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Newsletter of Departments of Pathology and Microbiology, and Radiology

LABRAD

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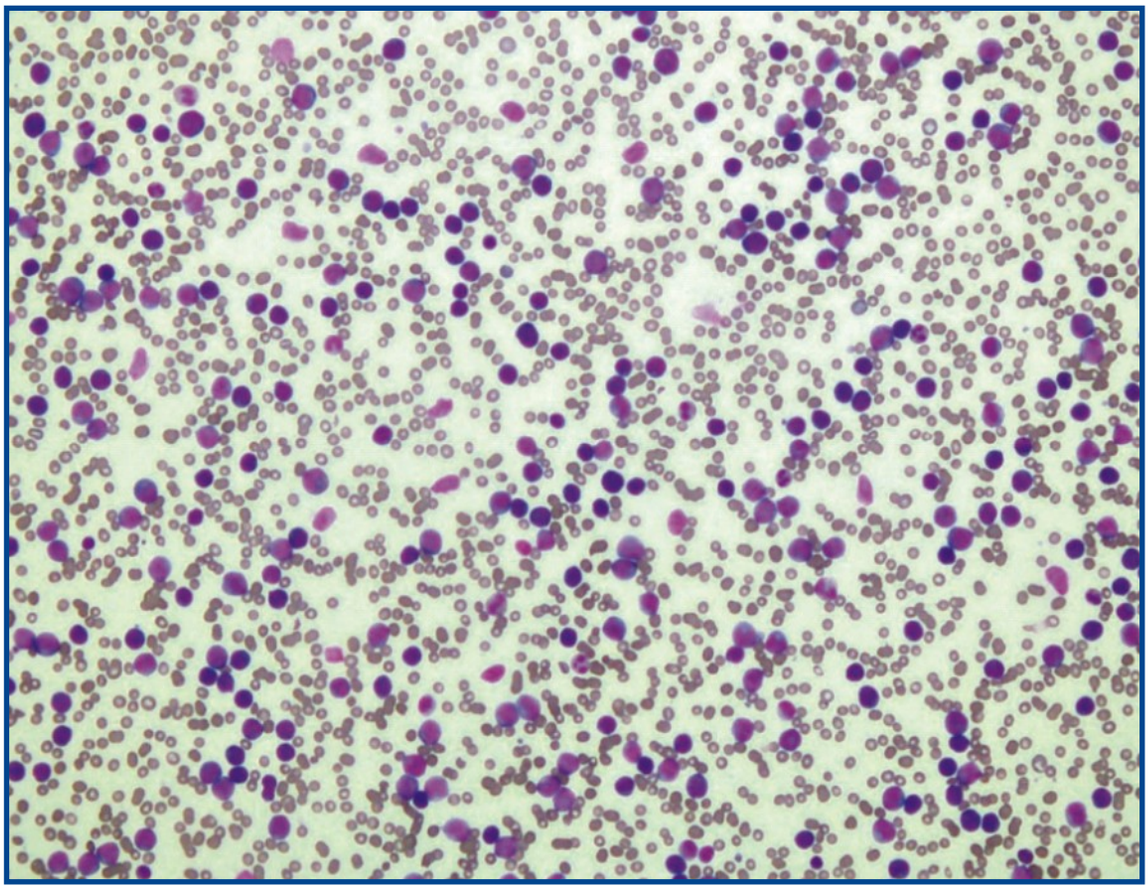

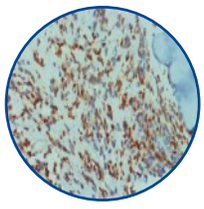

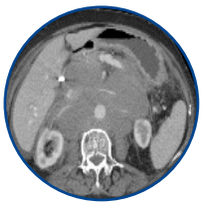

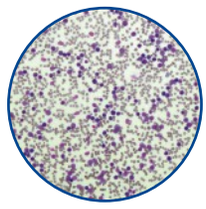

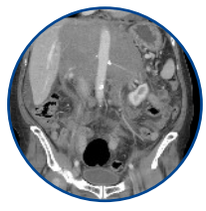

In this issue

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The Aga Khan University Hospital, Karachi

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Acute Leukemia Immunophenotyping with Pakistani Perspective

Dr Shahid Pervez, Histopathology

Immunophenotyping is currently an integral part of modalities in diagnosis of acute leukemia along with morphology, cytochemistry and cytogenetics. However in financially constrained regions like Pakistan, judicious usage in a cost-effective manner is of paramount importance.

Primary goals for immunophenotyping in acute leukemia are lineage assignment of blasts and further sub-classification. Secondary goals include prognostication and minimal residual disease assessment.

We recommend performing immunophenotyping after meticulous morphological assessment and histochemistry. This would help in the selection of panels in a cost – effective fashion.

The following approaches are used in various laboratories:

Upfront (single) comprehensive panel (Fig. 1, 2 and 3)

Primary screening panel followed by secondary directed panel

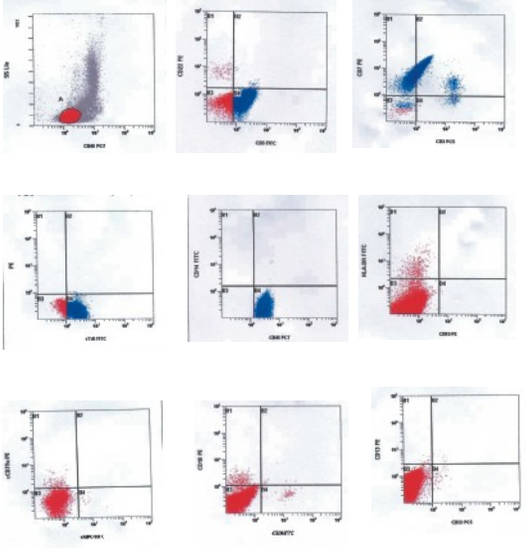


Figure 2: A comprehensive panel in a young, adult with acute leukemia. Note blast gating on a CD45 dim population. This population is showing prominent reactivity with T-Cell markers CD3, CD5 and CD7 along with cTdt consistent with 'Pre-T-ALL'.

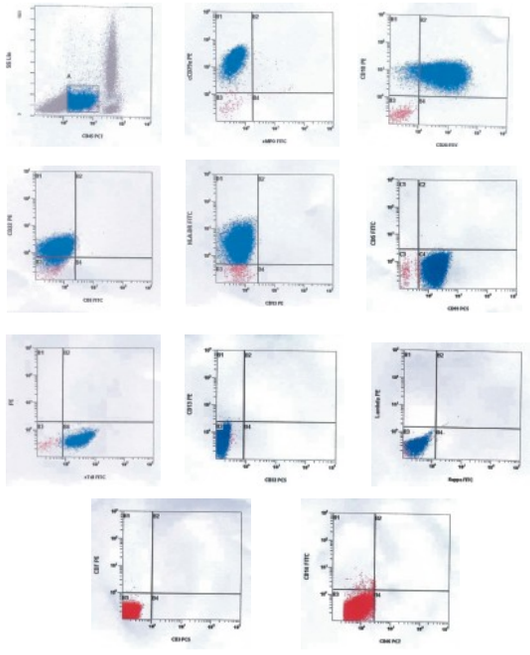


Figure 1: A comprehensive panel in a child with acute leukemia. Note blast gating on CD45 dim population. This population is showing prominent reactivity with B cell markers cCD79a, CD19, CD20, CD10, CD22 & cTdt along with HLA-DR consistent with 'Commen Pre-B-All'.

The second approach is more suitable in our scenario as it reduces the cost without compromising diagnosis. Here, primary panel composed of most sensitive markers for each lineage is able to diagnose most leukemias without additional testing. This should be as minimal a panel as necessary.

Following panels are recommended by Histopathology Section of AKUH,:

Primary Panel

B-cell:	CD19 and CD10
T-cell:	CD7 and CD3 (cyto)
Myeloid:	CD13 and CD33

Secondary Panel

B- Cell:	CD20, CD22, cCD79a, IgG, IgM, Kappa, lambda, HLA-DR and Tdt

T-Cell: CD5, CD4, CD8, CD56, HLA-DR and Tdt
Myeloid: MPO, CD14, HLA-DR, CD117, CD61

All samples must be tested for viability and gating (selecting) of the blast population by Leucogate. This is using CD45 (LCA) with side scatter (SS) and as blast population is invariably dim for CD45, it can be selected for further analysis.

Samples of bone marrow or blood should be obtained fresh possibly not over 48 hours in heparanised or EDTA tubes (3-4 cc). Transportation from different cities and distant or remote areas should be according to the defined guidelines. It is necessary that a viability check be performed on arrival of sample before proceeding further.

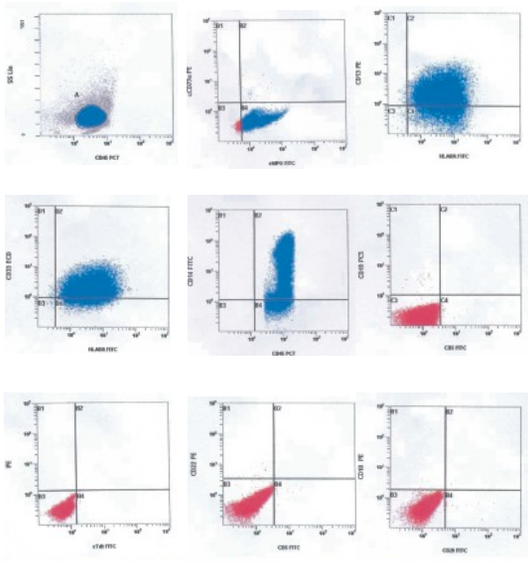


Figure 3: A comprehensive panel in a middle-aged patient with acute leukemia. Note blast gating on CD45 dim population. This population is showing prominent reactivity with myeloid markers cMPO, CD13 CD33 & CD14 alongwith HLA-DR consistent with 'Acute myelomonocytic leukemia (M4)'.

PAX5: Immunohistochemistry Marker for B cell Lymphoproliferative Disorders

Muhammad Rahil Khan; Arsalan Ahmed, Histopathology

PAX5 (B-cell-specific activator protein, BSAP) is a member of the paired-box domain gene family that encodes nuclear transcription factors. The latter are important in development, differentiation, cell migration and proliferation of B lymphocytes. PAX5 protein is expressed as a nuclear marker in B-lineage cells that span the differentiation spectrum in pro-, pre-, and mature B cells, but are not expressed in plasma cells at all. Hence, PAX5 protein is also a useful lineage-specific marker in hematopoietic neoplasms arising from B cells.

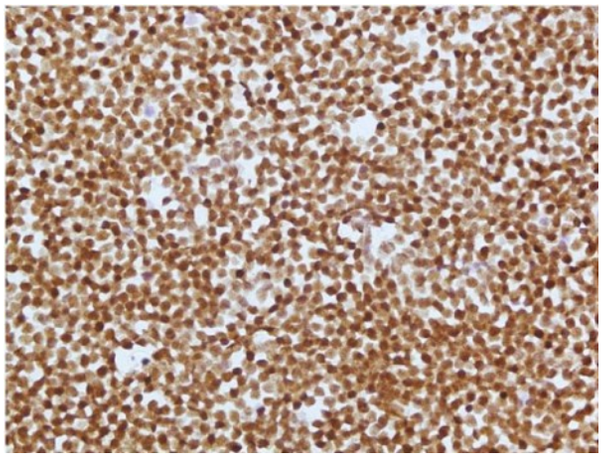


Figure 1:Bone trephine biopsy showing diffuse positivity to PAX5

Staining for PAX5 has utility in the diagnosis of B cell malignancies that lack expression of commonly used pan-B-cell markers such as CD20 and CD79a, especially acute lymphoblastic leukemia, lymphoma and post-Rituxamab treatment. In addition to its expression in B cells, PAX5 protein and/or mRNA have been reported to be expressed in neoplasms of central nervous system, testis and bladder.

PAX5 is the most sensitive and reliable immunohistochemical marker for B cell malignancies since PAX5 will always be expressed in the absence of expression of other pan-B-cell markers, suggesting that the inclusion of PAX5 in a panel of antibodies to diagnose B cell lymphomas would be very helpful. AKUH Laboratory has recently added this marker in the immunohistochemistry profile for tumors and lymphoproliferative disorders

Understanding the Water Deprivation Test

Dr Lena Jafri, Chemical Pathology

Water Deprivation Test is performed to distinguish among the two major forms of Diabetes Insipidus (DI): Central and Nephrogenic.

DI results from the deficiency or functional resistance of a pituitary hormone known as Antidiuretic hormone (ADH) or vasopressin. ADH helps in conserving water by the kidneys . Consequent to low or subnormal ADH, the kidneys are unable to retain water during filtering blood resulting in polyuria. Hence, urine output may exceed three litres in a day in adults and two litres/m^2 in children.

Central DI results from trauma or tumor in pituitary gland with subsequent failure of the posterior pituitary to secrete ADH. Rarely, it can be familial due to mutation in ADH gene. This is an autosomal dominant disorder leading to misfolded ADH precursors which are not stable and are destroyed easily.

In contrast to central type, ADH secretion is normal in nephrogenic DI but is associated with varying degrees of renal resistance to its water retaining effect. Causes of Nephrogenic DI can be structural kidney defects due to hypercalcaemia, hypokalaemia and chronic lithium usage or mutations in auaporin-2 gene or AVPR2 gene. [There are two different receptors for ADH: the V1 (AVPR1) and V2 (AVPR2) receptors. The AVPR2 gene is located on the X-chromosome (Xq-28).]

Differential diagnosis of DI includes other causes of polyuria such as diabetes mellitus and, chronic renal failure (caused by osmotic diuretics, glucose and urea). Psychogenic polydipsia is an important cause of polyuria, which usually occurs in anxious middle-aged women, psychiatric illnesses, individuals taking phenothiazines causing dry mouth.

An unusual form of transient ADH-resistance disorder is gestational DI that is observed in selected women during the second half of pregnancy. Pregnancy is associated with release of a vasopressinase from the placenta. This leads to rapid degradation of endogenous or exogenous ADH, but not of desmopressin. These women also present with polyuria.

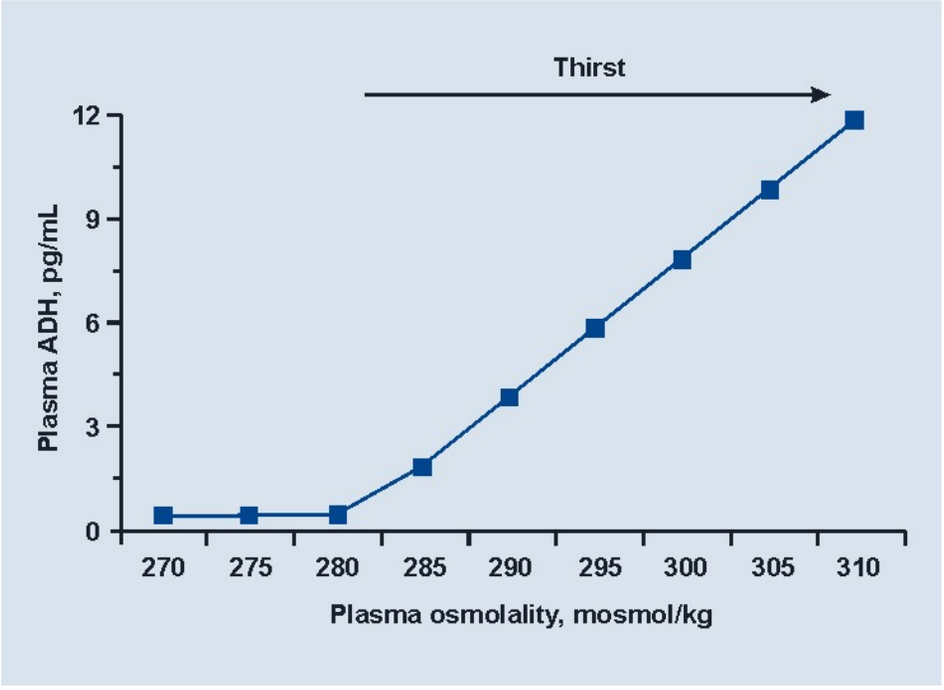


Figure 1: Relation between ADH and plasma Osmolality

The cause of polyuria is often suggested from the history, for example age of onset and eliciting the possible presence of the different causes of DI, and rarely by the plasma sodium concentration. Polyuria due to lack of ADH usually exceeds 5 litres daily. In DI there is a tendency for the serum osmolality to be increased above normal; the reverse is true in compulsive water drinkers. Specific testing is then performed to establish the diagnosis.

Water Deprivation Test helps in the diagnosis of DI. It is performed under constant medical supervision as it can potentially cause dehydration, fluid and salt imbalance.

Water is restricted from 9:00 pm the night before the test until conclusion of the test. At 7:00 am the next morning the bladder is emptied and this urine is discarded. The patient is weighed and is told to pass urine hourly beginning at 8:00 am. Urine osmolality is estimated and the test is continued until urine osmolality reaches 750 mmol/L or it reaches a plateau. (Plateau is the difference between consecutive estimations of urine osmolality of less than 30 mmol/kg). When plateau is reached blood sample is drawn for serum osmolality.

Now ADH (Desmopressin 10 microgram nasal insufflations or 4 microgram subcutaneously or 5 units of aqueous vasopressin subcutaneously) is given. One hour later urine is collected for urine osmolality estimation.

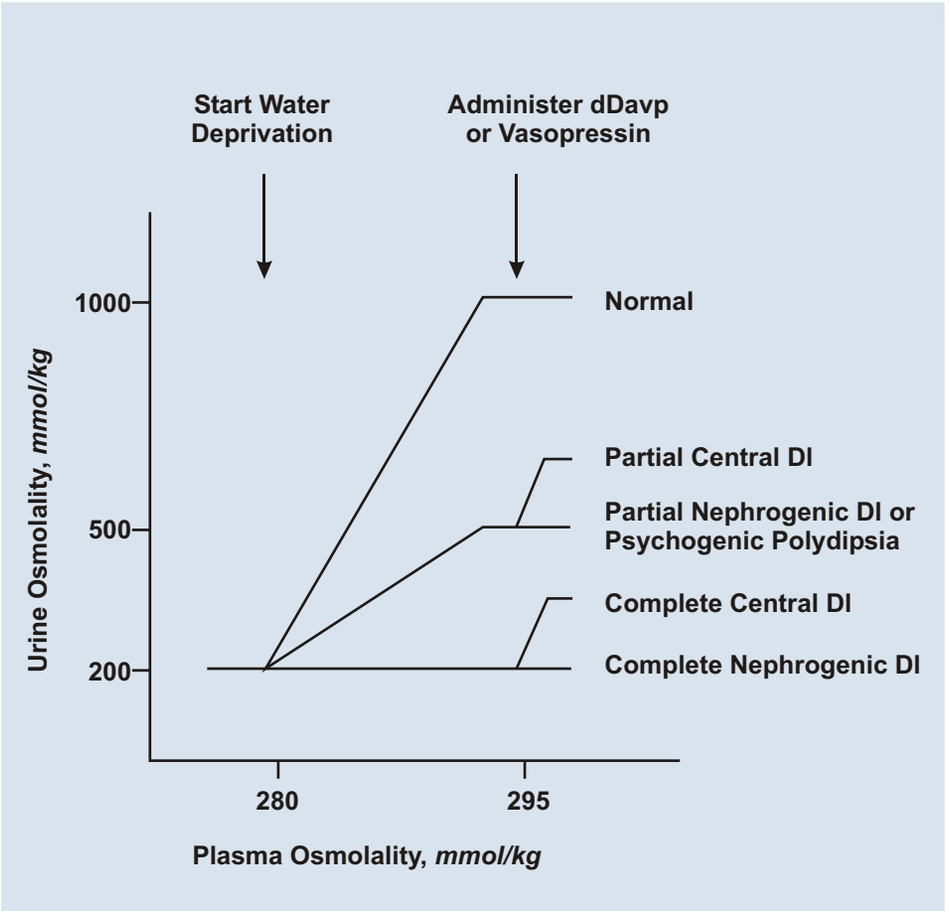


Figure 2: Interpretation of Water Deprivation Test

Aga Khan Hospital Clinical Laboratory should be notified the day before testing to arrange for stat determinations of urine and serum osmolality and for immediate processing of plasma vasopressin.

The test is discontinued if urine osmolality is stable on two or three successive measurements despite a rising plasma osmolality or if the plasma osmolality exceeds 295 to 300 mosmol/kg. The test is also halted if the patient loses >5% of their body weight.

Accurate interpretation of the water restriction test generally requires that exogenous ADH not be given before the urine osmolality has been stabilized or the plasma osmolality has reached 295 mosmol/kg. Below this level, maximum endogenous ADH effect may not be present and an antidiuretic response to ADH is of no diagnostic benefit, since it will raise the urine osmolality even in normal subjects (Figure 1). Central DI is usually partial. In the case of Central DI both ADH release and urine osmolality may increase as the plasma osmolality rises, but sub-maximally. Exogenous ADH will lead to a rise in urine osmolality of more than 100% in complete Central DI and 15 to 50% in partial Central DI (Figure 2). Nephrogenic DI is also associated with sub-maximal rise in urine osmolality in response to water restriction. Elevation in plasma osmolality stimulates ADH release. Most patients with acquired Nephrogenic DI are resistant to ADH hence no response is seen. If the history and water restriction test provide equivocal results plasma samples collected at baseline and following water deprivation (prior to ADH administration) are sent for measurement of ADH.

Note: This test can be done only under medical supervision as it can potentially cause dehydration, fluid and salt imbalance.

Gonadotropins Releasing Hormone (GnRH) Stimulation Test

Dr Noreen Sherazi, Chemical Pathology

The hypothalamic gonadotropin releasing hormone (GnRH) stimulates release of both luteinizing hormone (LH) and follicle stimulating hormone (FSH) in normal individuals. Subnormal responses are seen in some patients with pituitary and hypothalamic disorders. However, the magnitude of FSH and LH response to GnRH is usually predictable from the basal FSH and LH levels.

GnRH stimulation test is useful in patients in whom the clinical picture and basal gonadotropins measurements are inconclusive. It is indicated in patients with precocious puberty (suspect pathologic central cause) and delayed puberty (suspect hormonal cause)

The test may be performed without regard for previous feeding or time of day. After patient's consent, baseline specimens are obtained for LH and FSH determination.

After that 100 µg of synthetic GnRH is given intramuscularly or intravenously, followed by sampling for serum levels of FSH and LH at 30, 45, 60 minutes (can be taken up to 180 minutes).

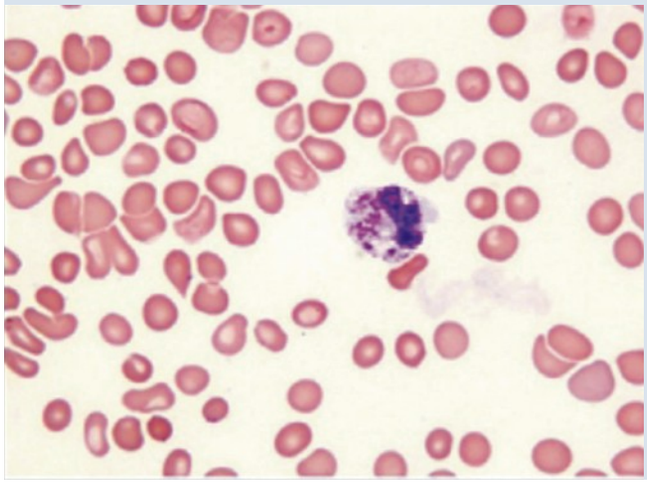
Instruction about use of medicine, dose and timings of samples can be followed as per physician request.

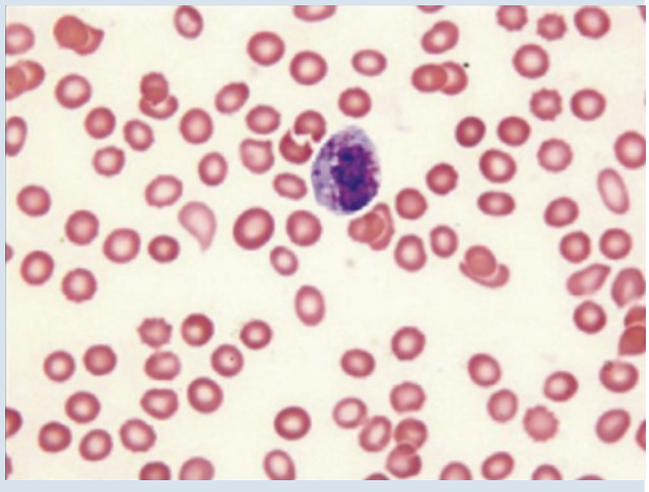
Peak responses to both FSH and LH occur between 30 and 45 minutes. Patients with pituitary disorders may have normal, diminished or absent response. Normally LH response should increase by 3-10 fold. The FSH response is of lesser magnitude, usually 1.5-3 fold increase in patients with hypothalamic disorders; the response may be exaggerated, normal, diminished or absent. In the case of Gonadotropins-independent precocious puberty, no increase over basal levels is observed. FSH and LH response is termed flat.

Haematology Quiz

Drs Natasha Ali, Kashif Khan, Haematology

A seven-year old child presented to haematology clinic with complaints of fever and failure to thrive since two months. Past history was significant for repeated upper respiratory infections. Examination revealed pallor. There was no hepatosplenomegaly. A complete blood count showed hemoglobin of 6.2 gm/dl, haematocrit





19%, normal red cell indices. WBC of 3.7 x10E9/L, ANC 1.6 x 10E9/L and Platelets 122 x 10E9/L. Peripheral blood picture is attached. Please comment on the peripheral film and give your most probable diagnosis

Red Cell Mass Study

Dr Izza Hussain, Haematology

Red cell mass (RCM) is the measurement of total volume of erythrocytes in the body. Its significance lies in the fact that Polycythemia Vera Study Group (PVSG) requires RCM to be measured for the diagnosis of polycythemia rubra vera (PRV) - a myeloproliferative disorder that is associated with absolute increase in red cells. The International Council for Standardization in Haematology (ICSH) has recommended that blood volume should be calculated in terms of body surface area.

RCM studies are based on dilutional analysis. The patient red cells are labeled with radioactive sodium chromate (Cr51) and injected intravenously. The dilution is measured after allowing sufficient time for Cr51 tagged red cells to become thoroughly mixed in circulation. From the dilution, the total blood volume of red cells can be calculated. Results are recorded as counts per seconds (cps) and background counting is measured by gamma counter. RCM is then calculated using body surface area.

It is considered elevated if it is >25% above the mean expected value. False positive results can be observed in obese patients with PRV who has had significant recovery or during gastrointestinal blood loss.

Red cell mass study helps to differentiate between absolute and apparent erythrocytosis. The former is the absolute raised red cell mass with normal plasma volume while the latter is spuriously high red cells counts secondary to reduced plasma volume. RCM is required for establishing the diagnosis of PRV. It is one of the chronic myeloproliferative disorders characterised by clonal proliferation of myeloid cells distinguished clinically from other myeloprpliferative disorders by the presence of increased red cell mass which results in increased red cell counts, elevated haemoglobin and increased haematocrit (packed cell volume).

Diagnostic Criteria for PRV

Major
• Increase red cell mass (25% above predictive value or PCV > 60 in males and 56 in females)
• Arterial oxygen saturation > 92% with no elevation of serum erythropoietin (EPO) concentration
• Palpable Splenomegaly
• Acquired clonal genetic abnormality except BCR-ABL fusion
Minor
• Platelet count > 400 X 10^9/L
• WBC count > 10 X 10^9/ L or 12 X 10^9/ L in smokers
• Radiological splenomegaly
• Endogenous erythroid colonies or low EPO

Diagnosis of PRV requires presence of two major criteria or presence of any major with any two minor criteria. Additionally, presence of JAK-2 mutation (exon 14 or 12), Karyotyping abnormality other than t9:22, bone marrow biopsy showing hyper cellularity with prominent erythroid, granulocytes and megakaryocyte proliferation with characteristic absence of storage iron may be required for diagnosis.

What should a patient know before RCM studies?

1.	It is a sufficiently long test requiring at least 2.5 hours for completion
2.	Ionic dyes are sometimes allergic, but this is a radio nucleotide scanning, it will not affect the patient's health (amount of chromium used in the study is <2 ìg/ml while toxic level is > 10 ìg/ml to inhibit glycolysis and > 5ìg/ml to inhibit glutathione reductase)
3.	Getting the blood back after tagging is part of the study and all the aseptic techniques are employed to ensure safety
4.	During travelling, the patient will not be detected by metal detectors

Semen Analysis: An Invaluable Tool for Infertility Work-up

Azra Ali and Dr Shahid Pervez, Histopathology

Semen analysis is the most useful front-line test in the fertility work-up in males. It is essential that semen is collected according to pre-defined strict guidelines, so that a true picture of the fertility status may emerge. The test is simple, cheap, non-invasive and most informative.

Sample Collection Guidelines

1.	The sample should be collected after a minimum of 48 hours but no longer than seven days of sexual abstinence
2.	Ideally the sample should be collected in the laboratory but if this is not possible it should be delivered to the laboratory within one hour of collection
3.	The sample should be protected from extremes of temperature (less then 20°C - more then 40°C) during transportation
4.	The sample should be obtained by masturbation into a clean, wide-mouth container (available at AKUH lab points)
5.	The container must be adequately labeled with the subject's name and identification number

Like all biological specimens, semen samples may contain harmful infectious agents (for example HIV, hepatitis B) and should therefore be handled carefully. A normal semen sample liquefies within 60 minutes at room temperature, although in most cases this occurs within 15 minutes. After liquefaction the physical and microscopic examination is performed.

The semen contains spermatozoa and seminal plasma which is a semi-gelatinous fluid. Testis produce spermatozoa while the assessory glands namely the epididymis, prostate, seminal vesicles and bulbo-urethral glands produce the seminal plasma.

The first part of ejaculate contains most of the spermatozoa suspended in prostatic and epididymal fluid while its last part has residual spermatozoa suspended in the vesicular fluid.

The spermatozoa constitute only 1-5% of the total ejaculate. Spermatozoon is a unique cell which neither grows nor divides. It consists of a head, a mid piece and a tail. It is a highly specialised cell with considerable power of movement in order to complete its task of fertilisation of the oocyte.

Physical characteristics of semen like appearance, volume, viscosity are noted. Its pH is measured and microscopic examination is also performed and reported.

Normal Values for Human Ejaculate

Volume	>2.0 ml
PH	7.2-7.8
concentration	20 x 10^6 spermatozoa/ml or more
motility	>50%
morphology	>30% with normal morphology
WBC	<1.0 millions/ml

Microscopic Examination

This is done to estimate total sperm count as well as percentage of motile sperms. Motility of the spermatozoa like rapid linear progression, slow/non linear progression and non progressive sperms. On morphology defects of head (e.g. large, small tapered pyriform, round and amorphous heads), neck and mid-piece (namely bent head, thick mid-piece) and tail (such as short, multiple hairpins and bent tail) are noted.

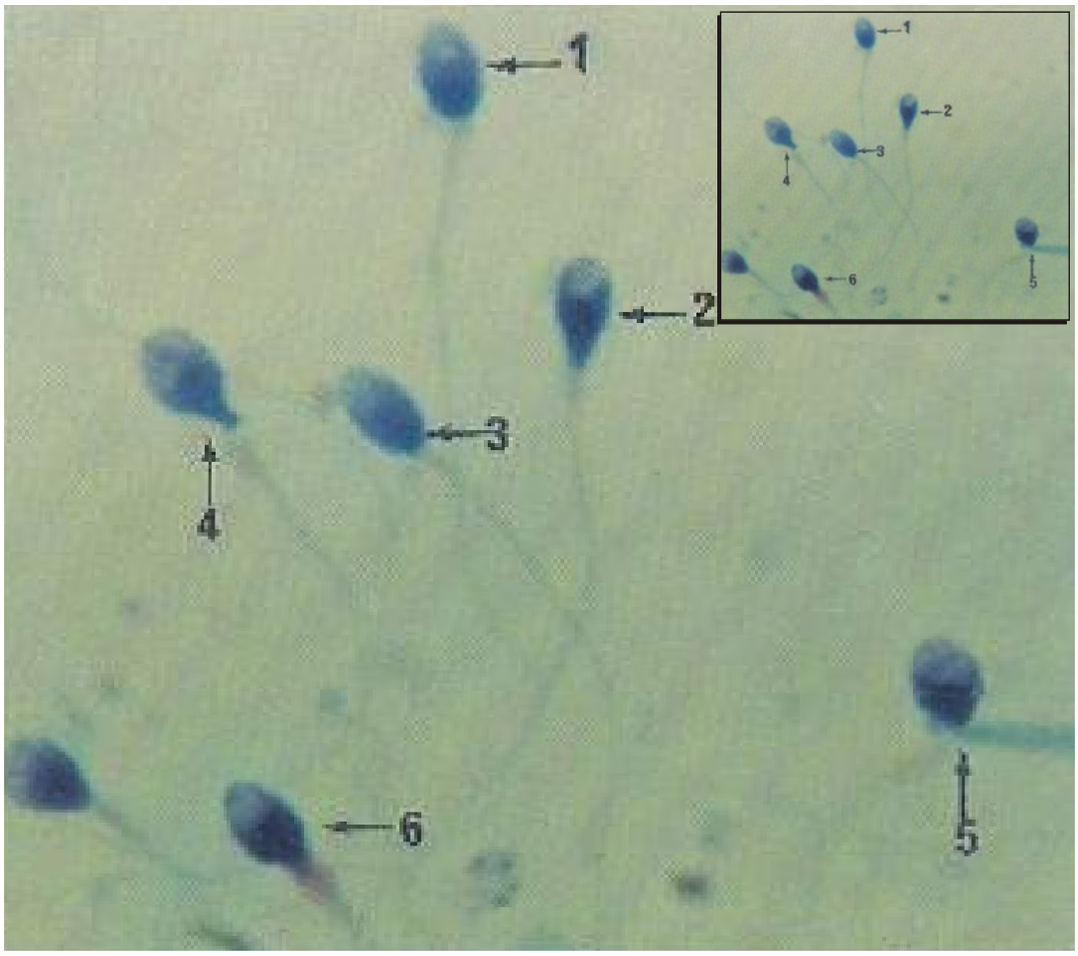


Figure shows: 1-Normal, 2-Pyriform head, 3-Normal, 4-Amorphous head, 5-Bent head, 6-Amorphous head with thick mid-piece. (Acquired from WHO Lab. Manual - 1)

Nomenclature for Semen Variables

Azoospermia: Total absence of sperms in an ejaculate
Oligozoospermia: Reduced number of sperms in semen (less then 20 millions/ml)
Polyzoospermia: Increased number of sperms in semen (greater then 200 millions/ml)
Normozoospermia: Normal sperm counts
Aspermia: Total absence of an ejaculate
Haematospermia: The presence of blood in semen
Leukocytospermia: White Blood Cells in the semen

Foetal Anomaly Scan

Dr Shaista Afzal; Muhammad Owais Khan, Radiology

Foetal Anomaly Scan is done at Aga Khan University Hospital with dedicated appointment and time slot.

The objective of this scan is to examine the anatomy of foetus and assessing its normal growth along with evaluation of placental position. The structures examined include the brain, spine, heart, kidneys, lips, legs, feet, lungs, stomach, kidneys, bladders, umbilical cord and limbs. The liquor volume will also be assessed at the same time. Foetal anomalies are sometimes associated with abnormal liquor volume. A second appointment may be needed for completion of examination if the foetus is in a position which makes scanning difficult or if the image is not very clear as in larger women. The best time to do this scan is around 20 weeks of pregnancy because the baby's parts are not crowded and easily seen. The scan usually takes about 20 minutes.

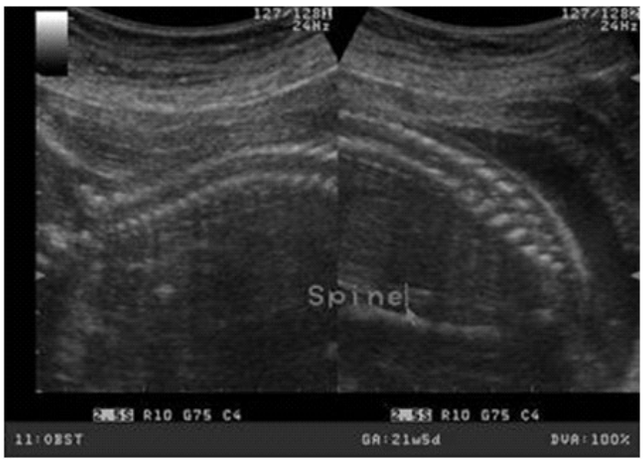


Figure: A foetal anomaly scans at 21 weeks.

An anomaly scan will detect approximately 50% of significant abnormalities Their early detection enables appropriate and timely intervention and thus can decrease the tremendous psychological trauma and financial burden on the family and society.

The foetal anomaly scan is done to reassure a woman that her baby has no structural abnormalities. It aids to identify anomalies not compatible with life or those that are associated with morbidity or disability. Most of the time, the scan will not review any abnormality. In fact, 98% of babies born are normal. If an abnormality is detected, rescanning may be carried out by another doctor to confirm the diagnosis. In case of life threatening anomalies, for example anencephaly of foetus, termination of pregnancy can be suggested.

If the problem requires surgery soon after birth, for example gastroschisis, then preparations are made for surgery to be done after birth. If the abnormality is associated with chromosomal abnormality, then cordocentesis will be performed to determine the karyotype.

The table below shows the major anomalies and their percentage chances of being detected.

Problem	What the problem is	Chance of being seen
Spina bifida	Open spinal cord	90%
Anencephaly	Absence of the top of the head	99%
Hydrocephalus	Excess fluid within the brain	60%
Major congenital heart problems		25%
Diaphragmatic hernia	A defect in the muscle which separates the chest and abdomen	60%
Exomphalos/gastroschisis	Defects of the abdominal wall	90%
Major kidney problems	Missing or abnormal kidneys	85%
Major limb abnormalities	Missing bones or very short limbs	90%
Cerebral palsy	Spasticity	Never seen
Autism		Never seen
Downs syndrome	May be associated with heart and bowel problems	About 40%

Reference: Royal College of Obstetrics and Gynaecologists (2000)

Diagnosis of Helicobacter pylori Infection

Sadia Omer, Microbiology

H. pylorus is a helix-shaped gram-negative pathogen responsible for gastritis, peptic ulcer disease and gastric MALTomas in humans. It is also associated with the development of gastric adenocarcinoma. Approximately 50percent of the world's population is affected by gastric *H. pylori* infection. Infection is more frequent in less developed countries like Pakistan, India and Bangladesh. Many invasive and non-invasive methods are available for the detection of *H. pylori* infection. If done properly all of these methods have a diagnostic accuracy of more than 95%. However, each test has its advantages and disadvantages.

NON INVASIVE METHODS

Serology (Blood Antibody Test)

Titers of serum immunoglobulin IgG and less frequently IgA to *H. pylori* is a quick and readily available modality for diagnosis. The sensitivity of this test is 76-84percent which is more sensitive than biopsy as in essence it samples the entire stomach. The biopsy only samples a small region and since the inflammatory process may be patchy, it may be missed. However it does not help in the determination of lesion or pathology and has no antimicrobial susceptibility. This test is available at AKUH laboratories.

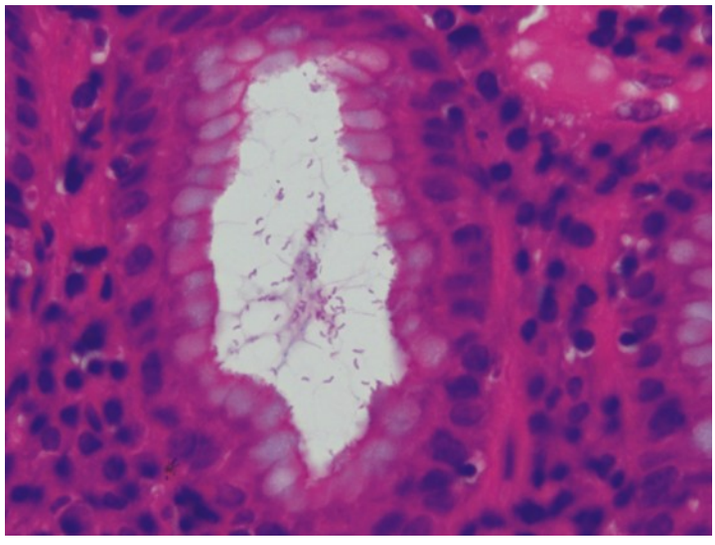


Figure 1: Helicobacter pylori H&E Stain
Courtesy Dr M Abrar Barakzai (Histopathology Section, AKUH)

Detection of Salivary *H. Pylori Antibody*

IgG antibodies detection from saliva could be used reliably for screening dyspeptic patients in general practice, especially in children in whom venesection is more difficult. However this test is not locally available up till now.

Stool Antigen Test

Stool antigen-testing allows non-invasive detection of *H. pylori* that is indicative of active infection. A positive result on the stool antigen test seven days after completion of therapy identifies patients in whom eradication of *H. pylori* was unsuccessful. The sensitivity of this test ranges from 86-94% and has a specificity of 92-97%. However it is not a quantitative test and like the serological test it does not help in the determination of lesion or pathology and has no antimicrobial susceptibility. This test is available at AKUH laboratories.

Urea Breath Test

Urea breath test is an effective diagnostic method for *H. pylori*. Results of these assays correlate with numbers of urease producing *H. pylori* organisms. This is the most valuable test for assessing response to eradication therapy after 6 to 8 weeks. It has a sensitivity of 90-95% and a specificity of 94-100% But the drawback of this test is that it is expensive, involves administration of radioisotopes and is not quantitative.

INVASIVE METHODS

Endoscopy with Biopsy

The gold standard method for detecting *H. pylori* infection is a biopsy taken during an endoscopy. This

permits the inspection of pathology and allows the detection of ulcers, strictures and neoplasm. Biopsy specimens may be cultured for *H. pylori* but require expertise and resources. Another advantage is that antibiotic susceptibility testing could be performed. However it is an expensive and invasive procedure, and as compared to other diagnostic modalities is time consuming.

Molecular Methods

PCR for the detection of *H.pylori* in tissue biopsy samples is available. Moreover polymerase chain reactions are available that could detect resistance genes and could therefore give an idea about the antimicrobial susceptibilities. However these tests are not widely available and are a research tool at this moment.

Hepatitis C Virus (HCV) Genotyping

Afsheen M. Ibrahim, Molecular Pathology

HCV has infected nearly 170 million people worldwide. Out of this, 3/4 million are newly infected. There are about 30percent cases of acute hepatitis and 80percent cases of chronic hepatitis that develop a risk of cirrhosis and hepatocellular carcinoma.

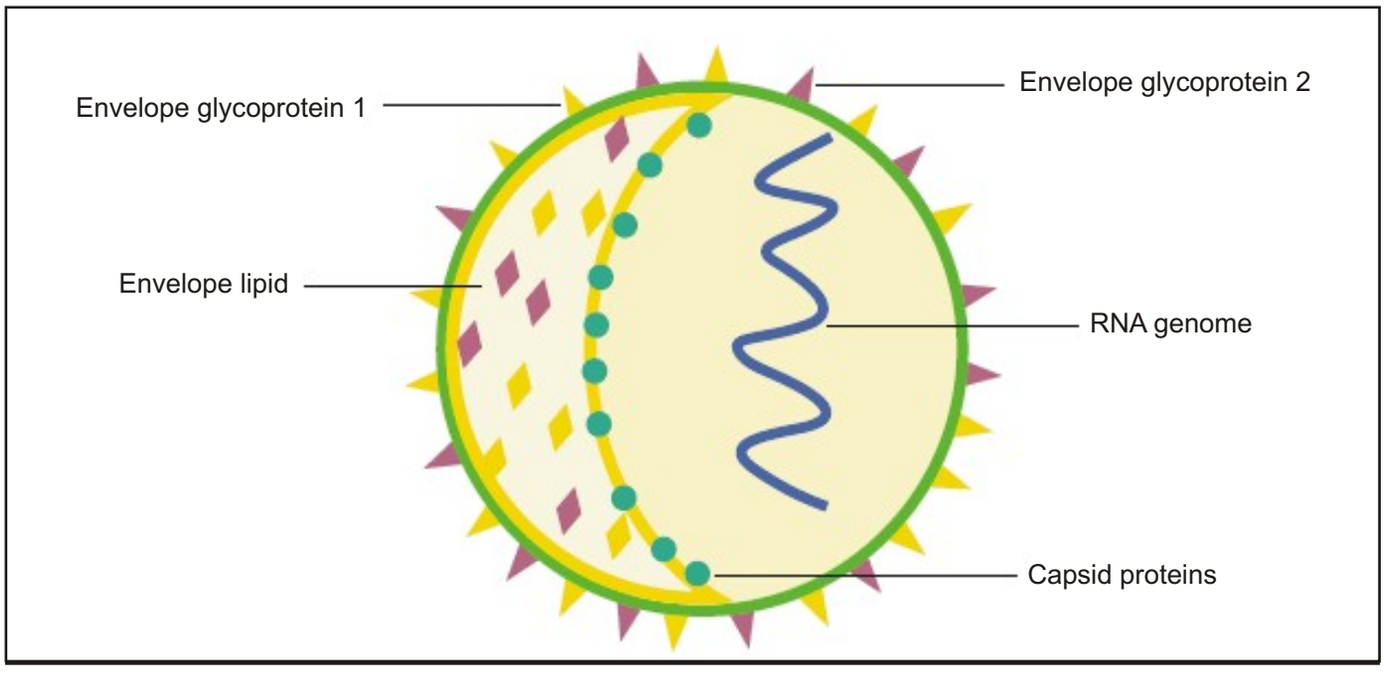


Figure 1: Model structure of HCV

The hepatitis C virus is a small 15 nm, enveloped, single stranded, positive sense RNA virus. It is a member of hepacivirus genus in the family flaviviridae. HCV genome is approximately 10,000 nucleotides which codes for 3,000 amino acids.

Due to different genetic variations several different strains of HCV are identified, called genotypes. With the advent of advanced molecular tests, HCV genome is classified into six main genotypes (1a-6a) and several subtypes (1a, 1b etc). The most common genotype in Asia including Pakistan is 3a.

Genotype information is important for patient management and prediction of treatment response. A genotype test requires a blood sample. RNA is extracted from serum and reverse transcribed (RT) to cDNA and amplified using polymerase chain reaction (PCR). The PCR product is denatured and hybridized to the nitrocellulose strip with HCV genotypes already bound to it. After hybridization of PCR product with the strip, conjugate is applied and substrate is added resulting in

purple brown precipitate. A line is considered positive when a distinct brown spot appears on the strip as shown in figure 2.

The success rate of antiviral treatment (Interferon plus Ribavirin) ranges from 50-90%. Genotype 1 has least response (50%) to therapy while genotype 2 and 3 show best response (nearly 90%). Genotype of a person remains the same throughout the treatment unless person is re-infected with another genotype.

At Aga Khan University Hospital, Molecular Pathology Section of Clinical Laboratory, HCV in serum is tested by RNA extraction and amplification using Amplicor HCV assay and HCV positive samples are then genotyped using Linear Array HCV genotyping kit based on hybridization to genotype specific probes.

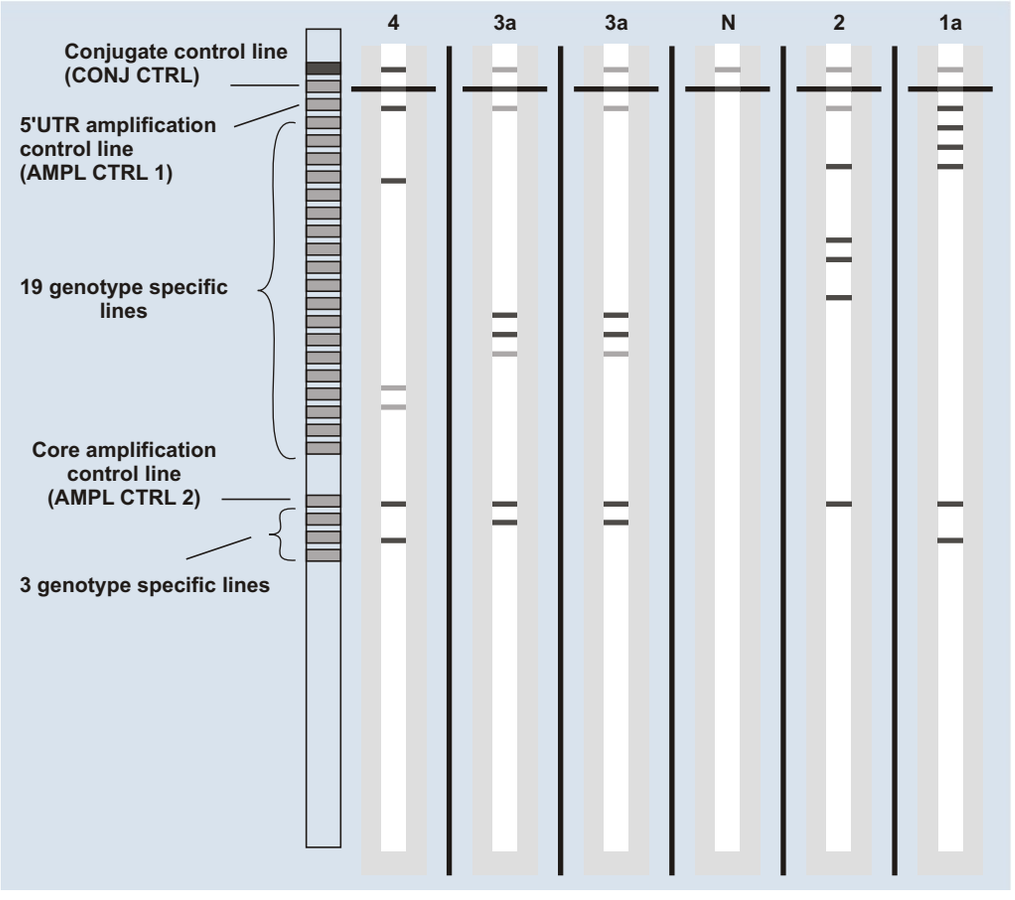


Figure 2: Banding pattern of genotypes on different strips.

Answer to Haematology Quiz

Drs Natasha Ali, Kashif Khan, Haematology

Peripheral blood film shows characteristic large granules in neutrophil (left) and monocyte (right) seen in Chediak Higashi syndrome.

Chediak Higashi syndrome is a fatal inherited autosomal recessive disorder characterised by a defect in formation of lysosomes in multiple cell lineages. Abnormally large granules in leucocytes and other granule containing cells is the hallmark characteristic and diagnostic feature. Haematological abnormalities are most apparent in the granulocytic series although anaemia and thrombocytopenia also occur. Homozygotes for defective genes suffer from partial albinism, neurological abnormalities, and recurrent bacterial infections.

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