1) 3 Major function of Kidney
   I) **Regulation:** Water, acid-base , electrolyte
   II) **Excretion:** Urea, Creatinine, organic acids, phosphate
   III) **Hormone:** Production and elaboration
   ➔**E.**g. Renin, erythropoietin, ADH

2) Basic facts about kidney
   I) Each kidney is made up of 10^6 nephrons (functional units)

   II) Glomerular function ➔ Filtering function

   III) Tubular function
   ➔ Reclamation of essentials
   ➔ Concentrating solution
   ➔ Secreting waste products

   IV) **Renal blood flow**: 1200mL / min (~20% of cardiac output)
   V) **Glomerular filtrate rate:** 125mL/min
   ➔The BEST measure of glomerular function
   VI) **Urine formation:** 1mL/min

3) Renal function Test
   ➔Depends on measuring the **glomerular filtration rate (GFR)**
   →Clearance of substances ****
   a) Creatinine Clearance (male: 80-115, female 53-97 mmol)
   I) Background
   ➔Convenient but not insensitive
   ➔End product of muscle metabolism
   ➔Freely filtered and not reabsorbed
   →**BEST indicator of GFR**

   II) Limitations
   1) Plasma level is dependent on **muscle mass**
   2) **Secretion** present in proximal tubules
   ➔OVER-estimation of GFR
   ➔Some drugs may also interfere with this secretion
   3) Various substances may causing bias by **Jaffe reaction**
   4) Dietary factors (E.g. Roasted meat have much creatinine)

III) Other conditions affecting creatinine independent of GFR

1) Factor decreasing creatinine (OVER-estimation of GFR)
   i) **Increasing age**
   ➔Physiological decrease muscle mass
   ii) **Cachexia**
   ➔Pathological decrease muscle mass

2) Factor Increasing creatinine (UNDER-estimation of GFR)
   i) Ingested cooked meat
   ➔Gastro absorption of creatinine
   ii) Drugs
   ➔Inhibit tubular creatinine secretion
   iii) **Cefoxitin, Cephalothin** (creatinine-like)
   iv) **Ketoacidosis** (Creatinine-like)

IV) Creatinine Clearance Formula (Cr Cl)

➔**Cr Cl = Ucr X V / Pcr**

→Ucr = Urine concentration of creatinine

➔Pcr = Plasma concentration of creatinine

➔V = Volume of urine produced over a fixed period

➔**Cockroft and Gault formula**

→Can eliminate the affecting factors (Age, body weight)

b) Urea Clearance

➔Depends on **Urine flow Rate**

➔**Very poor indicator of GFR**

I) **Background**

➔Waste product of Amino acid metabolism

➔Filter freely but reabsorb back by passive diffusion

II) **Reason for a POOR indicator**

1) Decrease production of urea can lower plasma urea
   ➔Decrease intake of protein will lead to
   ➔Renal insufficiency patient may have normal plasma level

2) GFR has to drop ~40% before urea level rise
3) Increase production of urea may not result in proportionately high level of plasma urea

III) Other conditions affecting creatinine independent of GFR

1) Factors increasing urea level
   - ➔High protein diet
   - ➔Gastrointestinal bleeding
   - ➔Tissue trauma
   - ➔Drugs: Glucocorticoids, tetracycline
2) Factors decreasing urea level
   - ➔Liver disease
   - ➔Malnutrition

c) Overall Clinical situations where clearance that necessary to estimate GFR

I) Extremes of age / body sizes
II) Severe obesity / inanition
III) Disease of skeletal muscle
IV) Paraplegia and tetraplegia
V) Vegetarian diet
VI) Rapidly changing renal function

4) Proteinuria

a) Basics

➔Normally small proteins can be freely filtered but can completely reabsorbed (<15kDA)

➔Normally daily excretion < 150mg, about 40-50% is albumin

b) Measurement

➔24 hr / 12-hr overnight / 4 hr

➔**Dipstick methods**

→Most sensitive to albumin

→Poor for detecting tubular proteinuria

→Based on protein association with pH indicator

→Test pad with dye **tetrabromphenol blue** at **pH 3**

→If proteins binds, **Yellow to Green**

c) Classification

I) Overload proteinuria

➔Haemoglobin

➔Myoglobin (crush injury, rhabdomylosis)

➔Bence jones (Multiple myeloma)

II) Tubular Proteinuria

➔Mostly low molecular weight proteins (Not albumin)

➔Heavy metal toxicity, cystinosis, galactosaemia

III) Glomerular Proteinuria

➔Mostly albumin at first

→Then larger proteins appear as membrane selectivity is lost

IV) Other

1) Orthostatic Proteinuria

➔Standing position increase protein excretion

→10-20% healthy subjects at prolonged upright posture have

2) Transient Proteinuria

➔Systemic illnesses not related to kidneys

→**Eg** High fever, congestive heart failure

d) Nephrotic Syndrome

➔Proteinuria > 3.5g / day / 1.73m^2

➔Associated with hypoalbuminaemia, hyperlipoproteinaemia, edema

→Hyperlipoprotein due to leaking of small molecules

5) Arterial Blood Gases Analysis (Acid-Base disorders)

➔pH, PO2, PCO2, HCO3-, O2 saturation

a) Concepts and vocab

➔By measuring H+, HCO3- concentration, pCO2

→The component of bicarbonate buffer system

I) Metabolic acid-base disorders

➔Primary Problem with hydrogen ion production or excretion

→Reflected in conc. Of HCO3-

II) Respiratory Acid-base disorders

➔Primary Problem with CO2 excretion

→Reflected in PCO2

III) Compensation process

➔The body got physiological mechanisms to try restore H+ conc.

⇨ Acid-base disorder = Balance between **primary disturbance** and **compensation**

b) Diagnosis of Acid-Base disorder

I) Compensated acidosis /alkalosis

II) Partially compensated

III) Fully compensated

c) Common cause

I) Acidosis

➔Impaired H+ excretion

➔Increased H+ production or ingestion

➔Loss of HCO3-

II) Alkalosis

➔Loss of H+ in vomiting

➔Alkali ingestion

➔Potassium deficiency

d) Management

➔Correct underlying disease

6) Immunological tests

a) **<u>Antinuclear antibodies (ANA)</u>**

<u>I)</u> Background

➔Antibodies that against nuclear constituents

➔Usually tested by **indirect immunofluorescence** (IIF)

<u>II)</u> Common Clinical use

1) Systemic lupus erythematosus (95%)

2) Rheumatoid arthritis (60%)

3) Scleroderma (90%)

4) Normal (3-4%)

5)

<u>III)</u> **Pattern of ANA**

1) **Diffuse**: Deoxyribonucleoprotein, Non-specific
2) **Speckled** 斑點: ENA, rheumatic disease
3) **Rim** 環繞: dsDNA, SLE
4) **Centromere:** CREST
5) **Nucleolar:** Ribonucleoprotein precursors, scleoderma

IV) **Classification**

1) **Anti-dsDNA**

➔Specific to SLE, but present only in 70% of SLE patient

➔Level correlate with activity in most patient

→May have a delay of weeks

➔Detected by ELISA / Farr assay /IIF

2) **Anti-ENA (Anti extractable nuclear antigen)**

➔At least 30 different specificities

➔Detected by Double immunodiffusion, ELISA

➔Sub-division

I) **Smith:** highly specific for **SLE (30%** present)

II) **nRNP**:

→**High titre**: Associated with mixed connective tissue(MCTD)

→**Lower titre:** SLE and other connective tissue disease

III) Ro(SS-A)

→Associated with heterogeneous clinical manifestations

→E.g. Neonatal lupus, subacute cutaneous LE

IV) La(SS-B)

→Similar to RO, have affinity to one another

3) **Anti-centromere (C3,C4)**

➔Related to **CREST**

→Calcinosis, Raynaud's phenomenon, Esophagus dysmotility

→Sclerodactyly, Telangiectases

➔Subdivision

I) Decrease in C3 and C4

➔Normally secondary cause

→Consumptive: AP / CP

→Decreased production: chronic liver disease

➔Also related to SLE, C1-inhibitor deficiency

II) Increase in C3 and c4

➔In acute phase response

b) **Anti-Thyroid antibodies**

➔Anti-thyroglobulin Ab / Anti-thyroid microsomal Ab

I) Methodology

➔By ELISA / particle agglutination

II) Clinical use

➔Associated with thyroid autoimmunity

➔Can be found in thyroid malignancy

c) **Anti-Smooth Muscle Antibodies**

➔Found in

→Chronic active hepatitis 70%

→Primary biliary cirrhosis 20%

→Cryptogenic cirrhosis 30%

d) **Anti-Mitochondrial Antibodies**

➔Found in

→Chronic active hepatitis 25%

→Primary biliary cirrhosis 90%

→Cryptogenic cirrhosis 25%

e) **Rheumatoid factor**

➔IgM against IgG Fc

I) Methodology

➔Nephelomtry

➔ELISA

➔Agglutination method

II) Diagnostic significance

1) **Rheumatoid Arthritis *****

→Not sensitive / specific

2) **Other AI diseases:** SLE, scleroderma, CAH

3) **Chronic infeections:** TB, OSteomylitis

4) **Normal**

III) High titre: Active disease

IV) Very High Titre: Rheumatoid vasculitis

f) **Anti-Neutrophil cytoplasmic antibodies (ANCA)**

➔By IIF, ELISA

➔2 staining pattern

→Cytoplasmic, pernuclear

➔Clinical use

1) **Small vessel vasculitis**

➔**cANCA → Wegener's granulomatosus**

➔**pANCA → Microscopic polyarteritis**

g) <u>Anti-Phospholipid antibodies</u>

I) **Methodology**

1) **VDRL:** Least sensitive
2) **Lupus anticoagulant(LA):** Most specific
3) **Solid-phase assays:**
4) **Anti cardiolipin antibody test:** by ELISA
5) **Anti-beta2-glycoprotein I antibody test:** by ELISA

h) **<u>Paraproteins</u>**

<u>I)</u> Definition of paraprotein

➔Abnormal discrete bands seen on electrophoresis of serum or urine

➔Comprise intact / fragmented homogenous Ig derived from a single clone of B cells

➔Benign /Malignant

<u>II)</u> Disease associated

a) Malignant

➔**Multiple myeloma ****

➔B cell lymphoma

➔Heavy-chain disease

➔Amyloidosis

b) Benign

➔Infectious processes

➔Conditions associated with hyper-gamma-globulinaemia

i) IgG, IgA, IgM abnormalities

I) Antibody deficiency

➔Primary cause: CVID, selective IgA deficiency

➔Secondary: Myeloma

II) Raised Ig

➔Chronic liver diseases, **AIDs**

甲、 **Quantitation of paraprotein**

➔Cheaper and easier than densitometry

→But can give gross error

7) Diagnosis of multiple myeloma

I) **Serum and urine presence of paraprotein**

II) **Bone marrow biopsy (increased number and abnormal morphology)**

III) **Skeletal X ray – lytic lesions**

8) Basics about microbiology investigation of infectious disease

a) <u>Common Roles of microbiology laboratory</u>

1) Microbiological examination of specimen
2) Consultation on investigation and management of patient
3) Control of hospital infection
4) Public heath surveillance 監視

b) Principle of laboratory diagnosis of infection

I) Specimen

1) quality
2) timing
3) collection technique
4) preservation

II) Requests

➔Right test, Right purpose

9) Methods of microbiology investigation

a) <u>Microscopic examinations</u>

I) Direct light microscopic examination

II) With staining

➔*Gram-stain:* Identify **Gram+ve organism**

➔*Ziehl-Neelsen stain*: Identify **Acid-fast organism**

➔E.g. Mycobacterium tuberculosis

➔*Silver stain:* To visualize DNA, proteins

III) With immunofluorescence

IV) Electron microscopy

b) Identification of microorganism

I) Phenotypic

➔Colony morphology, microscopic-morphology, biochemical tests

II) Genotypic

➔Probe hybridization, DNA sequencing

III) Mass Spectrometry

c) <u>Culture</u>

I) Solid media
II) Liquid Media
III) Tissue culture
IV) Animal inoculation 接種

d) <u>Antigen / antibody detection</u>

➔By serology on blood and other fluid

➔**Antimicrobial susceptibility testing**

➔**To** guide the choice of treatment (Anti-microbial agents)

➔Report as Sensitive / Susceptible / resistant

I) Pros of Antibody:

1) Fast
2) No dependence on culture
3) Non-invasive

II) Cons of Antibody:

1) Cross reaction
2) Cannot differentiate **new /old** infections
3) Time needed for antibody immune response
4) Patients with immunosuppression

III) Antigen

➔Can be performed in various body fluids

➔Less problem than antibody detection , but not often available

e) <u>Nucleic Acid Amplification and Detection</u>

➔By Polymerase chain reaction (PCR)

I) **Pros**

1) Relatively fast
2) Does not depend on culture
3) Usually Very sensitive

II) **Cons**

1) May not differentiate between **live / dead**

2) Inhibitor affecting

3) High **cost**

f) Blood culture criteria

I) Must only be taken in suspected sepsis / severe infection

II) Aerobic + Anaerobic culture

III) At least 2 set from different sites

IV) Strict aseptic techniques

V) Adequate volume: 5-10mL per bottle

10) Clinical features of Microbiological investigation of infectious disease

A) CNS infection

a) Common types of infection

1) Meningitis
2) Encephalitis
3) Brain abscess, epidural / subdural abscess
4) Ventricular shunt infections
5) Spine epidural / subdural abscess

b) Common types of specimen

1) Cerebrospinal fluid
   ➔Lumbar puncture / Ventricular drains
2) Brain abscess drainage
3) Brain biopsy
4) Blood culture
5) Serology
   ➔Antigen / antibody

B) Upper respiratory tract infection

a) Tonsillopharyngitis

I) *Streptococcus pyrogens*
   ➔By throat swab

II) Viruses

III) *Corynebacterium diphtheria* (Rare)

b) Epiglotitis

c) Sinusitis

I) Cause
   ➔Streptococcus pneumoniae
   ➔Haemophilus influenza
   ➔Moraxella catarrbalis

II) **Culture**
   ➔Nasal pus / sinus exudates **NOT reliable**
   ➔Sinus puncture **Preferred**

d) Otitis media

I) Cause same as sinusitis

II) Culture
   ➔External auditory meatus **NOT reliable**
   ➔Tympanocentesis **Preferred** only seriously ill

e) Common cold: No need, viral infection

C) Lower respiratory tract infection

a) Pertussis (whooping cough 百日咳)

➔Caused by ***Bordetella pertussis***

➔Culture of nasopharyngeal aspirate or swab on special medium

b) Lung abscess

c) Empyema thoracis 蓄膿

d) Pulmonary tuberculosis

e) Pneumonia

I) Blood count, Blood gas

II) Cultures: blood, respiratory tract specimen, pleural fluid

III) CT + X-ray

IV) Sputum examination

➔Gram stain: Leukocytes, epithelial cells, predominant flora

➔Culture: Blood agar, chocolate agar, selective media

V) Other respiratory tract specimen

➔**Balance the risk** of procedure (Deeper, higher yield)

→Nasopharyngeal aspirate for viruses

→Tracheostomy aspiration

→Transbronchial biopsy

→Open Lung biopsy

→Urine antigen detection assays

→**For** Strep.pneumoniae + Legionella pneumophilia

D) Urinary tract infection

a) Clinical Diagnosis

➔Urinary symptoms + Systemic symptoms

b) Specimens

I) Midstream urine

II) Catheterized urine

III) Suprapubic aspiration

IV) Ureteric catheterization

V) Percutaneous nephrostomy urine

VI) Ileal conduit urine

VII) Bag urine

VIII) Blood culture

c) Transporting criteria + Measures

1) Quantitation of bacterial count **

I) Significant bacteriuria

➔>10^5 CFU / mL urine

➔80% indicative for 1sample, 95% for 2 samples

II) Low-level bacteriuria

➔10^4 – 10^5 / mL urine

➔Asymptomatic women: 95% = contamination

➔Symptomatic women: 33% having infection

2) Within 2 hrs

3) Dip-slide technique

4) **Boric acid(1.8%) for preservation if can't be transported in time**

d) Urinalysis

I) Chemistry

➔Nitrite, leukocyte esterase, haemoglobin, protein

II) Microscopy

➔Bacteria, Leukocyte, RBC, Casts, Squamous epithelial cells

E) Gastrointestinal tract infection

a) Infectious agents

I) Bacteria

➔*Helicobacter pylori*

➔*C. difficile*

➔*Staphylococcus aureus*

➔*Enterobacteriaceae*

→*Salmonella, Shigella*

II) Viruses

➔Rotavirus, Astrovirus, norovirus, adenovirus etc.

➔HepatitisA, E

III) Parasites

➔Protozoa, nematodes, trematodes, cestodes

b) Specimens

➔Stool, rectal swab

➔Gastric / intestinal biopsy

➔Duodenal aspirates

➔Blood culture / serology

➔Incriminated food /water samples

c) Investigations

I) Culture:

➔**Selective media:** Routine culture for common pathogens

→**e.g.** Salmmonella, shigella, vibrio, aeromonas

➔**Microscopy:** For leukocytes parasites

➔**Anaerobic culture**: For C.difficile

II) Cytotoxin assay: For Clostridium difficile

III) Antigen detection: For virus

IV) Electron microscopy: For virus

d) Special requests **

I) Enterohaemorrhagic E.Coli (EHEC)

➔**Bloody diarrhea, food history, travel history**

II) Verocytotoxigenic E.Coli (VTEC)

➔**Bloody diarrhea, food history, travel history**

III) Enteropathogenic E.Coli (EPEC)

➔**Infantile diarrhea**

IV) Clostridum diffcile culture and cytotoxin

➔**Antibiotic-associated diarrhea**

V) Parasites

➔Entameba bistolytica, Giardia lamblia

VI) Helicobacter pylori

11) Basics about cytological examination

⇨ By looking at the specific morphological features under microscopy

a) Source of specimen

I) Exfoliation

➔Cells exfoliated from linings of body cavities

→Due to natural cell turnover

II) Fine needle aspiration biopsy

➔Obtained by needle suction

b) Major application

I) Detection of dysplasia / malignancy

➔More sensitive to central tumours

➔**More** sensitive to high grade tumours

1) Variable size, shape
2) Irregular nuclear outline, staining
3) Large nucleoli

II) Diagnosis of specific infections

➔Organisms with characteristic appearance

c) Diagnostic categories

I) Normal / Negative

II) Atypical cells

➔May be reactive / hyperplasia / benign / malignant

III) Suspicious cells

IV) Malignant cells

➔Can suggest tumour type

→Carcinoma / sarcoma / lymphoma

12) Examples of Exfoliation cytology

A) Bronchial cells examination

a) Normal bronchial cells

I) Epithelial cell

➔Columnar shape

➔Basal nucleus

➔Terminal plate & cilia

II) Goblet cells

➔Apical mucin globule

b) Preparation of specimens

I) Sputum

1) Produce sputum by steam inhalation
2) Examined with naked eye for **small cell clumps**
3) Pick and smear the cell clumps on a glass slide

II) Bronchial fluid

1) Inject saline
2) Re-aspirate by bronchoscope
3) Stain with **Papanicolaou stain**

c) Small cell carcinoma

I) **Small, Dense, hyper-chromatic nuclei**

➔<4X lymphocyte / normal bronchial epithelial cell diameter)

II) **Fine chromatin, uniform distribution**

III) **Nuclear molding**

IV) **Absent nucleoli**

d) Squamous cell carcinoma

I) **Keratinization:** Dense cytoplasm

II) **Nucleus:** Dense, dark, irregular size & shape

III) **Bizarre cell shape:** Tadpole, Caudate, fibre

e) **Adenocarcinoma**

I) **Columnar / round**

II) Eccentric nuclei 古怪

III) Vacuolated, foamy cytoplasm

IV) Gland-like arrangement of cells

f) **Fungal infections**

I) Aspergillosis

➔Long uniform septate hyphae

➔Acute angle-branching

II) Cryptococcosis

➔Spherical to elliptical uninucleate

➔**Thin-walled yeast forms**

➔Thick mucinous capsule

III) Candidiasis

➔Narrow-based budding yeast, pseudo-hyphae

IV) Mucormycosis

➔Non-septate

➔Non uniform width, wavy, branching at 90oC

g) **HSV infection**

➔Ground-glass chromatin

➔Chromatin margination to nuclear membrane

B) Gynecological Cytology

a) Pathogenesis of cervical carcinoma

I) Majority due to **HPV infection**

II) **Viral proteins interact** with hot cell cycle proteins

➔Lead to increased cell proliferation

→Eventually cancer development

III) **Progression** from pre-invasive to invasive phase

➔May take many years

IV) **Stop cancer progression** at the pre-invasive phase

b) Squamous Intraepithelial Lesion(SIL)

➔**Low grade:** Low nucleus to cell ratio

➔**High grade:** High nucleus to cell ratio

13) Fine needle Aspiration biopsy

a) Advantages of FNA

I) Simple, safe

II) Painless ??

III) Outpatient procedure

IV) Readily repeated

V) Speedy results

VI) Cheap

VII) Obtain material for other tests

b) Complications

I) Infrequent

II) Usually minor degree, resolve spontaneously

III) Site may influence

IV) Experience of operator dependent

14) Comparison between exfoliative cytology and FNA

Exfoliative cytology advantages	**FNA Advantages**
Specimens collected with minimal discomfort	I) Active sampling of otherwise not reachable lesions
Procedure can be repeated many times	II) Cells fresh, well-preserved
Specimen samples a wide area	III) Inexpensive, out-patient
Equipment for collection is inexpensive	IV) May allow application of histological criteria if material adequate

15) Basics about Haematological system

a) Elements

I) **Organs**: Bone marrow, thymus, spleen, lymph nodes

II) **Cell:** WBC, RBC, platelets

III) **Plasma:** Coagulation factors, Anticoagulants

b) Nature of haematological disorder

I) Hereditary VS acquired

II) Benign/reactive VS malignant

III) Primary VS secondary (Systemic disease)

c) Aim of lab investigation

1) Establish **diagnosis**

2) Predict **prognosis**

3) Guide **treatment**

4) Help **monitoring**

d) Basic principle of laboratory investigation

I) **Simple fast screening to complex confrmatory test**

II) **Cheap to expensive test**

III) **Non-invasive to invasive tests**

16) Clinical features of haematological tests

A) Blood cell investigation

➔Complete Blood count

→Fast, Simple, Cheap, Non-invasive, Excellent

a) **Iron deficiency Anaemia** **(**Microcytic)

I) Small and pale RBC

II) Low serum iron

III) Low serum ferritin (**Low storage)**

IV) High serum transferrin **(Compensatory aiming at increase transport)**

V) Lower transferrin saturation

b) **Alpha-Thalassemia** **(**Microcytic)

I) Small RBC

II) Detection of HbH(beta-4) Inclusion Bodies

c) **Megaloblastic anemia (Vit B12 and folate deficiency)**

I) Hypersegmented neutrophils

II) Oval macrocytes

d) **Sickle cell anaemia (Hereditary)**

➔Sickle blood cells

e) **Bone marrow disease**

I) Circulating blasts

II) Unexplained cytopenia

B) Bone Marrow investigation

➔Invasive but safe

➔Requires expertise in assessment

➔Determine if it is **inadequate vs ineffective** haemopoiesis in cytopenia***

a) Congenital dyserythropoietic anaemia

➔Ineffective erythropoiesis

➔Erythrocytopenia

b) Aplastic Anaemia

➔Damage in bone marrow cells

➔Pancytopenia

c) Miliary tuberculosis

d) Acute promyelocytic leukaemia

➔Cancer of WBC

➔Abnormal accumulation of immature granulocytes (Promyelocytes)

e) Myelodysplastic syndrome

➔Ineffective production of all blood cells

➔Pancytopenia

f) Primary myelofibrosis

➔Bone marrow cancer

➔Proliferation of abnormal bone marrow cells

g) Other malignant cases

➔Provide optimal material for further special investigations

C) Special investigation for malignant haematological diseases

a) **Aim**

I) To classify malignant disease for choice of specific treatment

II) To predict prognosis for counselling and risk-adapted therapy

III) To monitor residual disease after treatment

b) **Measures**

I) Cytochemistry

➔To classify acute leukaemia

➔Demonstrate enzymatic function of blast

II) **Immunophenotyping**

➔To classify leukaemia

➔Using antibodies to detect lineage-associated antigens in abnormal cells

➔By **Flow cytometer**

D) Genetic Testing

a) Aim

➔Confirmation for inherited haematological diseases with known genetic defects

→**E.g. Thalassemia**

➔Some malignant hematological disease are also genetic diseases

→Acquired mutations

b) **Measures**

I) Cytogenetic studies

→Culture malignant cells and examine their chromosomes

→Predict prognosis and examine their chromosomes

II) **Molecular genetic tests**

→Classification, prediction of prognosis and MRD monitoring

→Determine lineage of abnormal cells, gene mutation, fusion

E) Bleeding and Thrombosis investigation

a) Prothrombin Time (PT)

➔Add tissue factor + phospholipid + calcium

→Measure **extrinsic** + **common** pathway

→**Factor VII, X, V, prothrombin, fibrinogen defect *****

➔Liver disease (production)

➔Disseminate intravascular coagulation (consumption)

➔Warfarin therapy (inactivate)

b) Activated partial thomboplastin time (APTT)

➔Add phospholipid + calcium

→Measure **intrinsic + common** pathway

→Factor **XII, XI**, X, **IX, VIII**, **V, prothrombin, fibrinogen**

➔Liver disease (production)

➔Disseminate intravascular coagulation (consumption)

➔Heparin therapy (inhibition)

c) Thrombin time (TT)

➔Add thrombin

→Measure **common** pathway

→**Fibrinogen**

➔Liver disease (production)

➔Disseminate intravascular coagulation (consumption)

➔Heparin therapy (inhibition)

d) Von Willebrand Factor (vWF) Testing

e) Platelet function test

f) Coagulation inhibitor testing

g) Specific coagulation factor assay

h) PC,PS,AT assay

17) 1

18) 1

19) 1