infusion than after bolus injection of the hormone. Significant increases in plasma cholecystokinin, however, were observed for longer during infusion than after bolus injection. We therefore conclude that both the degree and the duration of the rise in plasma cholecystokinin are important for inducing gall bladder contraction. The relative ineffectiveness of the large increase in plasma cholecystokinin after bolus injection in inducing a more efficient gall bladder contraction may be related to various factors, such as sluggishness of the gall bladder to respond to stimuli and spasm of the cystic duct induced by supraphysiological plasma cholecystokinin concentrations.³ Interestingly, plasma cholecystokinin concentrations found during infusion of the hormone were comparable to those observed after intraduodenal instillation of fat and were accompanied by similar degrees of gall bladder contraction.

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Lack of correlation between fulminant form of viral hepatitis and retrovirus infection associated with the acquired immune deficiency syndrome (AIDS) in drug addicts

The observation in the past two years of a spread of infection of the acquired immune deficiency syndrome (AIDS) in our area¹ and a remarkably increased use of intravenous drugs in cases of viral fulminant hepatitis (not entirely explained by the wide circulation of hepatitis viruses in drug addicts, as the prevalence rises from 20% in uncomplicated cases to about 70% in fulminant ones)² has led us to investigate a possible role of AIDS associated retroviruses in determining this condition.

Patients, methods, and results

We investigated antibodies to AIDS associated retroviruses in 18 consecutive patients referred to our department over the past 24 months (May 1983-May 1985) for viral fulminant hepatitis: 13 had hepatitis B virus, six of whom had hepatitis delta coinfection and three hepatitis delta superinfection, and five had non-A, non-B virus (15 men aged 17-24); 13 of whom had a declared history of prolonged use of intravenous drugs. We also examined 156 cases of acute viral hepatitis as control patients (90 had hepatitis B virus, of whom 28 had associated hepatitis delta, and 66 had non-A, non-B virus), made up of 78 consecutive drug addicts and 78 patients matched by age, sex, and geographical provenance, admitted to our department during the same period.

Diagnoses were made according to international criteria and confirmed by necropsy in the 15 patients who died (83%). Antibodies to AIDS associated retroviruses were determined, as previously described,³ by indirect immunofluorescence on a human T cell line infected with AIDS associated retroviruses (E11/HUT-78), controlling specificity of the test on non-infected HUT-78 cells.

Among our 18 patients with fulminant hepatitis, one of the 13 who were drug addicts and none of the five who were not drug addicts had antibodies against AIDS associated retroviruses. Among the 156 patients with uncomplicated acute hepatitis, six of the 78 who were drug addicts had antibodies but none of the 78 who were not drug addicts had them. Antibodies against AIDS associated retroviruses were thus significantly more common among drug addicts than

among non-addicts but were equally common among those addicts who developed uncomplicated acute hepatitis as among those who developed fulminant hepatitis.

Comment

Though we cannot presume that they are present in all infected subjects, antibodies to AIDS associated retroviruses seem to represent their past or present infection.⁴ Moreover, the immunofluorescence test constituted a sufficiently sensitive and specific method and valid alternative to the Western blot procedure.³ Available information indicated that AIDS associated retroviruses replicate preferentially in the OKT4 positive lymphocytes, inducing a strong cytopathogenic effect in vitro on these cells, which are crucially decreased in AIDS, and interfering with the immunological balance of the host.³ Theoretically, therefore, their infection may affect the development of a fulminant form in association with a hepatitis virus.

Our findings show basically the same prevalence of antibodies against AIDS associated retroviruses in both uncomplicated and fulminant viral hepatitis in drug addicts. Even considering that, as in a few subjects with AIDS, these antibodies are not detectable in a few cases of fulminant hepatitis, our observations seem to exclude any responsibility of AIDS associated retroviruses in determining this condition.

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Family outbreak of cryptosporidiosis

Cryptosporidium spp are a fairly common cause of gastroenteritis in both immunocompetent and immunosuppressed subjects.¹ Transmission of infection may occur from direct contact with infected animals,² though many patients have no such history. The possibility of food and water borne infection and direct person to person transmission is being explored. We report a family outbreak of cryptosporidiosis that was probably acquired from direct animal contact and spread within the family.

Patients, methods, and results

A family of three children, two parents, and two grandparents, on holiday in Devon, visited a dairy farm on 8 April 1985 that was open to the public. Two of the family (cases 5 and 7) drank raw milk on the farm as milk shakes. The family witnessed the birth of twin calves, standing within 2.7 m (3 yards) of the birth. Both calves were heavily contaminated with faeces. The family were also in close contact with kid goats and lambs.

From 11 April to 20 April one child (case 1) suffered from diarrhoea, with three to four watery pale stools each day that had an offensive smell, and sporadic abdominal pain. No blood or mucus was present in the stool. Also on 11 April the grandmother (case 2) developed vomiting and malaise, and by the next day she suffered from nausea and severe pain in the right iliac fossa but had no diarrhoea. She was admitted to hospital with suspected appendicitis, but symptoms subsided over 48 hours. On 16 April, however, she had abdominal pain and diarrhoea (six episodes) for one day. Also on 16 April a child (case 3) who shared the grandmother's bedroom vomited and had abdominal pain and malaise. Two days later he developed diarrhoea that gradually worsened until 25 April. On 27 April another child (case 4) vomited and later developed diarrhoea and was unwell and lethargic for two to three days. On 8 May the mother (case 5), in the 38th

week of pregnancy, developed upper abdominal pain and on 9 May explosive profuse water diarrhoea with the characteristic odour of the other cases. Symptoms subsided before delivery on 22 May of a healthy infant, who did not develop diarrhoea.

Faecal smears were stained for cryptosporidium oocysts by the modified Ziehl-Neelsen method.³ Positive results from stools were confirmed by Rhyl Public Health Laboratory. Smears of stools from three patients (cases 3, 4, and 5) obtained on days 9, 10, and 3 after onset of symptoms, respectively, were positive for oocysts (table); but oocysts were not detected by day 18 in all three. Smears of stools from two patients (cases 1 and 2) obtained 36 and 34 days after onset were negative for oocysts. Scanty oocysts were identified in the mother's (case 5) stool sample two days before delivery, and stool samples three and 20 days after delivery were negative for oocysts. The infant remained asymptomatic, and oocysts were not seen in samples obtained on days 1, 2, 4-6, 8, 9, 15, and 21.

Details of family members by age, sex, onset of symptoms, and results of stool samples

Case No	Member of family	Age (years)/Sex	Date of onset of symptoms	Days after onset, or date, when stool samples collected	Positive stool samples (days after onset)
1	Child	5/F	11 April	36	
2	Grandmother	56/F	11 April	34	
3	Child	6½/M	16 April	9, 17, 25	9
4	Child	2½/M	27 April	10, 18, 24	10
5	Mother	33/F	8 May	3, 7, 13, 18, 35	3, 7, 13
6	Father	34/M		15 May	
7	Grandfather	66/M		15 May	

Initially, stool samples were examined for shigella, salmonella, and campylobacter by standard methods and all yielded negative results. Antibodies to campylobacter were not detected in serum from the grandmother (case 2) obtained 34 days after onset of symptoms.

Faecal samples from animals on the farm were not obtained at the time of the outbreak, but samples taken from cattle seven weeks later were negative for cryptosporidium.

Comment

Three confirmed and two probable cases of cryptosporidiosis occurred after a visit to a dairy farm. Symptoms were typical of cryptosporidiosis in immunocompetent subjects.⁴ The source of infection for two patients (cases 1 and 2) could have been direct contact with farm animals; calves are a known source of infection.² If this did occur the incubation period in both was three days. One patient (case 3) could have been infected at the same time with an incubation period of eight days, though secondary spread from the patient in case 1 could have occurred. The infection of two patients (cases 4 and 5), who were ill 16 and 27 days after the first cases, probably resulted from secondary spread within the home. One patient (case 4) developed symptoms nine days after onset of diarrhoea in case 3 and another (case 5) became ill 11 days after onset of diarrhoea in case 4.

We were concerned that the mother could have transmitted infection to her newborn infant, but excretion of oocysts was not detected at delivery. Further excretion was not stimulated by the stress of delivery, and transmission to the infant was not detected.

This outbreak suggests that cryptosporidium infection can cause illness with severe abdominal pain before onset of diarrhoea, mimicking appendicitis, as in infections with campylobacter, yersinia, and some strains of escherichia. There was evidence of spread within the family between siblings and from child to mother, and the incubation period ranged from three to 11 days.

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