THE HEPATITIS VIRUSES

I. HEPATITIS A VIRUS - INFECTIOUS HEPATITIS
A. CLASSIFICATION
1. AN ENTEROVIRUS IN THE PICORNAVIRIDAE -
2. WAS HUMAN ENTEROVIRUS-72, NOW IN OWN GENUS, HEPATOVIRUS
B. STRUCTURE
1. 27 nm IN DIAMETER, ICOSAHEDRON, NON-ENVELOPED
2. SEQUENCED SS RNA WITH Vpg AT THE 5'-END AND POLY A AT 3'-END
3. TYPICAL PICORNAVIRUS
C. REPLICATION
1. LIKE PICORNAVIRUSES
2. CODES FOR COAT PROTEINS, REPLICASE, ETC
3. IRES STARTS WHOLE-GENOME POLYPROTEIN SYNTHESIS
D. IMMUNOLOGY
1. HA Ag (MAJOR ANTIGEN)
2. ANTI-HA IgG AND IgM PRODUCED
E. CLINICAL DISEASE AND PATHOLOGY
1. USUALLY ACUTE INFECTION WITH FEW SEQUELAE/COMPlications
2. FULMINANT HEPATITIS IN 1-4 %
3. STILL 20-30,000 CASES/YEAR IN USA (OUTBREAKS COMMON)

II. HEPATITIS B VIRUS - SERUM HEPATITIS
A. CLASSIFICATION
1. ONLY HUMAN VIRUS IN THE HEPADNAVIRIDAE
2. HEPADNAVIRUS TYPE 1
B. STRUCTURE
1. 42 nm DANE PARTICLE, ENVELOPED, ICOSAHEDRAL 28 nm CORE
2. CIRCULAR, PARTIALLY DS DNA, SEQUENCED, 5'-PROTEIN ON L STRAND
3. FOUR ORFs-OVERLAPPING, ONE DIRECTION
C. REPLICATION
1. LIKE "OUT-OF-PHASE RETROVIRUS"
2. ORF 1 CODES FOR A REVERSE TRANSCRIPTASE
3. INTEGRATION OF DS DNA INTO HOST GENOME MAY OCCUR
4. ORF1-RT; ORF2-THREE SURFACE PROTEINS, S, S-1 AND S-2; ORF3-CORE PROTEIN, C; ORF4-UNKNOWN
D. IMMUNOLOGY
1. THREE MAJOR ANTIGENS:
   a. HBsAg--surface antigen protective Ab produced
   b. HbcAg--core antigen denotes acute or chronic infection
   c. HBeAg--core-related antigen ditto
E. CLINICAL DISEASE AND PATHOLOGY
1. LONG INCUBATION PERIODS--2 MO. OR MORE
2. ACUTE INFECTION WITH EXTRAHEPATIC (IMMUNE-MEDIATED) MANIFESTATIONS
3. FULMINANT FORM (1-4%, AS IN HAV INFECTIONS)
4. CHRONIC: PERSISTENT (3%); AGGRESSIVE (3%); CARRIER (5%)
5. CIRRHOSIS AND HEPATOCellular CARCINOMA
6. PERINATAL TRANSMISSION LEADING TO CHRONIC INFECTION (90%)

III. HEPATITIS C VIRUS--NANB HEPATITIS--POST TRANSFUSION HEPATITIS
A. CLASSIFICATION--FLAVIVIRIDAE, HEPACIVIRUS
B. STRUCTURE--UNKNOWN--(LIKE OTHER FLAVIVIRUSES)
1. SENSITIVE TO ORGANIC SOLVENTS - ENVELOPED
2. SMALLER THAN 80 nm IN DIAMETER
3. CONTAINS A PLUS STRAND RNA OF 10 KB
C. REPLICATION--UNKNOWN--LIKE FLAVIVIRUSES
D. IMMUNOLOGY--WAS A DIAGNOSIS OF EXCLUSION (eg. NANB)
   NOW HAVE FLUORESCENT AB TESTS, ETC., ELISAs
E. CLINICAL DISEASE AND PATHOLOGY
1. POST TRANSFUSION HEPATITIS (PTH)
2. WIDE RANGE OF INCUBATION PERIODS
3. LIKE HBV INFECTIONS WITH:
   a. less fulminant disease
   b. much more chronic disease - 60%

IV. HEPATITIS D VIRUS--THE DELTA AGENT - A SATELLITE VIRUS OF HBV
A. CLASSIFICATION--NOT CLASSIFIED--PROBABLY UNIQUE
B. STRUCTURE
   1. 36 nm PARTICLE, ENVELOPED WITH A 27 nm DELTA CORE
   2. CONTAINS HBsAg (HBV SURFACE ANTIGEN)
   3. CORE PROTEIN IS DELTA SPECIFIC
   4. RNA IS SS, CIRCULAR, 1678 N; VIROID-LIKE
   5. CODES FOR A 215-AA PROTEIN
C. REPLICATION
   1. SELF REPLICATES RNA ?
   2. **REQUIRES HBV FOR TRANSMISSION** (COATING)
D. IMMUNOLOGY
   1. DELTA ANTIGEN--PROBABLY THE CORE PROTEIN
   2. ANTI-DELTA Ab MEANS IMMUNITY
E. CLINICAL DISEASE AND PATHOLOGY
   1. THOUGHT TO MODIFY HBV INFECTION--ACTUALLY INHIBITS
   2. FIRST FOUND IN CHRONIC HBV PATIENTS (20%)
   3. ACUTE (5%); CHRONIC CARRIERS (3%)

V. HEPATITIS E VIRUS--ET-NANB--ORAL-FECAL TRANSMISSION
A. CLASSIFICATION--UNKNOWN - "CALICIVIRUS-LIKE"
B. STRUCTURE
   1. NON-ENVELOPED
   2. 32-34 nm IN DIAMETER
   3. POLY A-CONTAINING RNA OF 7.6 KB
   4. cDNA CLONES HAVE BEEN MADE
C. REPLICATION--UNKNOWN
D. IMMUNOLOGY--CURRENTLY NANB
   1. ABs DO DEVELOP POSTINFECTION AND THEY AGGREGATE
      VLPs (VIRUS-LIKE PARTICLES)
   2. THUS FAR ALL ET-NANB OUTBREAKS RESULT IN SIMILAR ABs
E. CLINICAL DISEASE AND PATHOLOGY
   1. ENTERICALLY TRANSMITTED--ENDEMIC IN ASIA/APRICA
   2. AFFECTS MAINLY ADULTS, MORTALITY ABOUT 4%
   3. HIGH MORTALITY AMONG PREGNANT WOMEN
   4. USUALLY AN ACUTE DISEASE--LIKE HAV DISEASE

VI. TRANSMISSION
A. BLOOD AND BLOOD PRODUCTS
   1. HBV, HCV (NANB), AND DELTA AGENT
   2. HBV AND DELTA ALSO SEXUALLY TRANSMITTED
   3. VERTICAL TRANSMISSION ALSO WITH HBV AND DELTA
   4. HBV TRANSMITTED IN MALE GAY POPULATION
B. ORAL-FECAL ROUTE
   1. HAV AND HBV
   2. ENDEMIC AREAS
   3. PROBABLY NO SEXUAL OR VERTICAL TRANSMISSION
   4. USUALLY ASSOCIATED WITH POOR SANITATION AND
      CONTAMINATION OF WATER SUPPLIES
   5. HAV ASSOCIATED WITH SHELLFISH ON GULF COAST