CELLULAR PHYSIOLOGY

• CELL ORGANELLS
IRREVERSIBLE CELLULAR INJURY

• APOPTOSIS
  ◦ Cellular membrane dissolves first
  ◦ Programmed cell death
  ◦ Noninflammatory
  ◦ Pyknosis
  ◦ Karyorhexis
  ◦ Karyolysis

• NECROSIS
  ◦ Nucleus dissolves first
  ◦ Unexpected
  ◦ Involves inflammation
  ◦ Pyknosis
  ◦ Karyorhexis
  ◦ Karyolysis
Necrosis

- **ISCHEMIC** (COAGULATIVE)
- PURULENT
- GRANULOMATOUS
- FIBRINOUS
- CASEOUS
- FAT
- HEMORRHAGIC
- LIQUEFACTIVE
Necrosis

- **Ischemic** (Coagulative)
- **Purulent**
- **Granulomatous**
- **Fibrinous**
- **Caseous**
- **Fat**
- **Hemorrhagic**
- **Liquefactive**
Necrosis

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- Purulent
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Necrosis

- ISCHEMIC (COAGULATIVE)
- PURULENT
- GRANULOMATOUS
- FIBRINOUS
- CASEOUS
- FAT
- HEMORRHAGIC
- LIQUEFACTIVE
MESS WITH THE CHROMOSOMES

• **MONOSOMIES**: DIE! DIE! DIE!

  – MCC: NONDISJUNCTION

  • 90% IN DAD, USUALLY IN MEIOSIS 1; BUT SPERM DIE ON A DAILY BASIS

  • FEWER OCCUR IN MOM; BUT MOM KEEPS HER EGGS FOR LIFE AND IS THEREFORE MORE LIKELY TO TRANSMIT HERS

  • IF ONE WERE TO SURVIVE TO BE BORN, IN THE LEAST, THINGS WILL NOT GROW
TURNER SYNDROME

- WEBBED NECK
- CYSTIC HYGROMA
- GONADAL STREAKS
- SHIELD-SHAPED CHEST
- COARCTATION OF AORTA
Differential Pulses
Differential Cyanosis
Rib Notching
TRISOMIES

• DIE! DIE!
• FEW LIVE
• TRISOMIE 13: **PATAU SYNDROME**
  – POLYDACTYLY
  – PALATE IS HIGH-ARCHED
  – PEE-ING SYSTEM ABNORMALITY
TRISOMIES

• TRISOMIE 18: **EDWARDS SYNDROME**
  – ROCKEBOTTOM FEET (IN 95%)
TRISOMIES

• TRISOMIE 21: **DOWNS SYNDROME**
  - MCC: NONDISJUNCTION
  - ROBERTSONIAN TRANSLOCATION: HIGHEST INCIDENCE (33% OF OFFSPRING)
  - HAS MANY THINGS TO CONSIDER
DOWN’S SYNDROME

- **MENTAL RETARDATION** – 100%
  - IQ: AVERAGE IS 85 TO 100 WITH A STANDARD DEVIATION OF 15
  - SUPERIOR INTELLIGENCE: IQ > 130
  - MILD MR: IQ < 70
  - MODERATE MR: IQ < 55
  - SEVERE MR: IQ < 40
  - PROFOUND MR: IQ < 25 – NEEDS 24HR CARE
  - MILD TO MODERATE MR CAN BE TAUGHT BASIC ADLS
DOWN’S SYNDROME

• EARLY-ONSET **ALZHEIMER DISEASE**

• HIGHER FREQUENCY OF **AML**; BUT **ALL** IS THE MOST COMMON LEUKEMIA

• 20 TO 40% HAVE **congenital heart DISEASE**

• -ENDOCARDIAL CUSHION DEFECTS
  – VSD and ASD
  – VSD
  – ASD
DOWN’S SYNDROME

• CYANOTIC CONGENITAL HEART DISEASE
  – TRANSPOSITION OF GREAT ARTERIES
  – TETROLOGY OF FALLOT
DOWN’S SYNDROME

• 50% HAVE **HYPOTHYROIDISM**
• WIDELY-PACED CRANIAL SUTURES
• **MACROGLOSSIA**
• **DUODENAL ATRESIA**
• **HIRSCHSPRUNG’S DISEASE**
• CLUES:
  – MONGLIAN SLANT TO EYES
  – WIDELY SPACED FIRST AND SECOND TOES
  – SIMIAN CREASE
TRISOMIES

• **XXX**: Normal female; has two Barr bodies
• **XXY**: Klinefelter’s syndrome. Tall male with gynecomastia, small penis and testicles
• **X- Fragile X syndrome**
  – Mcc of chromosomal induced MR
  – Short stature; macrochordism
  – Collagen disorder (increased risk of MVP)
  – Isolated using the drug METHOTREXATE
CHEMOTHERAPY

- Stops rapidly dividing cells
- Attacks the nucleus in some way
- Causes irreversible cellular death
- WILL kill some patients
- No such thing as safe chemo
ANTIMETABOLITES

- **ARA-A**
- **ARA-C**
- **5-FU**: blocks thymidylate synthetase
- **6-MERCAPTOPURINE**: promotes gout; recognized by xanthine oxidase
- **THIOGUANINE**
- **METHOTREXATE**: inhibits dihydrofolate reductase (as does TRIMETHOPRIM and PYREMETHAMINE)
  - Most commonly used antimetabolite
  - Used to treat molar pregnancies
  - Used to treat STEROID RESISTANT disease (followed by AZOTHIOPRINE and CYCLOSPORINE)
ANTIMETABOLITES

• METHOTREXATE
  – Causes folate deficiency and megaloblastic anemia
  – Give LEUCOVORIN > FOLINIC ACID to prevent the anemia
ANTIMETABOLITES

• AZOTHIOPRINE

  – Used for steroid resistant diseases
    (behind METHOTREXATE and before CYCLOSPORINE)
ALKYLATING AGENTS

• Bind to double stranded DNA
• Used primarily for slow growing cancers
• Cause the most nausea and vomiting
  – ONDANSETRON: serotonin blocker used to treat nausea and vomiting in chemotherapy
ALKYLATING AGENTS

- Bleomycin
- Busulphan
- Adriamycin
- Cisplatin
- Cyclophosphamide
- Isophosphamide
- Mitomycin
- Antimycin
- Acridine dyes

- Hydroxyurea
- Melphalan
- Mechlorethamine
- Procarbazine
- Dacarbazine
- Chlorambucil

FOR RESCUES
- Desroxyzasane
- Mesna
MICROTUBULE INHIBITORS

- Vinblastine
- Vincristine
- Paclitaxel
NUTRIENT DEPLETION

- L-ASPARAGINASE
IMMUNEMODULATORS

- LEVAMISOLE
Phosphatidylserine

- Marker for **Apoptosis**
- Activates **Caspases**
Metalloproteinases

- Require zinc to be activated
- Digests connective tissue, allowing cells to migrate
- Very active in cancer cells, allowing metastasis
IRREVERSIBLE CELLULAR DEATH

- NUCLEAR DAMAGE
- LYSOSOMAL DAMAGE
- MITOCHONDRIAL DAMAGE

- OCCURS IN **6 HOURS** in all tissues
IRREVERSIBLE CELLULAR DEATH

- NUCLEAR DAMAGE
- LYSOSOMAL DAMAGE
- MITOCHONDRIAL DAMAGE

- OCCURS IN 6 HOURS in all tissues except the brain
IRREVERSIBLE CELLULAR DEATH

• OCCURS IN **20 MINUTES** IN THE BRAIN
The End?

To Be Continued...