Therapeutic areas & Diseases

Laboratory parameters analysed for Clinical trials

Module 4 Topic 3

Why are laboratory tests ordered

- Diagnosis
- Monitor progression of disease
- Monitor effectiveness of treatment
- To identify complications of treatment
- Screening population for diseases

Common Laboratory Tests

Most commonly ordered lab tests

- CBC (Complete Blood Count)
- BMP (Basic Metabolic Panel)
- CMP (Comprehensive Metabolic Panel)

CBC

- Red blood cell data
  - Total red blood cell count (RBC)
  - Hemoglobin (Hgb)
  - Hematocrit (Hct)
  - Mean corpuscular volume (MCV)
- White blood cell data
  - Total white blood cell (leukocyte) count (WBC)
  - A white blood cell count differential may also be ordered
- Platelet Count (PLT)

Red Blood Cell Count

- Count of the number of circulating red blood cells in 1mm^3 of peripheral venous blood (4.7 to 6.1 cells ? microlit
- **Hematocrit** is a measure of the percentage of the total blood volume that is made up by the red blood cells
  - Normal Hct in adult males - 40-54%
  - Normal Hct in adult females - 34-51%
- The **Mean Corpuscular Volume** (MCV) is a measure of the average volume, or size, of an RBC
- The MCV is important in classifying anemias
  - Normal MCV = normocytic anemia
  - Decreased MCV = microcytic anemia
  - Increased MCV = macrocytic anemia

White Blood Cell Count

- A count of the **total** WBC, or leukocyte, count in 1mm^3 of peripheral blood. Normal is 4 – 11000/microlit
- A decrease in the number of WBCs
  - Leukopenia
- An increase in the number of WBCs
  - Leukocytosis

Types of leukocytes (Differential count)

- Neutrophils 55-70%
- Lymphocytes 20 – 40 %
- Monocytes 2-8%
- Eosinophils 0-4 %
- Basophils 0.5 – 1 %

Platelet Count

- A count of the number of platelets (thrombocytes) per cubic milliliter of blood – 150,000 to 450,000 / microlit
  - A decreased number of platelets
    - Thrombocytopenia
  - An increased number of platelets
    - Thrombocytosis

CBC as reported by Lab

Component	Value	Flag	Low	High	Units
WBC	9.4		4.0	10.0	K/UL
RBC	4.81		3.60	5.50	M/UL
HGB	13.7		12.0	16.0	GM/DL
HCT	41.1		34.0	51.0	%
MCV	85.4		85	95	FL
MCH	28.6		28.0	32.0	PG
MCHC	33.4		32.0	36.0	GM/DL
RDW	14.3		11.0	15.0	%
PLT CNT	220		150	400	K/UL

CBC as reported by Lab

Component	Value	Flag	Low	High	Units
DIFF TYPE AUTOMATED					
LYMPH #	3.6		1.0	4.0	K/MM3
MONO #	0.6		0.0	1.0	K/MM3
GRAN #	5.1		2.0	7.0	K/MM3
EO #	0.0		0.0	0.7	K/MM3
BASO #	0.0		0.0	0.2	K/MM3
LYMPH	39		20	45	%
MONO	6		0	10	%
GRAN	55		45	70	%
EO	0		0	7	%
BASO	0		0	2	%

BMP as reported by Lab

Component	Value	Flag	Low	High	Units
Sodium	142		136	144	mm/l
Potassium	3.9		3.3	5.1	mm/l
Chloride	107		98	108	mm/l
Co2	27		20	32	mm/l
Bun	10		7	22	mg/dl
Creatinine	0.80		0.7	1.5	mg/dl
Glucose	100		70	100	mg/dl
Calcium	8.5	I	8.9	10.3	mg/dl

CMP from a patient with Congestive Heart Failure

Glucose	112	H	[70 – 100]	mg/dl
Blood Urea Nitrogen	39	H	[7 - 22]	mg/dl
Creatinine	1.6	H	[0.7 - 1.5]	mg/dl
Calcium	8.9		[8.5 - 10.5]	mg/dl
Sodium	132	L	[136 - 146]	mmol/L
Potassium	4.0		[3.5 - 5.3]	mmol/L
Chloride	93	L	[98 - 108]	mmol/L
Carbon Dioxide	23		[20 - 32]	mmol/L
Albumin	3.1	L	[3.6 - 5.0]	gm/dl
Protein, Total	5.8	L	[6.2 - 8.0]	gm/dl
Alkaline Phosphatase	200		[25 - 215]	IU/L
AST	35		[5 - 40]	IU/L
Bilirubin, Total	1.9	H	[0.2 - 1.4]	mg/dl

Detection Tests

Microscopy

- Direct examination of a specimen (or may use stains) to detect the presence of organisms

Culture

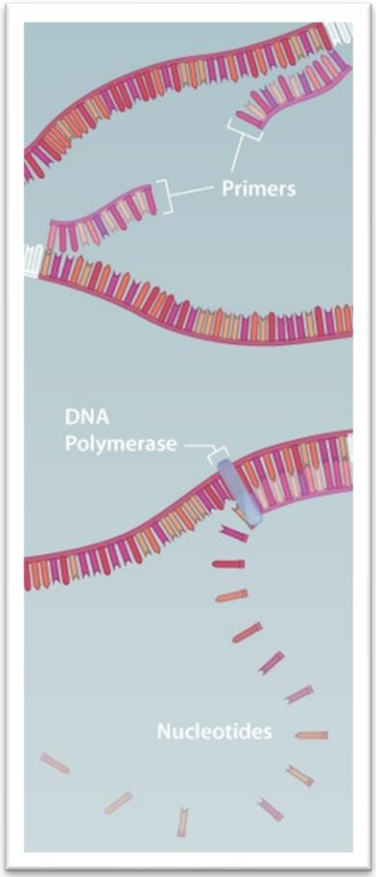
- The process of growing and pr
  media that is conducive for th
- Pros:
  - Confirm the organism
  - Reproduce the organism
  - Use for additional testing
- Cons:
  - Delay in confirmation
  - Require viable organism
  - Difficult for fastidious organisms

S. pneumoniae on blood agar plate

Identification Methods

Polymerase Chain Reaction (PCR)

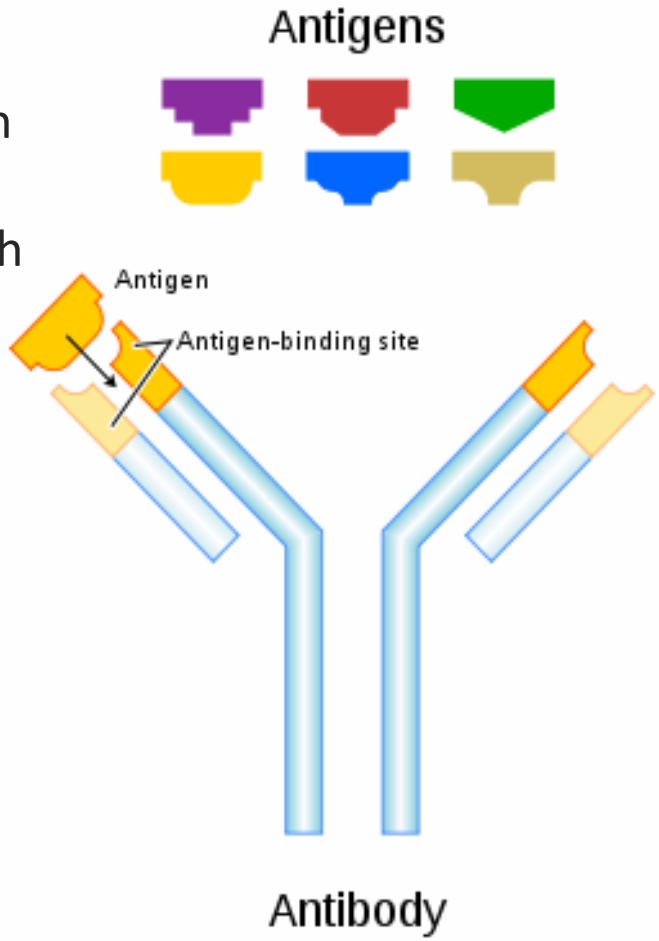
- Method used to amplify a specific region of a DNA strand
- Pros:
  - Simple process, eliminates tedious work,
  - Results available within a day
  - Does not require a viable organism as only a strand of DNA is needed
  - Sensitive test
- Cons:
  - Sensitive – can pick up environmental contaminants
  - Unable to distinguish between certain species



Identification Methods

Serology

- Study of blood serum, with emphasis on testing of antibodies in the serum
- **Antigen**: A 'foreign' substance which stimulates the body to produce antibody
- **Antibody**: A protein molecule produced by the body's immune system in response to a specific antigen. The antibody combines with the antigen and disables it.
  - Also called Immunoglobulins (e.g. IgG, IgM, IgA, IgE)
  - Referred to as **anti**-(name of antigen),
    e.g. anti-HCV, anti-HAV



Serology

Antibodies

- **IgM**: type of antibody produced by the body, usually the first antibody to appear in response to a foreign substance exposure, then eliminates the organism in the early stages of immunity before there is sufficient IgG
- **IgG**: type of antibody that provides the majority of antibody-based immunity against invading organisms, the only antibody that crosses the placenta to provide immunity to the fetus

Antibody Testing

Pros:

- Screening tool
- Readily available
- Indicates response to antigen (even if antigen is not detectable) – may indicate infection or immunity

Antibody Testing

Cons:

- Paired testing necessary for some diseases - may take a while to get results, impact on patient management
- Unable to differentiate between immunity and disease
- Sensitivity and specificity:
  - False-negative result: compromised immune system
  - False-positive result: liver disease, low disease prevalence

Detection Tests

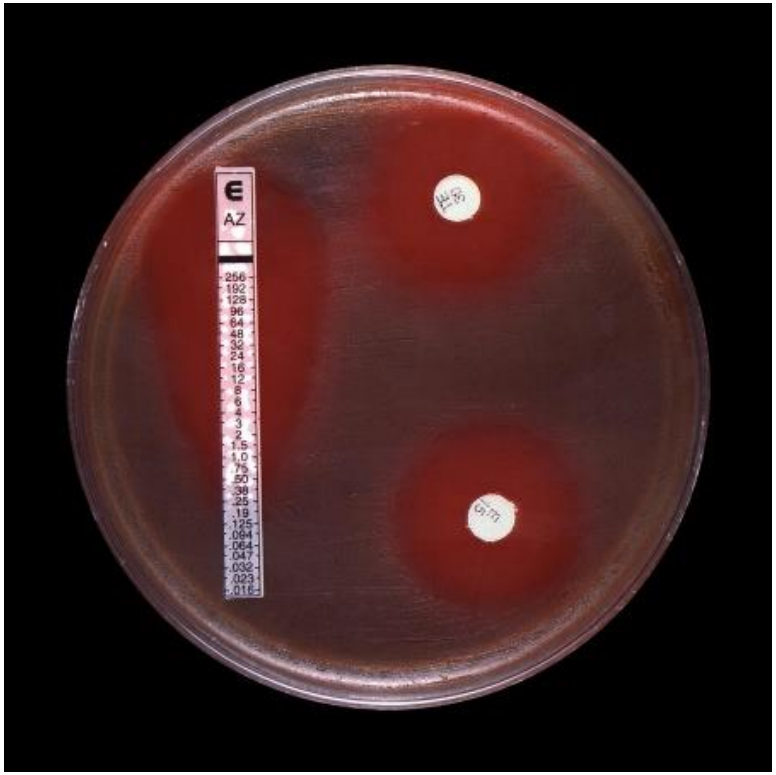
Antigen Test

Technique	Principle
Agglutination	Known antiserum causes bacteria or other particulate antigens to clump together or agglutinate
Complement fixation	Known antiserum mixed with the test antigen and complement is added. Sheep red blood cells and hemolysins are then added. Positive test: no hemolysis, negative test: hemolysis
Enzyme-linked immunosorbant assay (ELISA) ; Enzyme immunoassay (EIA)	A rapid test where an antibody or antigen is linked to an enzyme as a means of detecting a match between the antibody and antigen.
Fluorescent antibody	Fluorescent dye is attached to known antibodies. When the fluorescent antibody reacts with the antigen, the antigen will fluoresce when viewed with a fluorescent microscope.

Antimicrobial susceptibility

MIC (minimum inhibitory concentration)

- lowest concentration of antimicrobials that will inhibit the growth of organisms
- MICs are important to confirm resistance of organisms to an antimicrobial agent.



Methods:

- Disk diffusion test
- Broth dilution test

Monitoring for adverse effects

- May have begun with the observation that chloramphenicol could cause bone-marrow toxicity in case of prolonged or repeated administration
- Adverse events related to drug interactions e.g. oral anticoagulants, or exposure in vulnerable patients with disease states that predispose patients to NSAID toxicity

Drugs	Monitoring requirement
ACE inhibitors or angiotensin-II receptor antagonists	Creatinine
	Potassium
Diuretics	Electrolytes