RESPIRATORY TRACT INFECTIONS

LABORATORY
MEDICINE COURSE
2004
CLINICAL MICROBIOLOGY SERVICE

Dr. Preeti Pancholi 5-6237

BRIEF CASE

WHAT IS THE DIFFERENTIAL ?
WHAT TESTS TO ORDER ?
INTERPRETATION & EVALUATION

ACUTE PNEUMONIA

- PNEUMONIA & INFLUENZA WAS LEADING CAUSE OF DEATH 100 YRS AGO
- NOW LEADING INFECTIOUS CAUSE OF DEATH & 6TH LEADING CAUSE OF DEATH IN USA.

MAJOR VIRAL RESPIRATORY PATHOGENS

PATHOGEN	SEASON
• RSV	• OCT-MARCH
• INFLUENZA	• OCT-MARCH
• PARAFLU 1& 2	• OCT-JANUARY
• ADENOVIRUS	• YR ROUND
• RHINOVIRUS	• YR ROUND
• CORONOVIRUS	• OCT-MARCH

WHAT SPECIMENS SHOULD BE SENT TO R/O VIRAL INFECTION?

- WHAT SPECIMENS TO COLLECT?
  - ✓NASOPHARYGEAL ASPIRATE/WASH/SWAB
    - 89-96% SENSITIVE
  - ✓THROAT SWAB IN VIRAL TRANSPORT MEDIA
    - 70% SENSITIVE
- HOW TO SEND THEM
  - ✓QUICKLY – VIABILITY ISSUES
  - ✓VIRAL TRANSPORT MEDIA
    - HAS CALF SERUM & ANTIBIOTICS

WHAT TESTS ARE PERFORMED IN VIROLOGY?

- EIA VIRAL ANTIGEN DETECTION
  - ✓RSV, FLU A &B (30 MIN)
- DFA (2 HOURS)
  - ✓RSV
  - ✓FLU A & B
  - ✓PARA 1,2,3
- CELL CULTURE (RMK, MRC-5, A549)
  - ✓MIXED VIRAL INFECTIONS
  - ✓WHO REFERENCE LABS SENT CULTURES FOR SUBTYPING

TIME LINE FOR VIRAL TESTS

EIA (ENZYME IMMUNOASSAY)
30 MIN

↓

DFA (DIRECT FLUORESCENT ANTIGEN)
2HRS

↓

CELL CULTURE
2 DAYS - 1 WEEK

LAB DX RSV

TEST	SENSITIVITY	SPECIFICITY
EIA	52-98%	80-100%
DFA	75-97%	74-100%
SHELL VIAL	75-85%	100%

- SENSITIVITY varies with specimen quality, technical proficiency and test accuracy
- SPECIFICITY is normally good. True antigen positive, culture negative specimens exist

RAPID ANTIGEN TEST SEPARATING FLU A FROM B

- EIA INFLUENZA TYPES A & B

Flu A	SENSI	88%
	SPECIF	89%
Flu B	SENSI	70%
	SPECIF	100%

RAPID DFA TEST

DIRECT FLUORESCENT ANTIGEN

Flu A	SENSI	96%
	SPECIF	100%
Flu B	SENSI	87%
	SPECIF	100%

ADEQUATE SPECIMEN FOR DFA
- ✓> 200 CELLS/SLIDE
- ✓20 CILIATED EPITHELIAL CELLS

PEDIATRIC CASE

OCTOBER, 2003: A 3-MONTH OLD INFANT PRESENTED TO THE PEDS ED A "CROUP-LIKE" ILLNESS WITH LOW-GRADE FEVER. THE CHILD DID NOT HAVE A RECENT TRAVEL HISTORY

PATIENT RESULTS

- EIA
  - ✓POSITIVE FOR INFLUENZA A
  - ✓NEGATIVE FOR RSV
- DFA
  - ✓POSITIVE FOR INFLUENZA A
  - ✓NEGATIVE FOR RSV
- CULTURE POSITIVE
  - ✓POSITIVE FOR INFLUENZA
    - ✓SENT TO CDC & WHO FOR SUBTYPING

FLU A 2003

- FIRST CASE IN NYC-OCT
  - ✓COLUMBIA PRESBY CHONY
  - ✓ALSO WE HAD 1ST CASE IN 2002
- TEXAS HAS LARGEST # CASES
  - ✓SCHOOL OUTBREAK IN HOUSTON IN OCT
  - ✓STRAIN WAS H3N2
    - ✓ANTIGENICALLY SIMILAR TO VACCINE STRAIN

INFLUENZA A-C

- 114,000 HOSPITALIZATIONS, 20,000 DEATHS/YR IN U.S.
- TYPE A INFECTS HUMANS, OTHER MAMMALS (SWINE, ETC.), & BIRDS
- TYPES B & C HAVE BEEN ISOLATED ONLY FROM HUMANS (C IS VERY RARE)
- INFLUENZA A: AQUATIC BIRDS ARE NATURAL HOSTS & SERVE AS RESERVOIRS
- INFLUENZA A: PIGS PROPOSED AS "MIXING VESSELS" FOR GENETIC REASSORTMENT BETWEEN HUMAN & AVIAN FLU A

INFLUENZA SUBTYPES

- INFLUENZA SUBTYPES BASED UPON SURFACE GLYCOPROTEINS
  - ✓ Hemagglutinin Activity (HA)
  - ✓ Neuraminidase Activity (NA)
- NA CLEAVES CELL MUCIN BARRIER & HA FUSES TO CELLS SIALIC ACID RESIDUES, ENABLING VIRAL ADSORPTION & PENETRATION
- 15 HA & 9 NA SUBTYPES
  - ✓H1-H3 & N1-N2 CAUSE OF WIDESPREAD DISEASE IN HUMANS

INFLUENZA

- ANTIGENIC DRIFT
- ✓Mutations in HA & NA
- ✓Occurs during viral replication
- ANTIGENIC SHIFT
- ✓Only occurs with Influenza A
- ✓Trading of RNA segments between animal & human strains
- ✓2 influenza types co-infect same cell
- ✓Cause of pandemics

INFLUENZA PANDEMICS IN THE 20TH CENTURY

- "SPANISH FLU" (1918-1919)
- ✓ CAUSED BY H1NI STRAIN
- ✓ KILLED 20-40 MILLION WORLD WIDE (~200,000 AMERICANS)
- ✓ VERY VIRULENT
- ✓ GENETIC MATERIAL FROM 1918 BEING ANALYZED
- "ASIAN FLU" (1957)
- ✓ CAUSED BY H2N2 STRAIN
- ✓ KILLED 70,000 AMERICANS

INFLUENZA PANDEMICS IN THE 20TH CENTURY

- "HONGKONG FLU" (1968)
- ✓ CAUSED BY H3N2 STRAIN
- ✓ KILLED 28,000 AMERICANS

PANDEMIC INFLUENZA, MAJOR PLAGUE, WILL PROBABLY OCCUR IN THE NEXT SEVERAL YEARS

FLU
FROM CHICKENS TO HUMANS

1997 HONG KONG H5N1 INFLUENZA

- ✓INDEX CASE WAS A 3-YEAR-OLD BOY
- ✓PATIENT DIED OF EXTENSIVE INFLUENZA PNEUMONIA COMPLICATED BY REYE'S SYNDROME
- ✓FIRST DOCUMENTED OUTBREAK OF AVIAN INFLUENZA A VIRUS IN HUMANS
- ✓INCIDENT ESTABLISHED THAT AVIAN INFLUENZA VIRUSES CAN INFECT HUMANS WITHOUT PASSAGE THROUGH INTERMEDIATE HOSTS

FLU
FROM CHICKENS TO HUMANS

- H9N2 (CHINA & HONG KONG, 1999)
  - 2 CHILDREN
- H7N2 (VIRGINIA, 2002)
  - 1 SEROLOGIC EXPOSURE
- H5N1 AVIAN FLU (HONG KONG, 2003)
  - ✓at least 2 CASES, 1 DEATH
- H7N7 (NETHERLANDS, 2003)
  - ✓HIGHLY PATHOGENIC AVIAN FLU
  - ✓ALSO INFECTED PIGS & HUMANS
  - ✓83 POULTRY WORKERS & FAMILY
    - ✓79 CONJUNCTIVITIS
    - ✓6 RESPIRATORY SYMPTOMS
    - ✓FIRST DEATH WITH THIS STRAIN
  - ✓FIRST REPORT OF H7N7 CAUSING RESPIRATORY SYMPTOMS IN HUMANS

FLU
FROM CHICKENS TO HUMANS

- H9N2 (HONG KONG, 2003)
  - 1 CHILD
- H7N2 (NEW YORK, 2003)
  - 1 CASE (SERIOUS UNDERLYSING PROBLEM
  - INITIALLY THOUGHT TO BE H1N1
  - INVESTIGATION OF SOURCE ONGOING
- H5N1 (THAILAND & VIETNAM, 2004)
  - ✓STARTED JAN 2003
  - ✓HIGHLY PATHOGENIC (LIVER & KIDNEY INVOLVEMENT)
  - ✓OUTBREAK IN BIRD POPULATION IN MANY ASIAN COUNTRIES
  - ✓16 CONFIRMED CASES (Oct 4,2004); 11 fatal
- H7N3 (CANADA, 2004)
  - ✓POULTRY WORKERS
    - ✓EYE INFECTIONS

FIRST CASE OF HUMAN-TO-HUMAN TRANSMISSION -2004

An 11-YR OLD GIRL IN N. THAILAND

- DIED OF PNEUMONIA SEPT 8 (H5NI)
- RESIDED WITH 32-YEAR AUNT (ALSO INF.)
- BOTH HAD CONTACT WITH INF. CHICKENS
- GIRL'S MOTHER FROM BANGKOK PROVIDED BEDSIDE CARE FOR DAUGHTER UNTIL CHILD'S DEATH
- MOTHER FELL ILL & DIED (SEPT 20) UPON RETURN TO BANGKOK

FIRST CASE OF HUMAN-TO-HUMAN TRANSMISSION

INFLUENZA SEASON
USA (SEPT-JUN)

2002-03

- MILD SEASON
- FLU B
  - ✓44%
- FLU A (56%)
  - ✓H3N2 – 30%
  - ✓H1 – 70%

2003-04

- EARLY SEASON
- FLU B
  - 1%
- FLU A (99%)
  - ✓H3N2 -99.9%
  - ✓H1 -0.1%

CURRENT STATUS FLU A

- 33% H3N2 WORLDWIDE FEB-SEPT 2003 HAVE DRIFTED ANTIGENICIALLY FROM CURRENT VACCINE STRAIN
  - ✓VACCINE PROTECTION MAY BE LOWER BUT EFFICACY NOT PREDICTABLE
- H1N1 REMAINS THE SAME

HIGH ALERT

- RULE OUT INFLUENZA IS HIGH PRIORITY
- WHY? "FLU-LIKE" PRODROME
  - ✓INHALATIONAL ANTHRAX
  - ✓SARS
  - ✓H5 HONGKONG STRAIN !!!

INFLUENZA TREATMENT

INFLUENZA A PROPHYLAXIS

- AMANTADINE
- RIMANTIDINE

TWO NEW NEURAMINIDASE INHIBITORS FOR TREATMENT OF UNCOMPLICATED INFLUENZA A & B

- ZANAMIVIR
- OSELTAMIVIR

BRIEF CASE

WHAT IS THE DIFFERENTIAL ?
WHAT TESTS TO ORDER ?
INTERPRETATION & EVALUATION

CASE HISTORY

- 4 MTH OLD FEMALE WITH SEVERE RESPIRATORY DISTRESS
- 5 DAY PRIOR TO ADMISSION DEVELOPED COUGH & RHINITIS
- 2 DAYS LATER BEGAN WHEEZING, DEVELOPED FEVER
- BROUGHT TO ED WHEN LETHARGIC

CASE HISTORY

•ONE SIBLING REPORTED TO BE COUGHING, AND HER FATHER HAD A "COLD"

• PUT IN RESPIRATORY ISOLATION IN PICU PENDING MICRO RESULTS

RSV FACTS

- RNA VIRUS
- 2 ANTIGENIC SUBTYPES A & B
- SPREAD THROUGH RESPIRATORY SECRETIONS BY CLOSE CONTACT WITH INFECTED PERSONS/OBJECTS
- CAUSES REPEATED INFECTIONS THROUGHOUT LIFE
- VIRUS UNSTABLE IN ENVIRONMENT
- CAUSES COMMUNITY OUTBREAKS (DAY CARE) & NOSOCOMIAL INFECTIONS

LAB DX RSV

TEST	SENSITIVITY	SPECIFICITY
EIA	52-98%	80-100%
DFA	75-97%	74-100%
SHELL VIAL	75-85%	100%

RSV INFECTION

- ADULTS
  - ✓MILD COURSE
- ELDERLY & PEDIATRICS
  - ✓LOWER RESPIRATORY INFECTIONS
- INFANTS & CHILDREN <2 YRS
  - ✓FIRST MTHS OF LIFE
    - 40% PNEUMONIA
    - 90% BRONCHIOLITIS
  - ✓BY 2 YRS, NEARLY ALL HAVE HAD RSV INFECTION

HISTORY OF SIBLING

- THE SIBLING (7 YR) PRESENTED TO THE ED FEBRILE (103), DYSPNIA AND COUGHING EPISODES WITHOUT CHOKING
- PUT IN RESPIRATORY ISOLATION IN PICU PENDING MICRO RESULTS
- CHEST RADIOGRAPH SHOWED INFILTRATE IN RIGHT LOBE

PNEUMONIA

- X-RAY FINDINGS INDICATE LOBAR PNEUMONIA
  - ✓DISCRETE LOBE IN LUNG IS AFFECTED

WHAT BACTERIAL PATHOGENS ARE SUSPECT ?

- GRAM- POSITIVE BACTERIA
  - ✓*S. pneumoniae* - community acquired
  - ✓*S. aureus - nosocomial*
- GRAM-NEGATIVE BACTERIA
  - ✓Enterobacteriaceae - nosocomial
    - *K. pneumoniae, E. coli, Serratia*
  - ✓*P. aeruginosa* - nosocomial
  - ✓*H. influenzae* - community acquired
  - ✓*Legionnella sp.* - community & nosocomial

SPECIMENS SENT TO R/O BACTERIAL INFECTION?

- SPECIMEN COLLECTION
  - ✓SPUTUM
  - ✓BRONCHOSCOPIC ASPIRATES
- MICROBIOLOGY TESTS
  - ✓GRAM STAIN - MORPHOTYPES
  - ✓CULTURE
  - ✓ANTIMICROBIC SUSCEPTIBILITY
  - ✓STREP PNEUMO URINE ANTIGEN TEST

S. PNEUMONIAE

PNEUMOCOCCUS URINE AG

- DETECTS C-POLYSACCHARIDE CELL WALL ANTIGEN COMMON TO ALL SEROTYPES
- PEDS: NASOPHARYNEAL COLONIZATION
  - ✓5-10% HEALTHY ADULTS
  - ✓20-40% HEALTHY CHILDREN
- ADULTS: BEST CORRELATION
  - ✓DETECTS BACTEREMIC & NONBACTEREMIC PNEUMONIA

S. PNEUMONIAE

- MOST COMMON & IMPORTANT CAUSE OF BACTERIAL DISEASE
- OCCULT BACTEREMIA, MENINGITIS, PNEUMONIA – 17,000/YR; < 5 YEARS
- ACUTE OTITIS MEDIA, ACUTE BACTERIAL SINUSITIS

S. PNEUMONIAE

- ANTIBIOTIC RESISTANCE
  - ✓MANY STRAINS RESISTANT TO BETA-LACTAMS (PENICILLINS & CEPHALOSPORINS)
  - ✓MACROLIDE & TRIMETHOPRIM-SULFAMETHOXAZOLE RESISTANCE

THE CAP***#1*** PATHOGEN *S. PNEUMONIAE*

- NEARLY 500,000 CASES/YR U.S.A.
- FATALITY RATES 5-30%
- RISE IN PENICILLIN RESISTANCE

CPMC 2003 PEN RESISTANT PNEUMO

	PENICILLIN NON SUSCEPTIBLE
IN-PATIENTS	36%
OUT-PATIENTS	21%