In the case of non-A, non-B hepatitis, enteric infection in adults has been assumed because studies of acute hepatitis in Egypt and Sudan have not identified parenteral risk factors, but the absence of a specific serologic test for non-A, non-B hepatitis prevents definite conclusions. Blood transfusions, parenteral medical therapy, crowded living conditions, and tattooing have been identified as potential risk factors for hepatitis B infection. For most hepatitis B infections, however, a source of transmission has not been found. Studies conducted at NAMRU-3 of the plasma-derived hepatitis B vaccine have shown that this vaccine is efficacious when given to schistosomiasis-infected populations without hepatosplenic problems. In individuals with hepatosplenic schistosomiasis, vaccine response is inversely related to spleen size and may not be adequate for extended protection. Studies of the efficacy of yeast-derived recombinant hepatitis B vaccines in patients with low level infection with schistosomiasis are currently in progress. The determination of preventable sources of viral hepatitis transmission and the development of new hepatitis vaccines are of primary importance. These will be the principal areas of future hepatitis research at NAMRU-3.

EPIDEMIC NON-A, NON-B HEPATITIS: A MAJOR CAUSE OF ENDEMIC AND EPIDEMIC HEPATITIS IN DEVELOPING COUNTRIES, MS Khuroo, Riyadh Armed Forces Hospital

The availability of markers for HA and HB has provided the opportunity to recognize hepatitis which cannot be attributed to either. The diagnosis of NANBH is thus one of exclusion. There is convincing epidemiologic and experimental evidence for existence of two types of NANBH — one related to parenteral exposure and prevalent in Europe, the USA, and Japan (PT NANBH) and the other related to fecal-oral exposure, occurring in epidemic and endemic forms, prevalent in the Indian subcontinent (E NANBH). The former has eluded researchers attempting to define the causative agent while the latter is caused by a 27-nm virus, distinct from HA and other related viruses. E NANBH was recognized for the first time by the author in an epidemic of viral hepatitis occurring in the Kashmir Valley. The epidemiology of this disease was described by our group in a series of subsequent reports. E NANBH causes major outbreaks of waterborne or water-related epidemics of VH. The disease causes significant morbidity and mortality and deserves consideration as a major health problem in developing countries. In endemic hepatitis in the Indian subcontinent over one half of the disease is caused by E NANBH. The disease has been recently reported in epidemic form in West Africa, Algeria, Burma, and Nepal. Endemic disease has been described in Central Asia, Lebanon, and possibly in Jeddah, Saudi Arabia. The disease occurs in adults with slightly higher prevalence in males. Pregnant women develop icteric VH eight times more often than men and nonpregnant women of comparable age. The occurrence of fulminant hepatic failure is markedly increased in the third trimester of pregnancy. Over one fifth of the patients present with predominantly cholestatic disease needing differentiation from large bile duct obstruction. The transaminase elevation is of moderate degree. The liver biopsy changes are very distinctive and in a classical case can be easily differentiated from all other known VHs. The lobular disarray is minimal with lobular injury presenting as focal necrosis with intense cholestasis and with distinctive bile plugs with pseudo-acinar formation in the lobules. The hepatic cell injury seems to be related to the cytopathic nature of the virus. All nonfatal patients make an eventual recovery with no occurrence of chronic hepatitis in the follow-up. A transmissible agent from acute phase fecal samples from nine patients with endemic disease has been identified in a volunteer and finally passed into monkeys. The disease has been transmitted to many species of monkey by three independent groups. All groups have identified similar 27-nm particles by IEM. The etiologic agent for various countries — namely Burma, Pakistan, India and West Africa — are similar and serologically related. Further characterization of the virus, a serological test for diagnosis, and possible vaccine for use during epidemic (especially in pregnant women) are badly needed and the prospects seem to be bright.

THE EFFECT OF DELTA VIRUS ON THE COURSE AND PROGNOSIS OF HEPATITIS B: PROSPECTIVE COMPARATIVE STUDY, H Ghaznawi, SY Abed, HA El-Deeb, E El-Sherbiny, College of Medicine, King Abdul Aziz University and Jeddah Fever Hospital

Although the epidemiology and pattern of infection of hepatitis delta virus is still far from adequately studied, it has been established that this virus requires hepatitis B virus for its replication and survival. In this study, delta virus was looked for in all patients with acute hepatitis B admitted to Jeddah Fever Hospital and were followed over a period of 2 years. It has been found that 60% of delta hepatitis patients tend to run a more prolonged course compared to other patients with hepatitis B, but negative for delta virus. Also, chronicity was found among 40% of delta hepatitis compared to 12% in the other group, the difference being statistically significant ($P \pm 0.05$). It was concluded that delta virus plays a major role in the pathogenesis and chronicity of hepatitis B. These findings emphasize the importance of prevention of hepatitis B by all means, especially vaccination, to reduce the incidence of hepatitis B infection and consequently delta virus infection.

## Rotavirus Diarrhea

BACTERIAL, PARASITIC, AND VIRAL ENTEROPATHOGENS ASSOCIATED WITH DIARRHEA IN SAUDI CHILDREN, S Ramia, MAA Al-Bwardy, AR Al-Frayh, AA Chagla, AA Al-Omair, MAF El-Hazmi, A Lambourne, H Bahakim, H Salman, College of Medicine, King Saud University, and Sulaymania Pediatric Hospital, Riyadh

In addition to rotaviruses which are now recognized as the most common cause of diarrhea among infants and young children in both developed and developing countries, new enteric pathogens have recently been recognized. These include *Campylobacter jejuni*, enteropathogenic *Escherichia coli* (EPEC), enterotoxigenic *Escherichia coli* (ETEC), and *Yersinia enterocolitica*. A 2-year (January 1985–December 1986) study of the different enteropathogens associated with pediatric diarrhea in Riyadh, Saudi Arabia, showed that rotavirus was the pathogen most frequently detected either as a single agent (44.3%) or in combination with other enteropathogens (7%). There were two peaks of rotavirus infection, one during the cold months (January–April) and the other during the dry months (July–September) of the year. After rotavirus, *Salmonella* was the most frequent enteropathogen isolated (8% cases; 2.9% controls) followed by *Campylobacter jejuni* (2.9% cases; 1.0% controls). No *Yersinia enterocolitica* was isolated and the association of EPEC with diarrhea in our pediatric

population was not statistically significant ($P < 0.02$). *Giardia lamblia* was more isolated in controls than in cases and neither *Entamoeba histolytica* nor *Schistosoma mansoni* could be detected. The high frequency of the various enteropathogens and the phenomenon of mixed infections observed suggest that diarrheal disease in Saudi Arabia is a complex and multifaceted problem.

ROTAVIRUS INFANTILE DIARRHEA: EPIDEMIOLOGY AND CONTROL, IH Holmes, University of Melbourne, Australia

Rotaviruses typically cause acute diarrheal disease in infants or the young of many kinds of animals, and appear to be the major single agent producing severe infantile diarrhea in humans. They are highly contagious and incidence of infections is little affected by improvements in hygiene and water supply, so control will depend on development of effective vaccines. Diagnosis usually depends on antigen detection in fecal samples by ELISA, but electrophoretic analysis of extracted viral RNA is also practical and gives more information on strain variations. Five serotypes affect humans, but serotyping remains difficult. Live viral and genetically engineered bacterial-based oral vaccines are being developed and current progress will be reviewed.

VIRAL ETIOLOGY OF GASTROENTERITIS AMONG CHILDREN ATTENDING RIYADH ARMED FORCES HOSPITAL, D Fairclough, D Waller, AM Al-Rasheed, J Heapy, G Olewicz, AM Admawi, AO Osoba, Riyadh Armed Forces Hospital

Viral agents have emerged as important causes of diarrhea over the last few years, particularly in children in Third World countries, where diarrheal diseases constitute a major public health problem. Acute diarrheal diseases have been reported to be major causes of morbidity and mortality among neonates and children in developing countries. It is estimated that at least 70% of the causes of diarrheal diseases can now be explained with the recent identification of two relatively new agents, i.e., enterotoxigenic *Escherichia coli* and rotavirus. There are very few studies addressing viral etiology in diarrheal diseases in Saudi Arabia. Over 800 stool samples from children aged 5 years and under were examined by virus isolation and electron microscopy. The commonest agents identified were enteroviruses and rotaviruses.

CLINICAL PREDICTABILITY OF ROTAVIRUS DIARRHEA IN CHILDREN: A CASE-CONTROL STUDY IN THE RIYADH MATERNITY AND CHILDREN'S HOSPITAL, SS Islam, M Rahman, M Swailem, M Moagel, S Okasha, G Murtaza, W Alam, Q Shafi, M Yameen, Riyadh Maternity and Children's Hospital

In a case-control study, the clinical spectrum of rotavirus diarrhea was explored to identify factors differentiating it from other diarrheas of unknown etiology in children. Diarrheal patients who had evidence of rotavirus in stool as confirmed by ELISA (enzyme-linked immunosorbent assay) test and for whom no other enteropathogens (*Shigella*, *Salmonella*, *Vibrios*, *Campylobacter*, vegetative or cystic form of *Giardia lamblia*, *Entamoeba histolytica*) could be detected and for whom a microscopic examination of fresh stool specimen could be done, were included in this study as cases. Controls had similar criteria except that they were negative for rotavirus. Between April 1987 and October 1987, 7445 children attended the diarrhea center at Riyadh Maternity and Children's Hospital. A systematic random sampling was done for every tenth patient and 766 patients were screened for rotavirus. Our 52 cases and 52 controls came from these screened patients. Several clinical, microscopic, and feeding parameters were compared between cases and controls to identify factors associated with rotavirus. Two important factors that predicted rotavirus most were presence of neutral fat in the stool (odds ratio 8.9, $P < 0.0001$) and presence of fever ≥38°C (odds ratio 2.9). The relationship of rotavirus and neutral fat remained unchanged after controlling for fever. However, children above 6 months of age had a greater risk compared to children less than 6 months. Even after controlling for age and feeding pattern the neutral fat – rotavirus association remained strong. This study concludes that in a setting where no electron microscopy is available and where ELISA test is not available, neutral fat in stool microscopy is a strong predictor of rotavirus diarrhea.

CLINICAL SIGNIFICANCE OF ROTAVIRUS IDENTIFICATION IN STOOL, H Nazer, King Faisal Specialist Hospital and Research Centre, Riyadh

Acute gastroenteritis is one of the leading causes of morbidity and mortality of children throughout the world. The pattern of etiologic agents in gastroenteritis varies widely in different reports from developed and developing countries. Viral gastroenteritis is by far the commonest cause of acute diarrhea in childhood. Rotavirus has been firmly established as a major cause of infantile gastroenteritis. Group B rotaviruses have been responsible for annual epidemics of severe diarrhea affecting both adults and children. The etiologic role of other viruses such as Norwalk agents, caliciviruses, astroviruses, and adenoviruses has been recognized. However, the finding of more than one type of virus does not seem to be associated with worse manifestations or increased duration of diarrhea. Rotavirus infection may be readily transmissible especially in the environment of pediatric wards. Epidemiologic studies have suggested an association between rotavirus excretion and gastroenteritis. Rotavirus-associated gastroenteritis is a short-lived illness affecting mainly infants aged 6–12 months. Clinical manifestations include acute watery diarrhea rarely with blood, vomiting of sudden onset, concurrent upper respiratory tract infections, fever, and abdominal pain and distention. Dehydration is usually mild to moderate but sometimes severe enough to require intravenous rehydration. Conventional oral rehydration therapy using glucose electrolyte solution is effective in most cases. The duration of illness is usually a few days but may be prolonged to about 3 weeks. Recognized complications include monosaccharide intolerance, postenteritis enteropathy and cow's milk protein intolerance. The high rate of associated bacterial and viral pathogens make the description of specific features or clinical significance of rotavirus excretion rather difficult. Asymptomatic excretion of rotavirus has been reported, especially in neonates. The rate of excretion of rotavirus and its significance among neonates and young children has varied in different reports. While up to 50% of neonates may be excreting rotavirus by the time they are a few days old, most of these infections are asymptomatic. The incidence of infection is highest in winter. The incidence is lower in breast-fed than in bottle-fed infants. Many mild or undiagnosed rotavirus infections occur among children with 80% to 90% prevalence of rotavirus antibodies in certain com-

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# SYMPOSIUM ABSTRACTS

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