Online Pilot Webinar Series on Quality Assurance in Transfusion Transmissible Infections Testing

Introduction:

Blood transfusion is a life-saving intervention that has an essential role in patient management within the health-care system. The establishment of a system to ensure that all donated blood is screened for Transfusion transmissible infections is a core component of every blood transfusion setup. Blood safety depends on the recruitment and retention of blood donors who are at low risk of transmitting infection, safe blood collection procedures, reliable testing for transfusion-transmissible infections, blood grouping and compatibility testing, and the appropriate use and safe administration of blood. The World Health Organization Blood Transfusion safety program developed a plan of action to ensure blood safety, promote them at all levels, and provide support to member countries in achieving it.

This initiative of WHO is directed towards nurturing capacity building of safe blood transfusion practices through a unique model of online training imparted through pre-recorded videos, which in a short duration of time and with a wider regional and national reach to the healthcare providers, will help them in optimum utilization of their limited resources, capitalization of their inherent potential and capabilities.

Aims and objectives:

Aim of this project was to conduct a 3-day online pilot webinar series through pre-recorded videos on quality assurance of TTI testing for the health care providers engaged in blood transfusion services in the countries of the SEAR for the up-gradation of quality on TTI testing to promote blood safety.

Objective:

- To provide technical guidance and training to upgrade the quality of testing of TTI
- Capacity building of various areas of TTI testing including the selection of appropriate testing assay, formulation of SOPs, quality control performance and management of TTI testing equipment
- To provide insight into the recent advancements and future directions of TTI testing

Mode of Delivery and Event reporting:

Though the world around us stands still during this pandemic, AATM successfully completed a three-day online pilot webinar series in association with the World Health Organization. The training program was piloted to 4 countries, Bangladesh, Nepal, Indonesia and Maldives.

The webinar featured presentations by International speakers addressing basic aspects to the cutting-edge technology for screening of Transfusion transmissible infections. (Annexure 1 - Program Brochure)

Opening Session:

During the opening session, Dr. Philippa Hetzel is the Director of ‘National Reference Laboratory’, Australia spoke on ‘Quality Assurance Program in TTIs Testing Laboratory’. Dr.

Yuyun Maryuningsih Team Lead Blood and other Products of Human Origin (BTT) WHO presented the global perspective and Dr. Aparna Singh Shah, Regional Advisor World Health Organization (WHO)-SEARO, discussed the Quality Assurance in TTIs testing in South East Asia Region. Dr. N Choudhury, President of AATM and Dr Shamee Shastry, Professor and head of the department of Transfusion Medicine from Kasturba Medical College, Manipal were the main co-ordinators of the program.

The webinar series had pre-recorded lectures, video demonstrations and panel discussion. The main objective of the program was to strengthen the quality of TTI testing services in the blood centers of the participating countries

Topics and speakers: (Annexure 2 - Program Schedule)

Program Schedule with the details of the topics and the speaker

Day 1; 27th April 2021		
GMT –Hrs (IST)	**Topic**	**Speaker**
5.30-6.00 (11-11.30am)	**Inauguration**	
6.00-6.30 (11-30-12.00pm)	**Orientation on Quality Management System for Screening of TTIs**	**Dr. Armstrong Australia**
6.30-7.00 (12.00-12.30pm)	**Overview on Transfusion Transmissible Infections and Evolution of screening Techniques**	**Dr. Shivaram C India**
7.00-7.30 (12.30-1pm)	**Process Control of TTI laboratory**	**Dr. Sangeeta Pathak India**
7.30-7.45 (1-1.15pm)	**Q/A session**	**Speakers**
7.45-8.15 (1.15-1.45pm)	**Principles and Practices of ELISA for TTI Screening**	**Dr. Sadhana Mangwana India**
8.15-8.45 (1.45-2.15pm)	**Demonstration of ELISA Technique**	**Dr. Ganesh Mohan India**
8.45-9.15 (2.15-2.30pm)	**Q/A session**	**Speakers**
Day 2; 28th April 2021		

5.30-6.00 (11-11.30 am)	**Principles and Practice of Chemiluminescence Assay for TTI Screening**	**Dr. Ankit Mathur India**
6.00-6.30 (11.30-12.00 pm)	**Demonstration of Chemiluminescence Assay for TTI Screening**	**Dr.Dhivya Kandasamy India**
6.30-6.45 (12.00-12.15 pm)	**Q/A session**	**Speakers**
6.45-7.15 (12.15-12.45 pm)	**Principles and Methods of Rapid Testing in TTI**	**Dr. Aikaj Jindal India**
7.15-7.45 (12.45-1.15 pm)	**Demonstration of Rapid Testin**	**Dr. Chenna Deepika India**
7.45-8.00 (1.15-1.30 pm)	**Q/A session**	**Speakers**
8.00 – 8.30 (1.30-2.00 pm)	**Quality Control in TTI Laboratory**	**Dr. Wayne Dimech Australia**
8.30-9.00 (2.00-2.30pm)	**Demonstration of Preparation and validation of QC Samples for screening of TTIs**	**Dr. Ambuja K India**
9.00 – 9.30 (2.30-3.00 pm)	**Documentation and Records in TTI Laboratory**	**Dr. Sitalakshmi S India**
9.30-9.45 (3.00-3.15pm)	**Q/A session**	**Speakers**
Day 3; 29th April 2021		
5.30-6.00 (11-11.30 am)	**Equipment Management in TTI Laboratory**	**Dr. Nova Hippy Indonesia**
6.00-6.30 (11.30 – 12.00 pm)	**External Quality Assessment Scheme and Proficiency Testing**	**Dr. Gajendra Gupta India**
6.30-7.00 (12.00-12.30 pm)	**Root Cause Analysis and Process Improvement in TTI Laboratory**	**Dr. Shamee Shastry India**
7-00-7.15 (12.30-12.45 pm)	**Q/A session**	**Speakers**
7.15-7.45 (12.45-1.15pm)	**Recent Advances: Nucleic Acid testing for TTI Screening**	**Dr. Rahul Katharia SGPGIMS, Lucknow**
7.45-8.15 (1.15-1.45 pm)	**Recent Advances: Pathogen Inactivation and Blood Safety**	**Dr. C K Lee Hong Kong**
8.15-8.45 (1.45-2.15 pm)	**Donor Notification and Counselling**	**Dr. Nusret Nuri Solaz, Turkey**

8.45-9.15 (2.15-2.45 pm)	**Waste Management in Transfusion Centre**	**Dr. Nabajyoti Choudhury India**
9.15-9.30 (2.45-3.00 pm)	**Q/A session**	**Speakers**
9.30-10.15 (3.00-3.45 pm)	**Panel Discussion & Closing Moderator; Dr. Aparna Shah**	**Panelists: Dr. Philippa Hetzel, Australia Dr. Sandy Walker, Australia Dr. Lakhman E, Sri Lanka Dr. Ananda G. Sri Lanka Dr. Nabajyoti Choudhury, India Dr. Shamee Shastry**

Summary of the presentations:

- **Orientation on Quality Management System for Screening of TTIs by Dr Vee Armstrong**

Learning Objectives: To provide an introduction to:

- How TTI screening can improve the safety of blood donations
- Why TTI screening alone is not sufficient to ensure safety
- The differences between QC, QA & QMS, how they fit together & how they can improve our confidence in TTI screening

Brief Summary: One of the key obligations of a Blood Establishment is to provide safe blood for patients. While assurance of blood safety depends on several activities, screening of blood for transfusion transmissible infectious agents (TTIs) is a critical component. Donor blood screening has evolved over the years from largely manual screening tests for hepatitis B surface antigen to more efficient automated methodologies that include detection of newly emerging TTIs. This evolution has resulted in improved sensitivity and specificity of screening tests, with the ideal screening test having the highest level of sensitivity and the greatest degree of specificity. However, these improvements in sensitivity and sensitivity are not enough to ensure that blood screening is always effective, reliable and accurate. Different manufacturers' brands and methodologies have differing levels of performance, and in addition, there are a number of other factors and risks that can affect test performance, such as contamination, human errors, poor choice of materials, inadequate maintenance of equipment, poor record keeping etcetera. Confidence in the reliability of screening results can be significantly improved by implementing a quality management system (QMS) to manage these risks. Quality activities have also evolved over time. Initially, a screening laboratory's focus was on quality control (QC). Manufacturers provided known positive and negative controls with their screening kits, and these were included on every test run to validate the results, with runs rejected and repeated where the

controls did not give the expected results. Although these controls are an essential part of test run QC, they only identify problems after the problems have occurred and therefore do not prevent re-work or corrective action when used on their own. Optimised by the manufacturer for their own specific brand of test, the positive and negative controls are also ineffective at monitoring sensitivity and specificity. Quality assurance (QA), however, includes the performance of QC in addition to other activities that focus on preventing problems rather than simply identifying them after they have occurred. QA therefore not only enables test runs to be validated, but also increases confidence in the efficacy, reliability and accuracy of the test performance. A key QA activity is both the regular use of an independent control sample and the periodic use of external QA proficiency samples (or EQAS) on test runs to monitor test performance. Implementation of a quality management system (QMS) extends QA activities by providing a systematic organisational approach to quality. It provides a framework for quality activities that encompasses QC and QA as well as other activities such as the documented investigation, correction and prevention of problems, management of equipment and materials, staff training, and self-assessments or internal audits. A QMS is usually established for the whole organisation and sets out the quality requirements that all departments should follow. Establishment of a QMS is also currently a key component of good manufacturing practice (GMP) and good laboratory practice (GLP), focussing on the old adage "Prevention is Better Than Cure".

- **<u>Overview on Transfusion Transmissible Infections and Evolution of screening Techniques - By Dr Shivaram</u>**

  Learning objective: To understand

  Characteristics of TTI
  Mandatory screening of TTI
  Emergence and evolution of screening techniques
  Principles of TTI testing
  Residual risk of TTI and Donor notification

  Brief summary:

  All infections are not TTIs. The agent must survive in donor blood and produce a clinical outcome in the recipient. It includes viruses, bacteria, parasites and prions. WHO recommends quality-assured screening of all donated blood for HIV, hepatitis B, hepatitis C and treponema pallidum. Screening of donations for other infections, like malaria, Chagas disease or HTLV is based on local epidemiological evidence. The prevalence of TTI is calculated by the formula number of cases (Old + New) in a given population at a given time.

  Residual risk = Incidence rate x duration of window period /365 days

  To ensure blood safety donor counselling, TTI screening by serological assay like Enzyme linked immunosorbent assay (ELISA), Enhanced Chemiluminescence (ECi), particle agglutination, and rapid immunochromatography and molecular testing like nucleic acid detection should be followed as applicable. The critical factors involved in selection of

screening assay includes window period of the assay, rate of biological false positivity, complexity of the assay, qualified and trained manpower, and cost of the assay. The centralized testing helps better management, can be controlled for quality and provide economies of scale. The residual risk is one which remains despite screening and hence rational use of blood components is important. The reactive donors should be recalled, counselled, re-tested and notified.

- **Process Control of TTI laboratory - by Dr Sangeeta Pathak**

  Process control is an integral part of the quality management system implemented to monitor and control the various steps involved in routine blood banking practice. It helps to ensure the end point is delivered with minimum variations. The quality of the blood transfusion chain is affected by changes involved in each step, so it is important to have a process control (check points) in each step, starting from donor to the recipient.

  Teaching aims –

  a) To learn the importance of process control in TTI
  b) To monitor the process for a designed output
  c) To maintain a quality service
  d) Minimize variation in test result

  Process controls can be implemented in key check points such as –

  a) Transfusion chain
  b) Screening algorithms
  c) Various transfusion transmissible testing
  d) Selection of screening assays
  e) Evaluation and validation of screening assays
  f) Laboratory quality system
  g) Storage and transportation
  h) Sample handling and collection
  i) Test run
  j) Process verification

  Process control in TTI starts from donor selection and ends till the results are verified and certified. The aim of process control in TTI is to prevent any unwanted transfusion risk to the patient.

  Key check points in process control in TTI include –

  1. Donor selection strictly as per the national guidelines
  2. Retention of voluntary regular donor
  3. Sample collection and transportation as per the SOP
  4. Samples and Kit storage
  5. Sample validation criteria
  6. Process validations – IQ, OQ and PQ
  7. Departmental SOPs and QSPs
  8. Procedural validations – Internal as well as external controls
  9. Troubleshooting.
  10. LJ charts.
  11. Verification steps.

12. EQAS – inter laboratory comparison.

Three stage approach in TTI lab –

Stage 1 – method design

Stage 2 – method qualification (ELISA, CLIA or NAT)

Stage 3 – ongoing procedural evaluation

Summary –

Process control is the ability to monitor and adjust a process to provide the desired output. The aim is to maintain a process at a desired constant operating conditions in the face of routine working conditions or when a change is inevitable.

- **Principles and Practices of ELISA for TTI Screening - by Dr Sadhana Mangwana**
- **Demonstration of ELISA Technique - by Dr Ganesh Mohan**

Aims :Accurate testing of donated blood is vital to ensure blood safety. The different principles and types of ELISA will be discussed along the presentation and what are the quality control we can implement to improve the accuracy and safety of the procedure.

Different types:

a) Direct ELISA – Antigen is immobilized in microplate and soluble antibody is detected

b) Indirect ELISA – two step process. Antigen is immobilized on microplate. Primary antibody specific to the antigen binds to the target. Labelled secondary antibody binds to the primary antibody for detection.

c) Sandwich ELISA – two antibodies required for different epitopes of antigen. Antibody is coated on the microplate which detect the antigen. Conjugated antibody detects the captured antigen.

d) Competitive ELISA (Inhibition ELISA) – reference antigen pre coated on the microplate. Sample antigen competes with reference antigen to bind to the specific coated antibody. More target antigen, lesser free antibody thus weaker reaction.

ELISA procedure –

Follow manufacturer instruction in Kit insert. Make sure kits are stored in proper conditions. Samples should meet acceptance criteria. SOP need to be followed. Two level controls are an ideal practice, they are internal as well as external controls. Do not re use pipette tips. Washing is a crucial step as unbounded antibody / antigen might neutralize the stop solution. Result need to be verified as per kit insert and all controls need to be passed.

Trouble shoots:

Frequent problems encountered in ELISA are:

a) High background colour
b) No colour development (false negative results)
c) Low colour development
d) False positive results
e) Bad reproducibility

f) One row / one column colour development

Importance selecting the appropriate ELISA kits for TTI screen:

a) Window period – ideal to select a kit with higher sensitivity to reduce the detection window period.
b) Reasonable storage period.
c) Able to identify any locally specific mutations

Testing algorithms:

It is ideal to develop a testing strategy for routine blood banking.

It should be developed from national or international TTI screening recommendations.

Based on the algorithm, we can initiate look back / recall / trace back.

Every unit of blood that is donated need to be screened with a highly sensitive ELISA kit and negative results can be released for issuing. Positive results need to follow the testing algorithm to notify the donor.

- **Principles and Practice of Chemiluminescence Assay for TTI Screening - by Dr. Ankit Mathur an Demonstration of Chemiluminescence Assay for TTI Screening - by Dr Dhivya K**

  Learning objective: To understand

  - The principle of Chemiluminescent immunoassay (CLIA)
  - Methodology, calibration and maintenance of CLIA
  - Application of CLIA in TTI testing
  - Quality Control in CLIA
  - Benefits & limitations of CLIA over ELISA in TTI screening
  - Interpretation, validation and documentation of results
  - Troubleshooting and resolution

  Brief summary:

  Enhanced Chemiluminescence is an automated, highly sensitive serological immunoassay technique used in TTI screening of donated blood samples. In blood centres, ECI is commonly used for screening of Hepatitis B, Hepatitis C, HIV 1 & 2 and Syphilis.

  Principle: ECI is based on the principle of "Immunometric assay". The presence of Ag or Ab can be Quantified / Qualified by using a detection system using the enzyme Horse-Radish Peroxidase (HRPO). The Enzyme HRPO oxidises Luminol in the presence of Hydrogen Peroxide. The oxidized Luminol produces a glow of light. The light is measured using luminometer.

  Methodology: Chemiluminescence assay can be carried out by two modes

  1.Batch mode

  2.Random access mode (STAT mode) where EMERGENCY APHERESIS samples can be processed and the results can be released immediately even with a single sample

  In Chemiluminescence technology the calibration has to be carried out maybe once in 28 days because of its high standard of reproducibility with very less variation between each run. The TAT is faster with the Chemiluminescence technology system when compared to ELISA with less turn-around time.

  Benefits: It offers excellent precision and reliability, high-speed throughput, random access, and the technical simplicity of full automation

Interpretation of results: The interpretation of results is based on "Signal for test sample/cut-off value"

A value of < 0.9 - non reactive

0.9 to 0.99 – Borderline/grey zone sample

A value of 1.0 or more– reactive

Documentation: The hard copy of TTI test reports shall be filed after validation of the report and certification by Medical officer in-charge of blood centre.

Trouble-shooting: A few trouble shooting like sample dispense error, incubation temp out of range or reagent shuttle error, if encountered the appropriate resolution steps can be taken at laboratory level by following the instruction given in the operator manual. However, troubleshooting due to hardware error requires concerned technical expert's assistance to resolve and resume the assay.

- **Principles and Methods of Rapid Testing in TTI - by Dr. Aikaj Jindal**

  & Demonstration of Rapid Testing - by Dr Chenna Deepika

Learning Objectives

- Principle
- Demonstration
- Advantages
- Disadvantages

Rapid Diagnostic tests are designed for immediate and rapid testing of small numbers of samples

Their role in Transfusion centers includes:

- In low throughput blood banks
- Acute Crisis / Disaster
- Emergency release of blood

Principle

Rapid testing is done on the basic principle of visualizing the serological antigen antibody reaction. The 4 major types which have been described are:

- Immunoconcentration / Dot Blot immunoassay (vertical flow) : solid phase immunoassay where HIV antigens are immobilized on a porous membrane
- Immunochromatography Tests (Lateral Flow)
- Particle Agglutination Tests
- Dipstick and Comb Assay

Procedure

Universal safety precautions (use of a face mask, face shield, Head cap, gloves) needs to be followed for performing the test and other requisites like blood samples, reagent test kit, micropipette, tips, Marker pens, tissue paper, and arrangement for appropriate biomedical waste disposal to be kept ready..

Hemolysed samples or samples with turbid/lipemic plasma should not be used for the testing.

Ensure proper identification of the sample (Use the Unique identification number) assigned to the donation unit assigned (manually or barcode generated).

An appropriate kit based on the requirement of testing should be chosen.

The reagents and samples to be brought to room temperature if refrigerated during storage. Check for any external damage of the kit. Read the information leaflet thoroughly and perform the test as per the instructions provided in it.
The lot number, manufacturing and expiry date of the kit needs to be verified. Do not use the kit if it is not within the date of expiry.
Sample has to be identified appropriately and labelled. The device has a hole for the addition of sample. An area where the test results are read with two sections one is T – where the screening result is determined and C works as control and acts as a check for the test.
The tests are to be performed as per manufacturer instructions.
If multiple tests are being performed, write the time to read the result as well on the cassette.
Read and interpret the results as per manufacturer instructions.
After reading the result dispose all used and contaminated material as per Standard Biohazard Safety guidelines
Documentation
This is a sample format for documentation of test results. Each result should be read and interpreted by two trained personnel.
Advantages

- Easy to use, with minimal training
- Relatively rapid and results obtained within 10 – 30 minutes
- Shelf life of 1-2 yrs, at ambient temperatures, without need for refrigeration
- Limited/no need for instrumentation
- No electricity requirement
- Results can be read visually

Disadvantages

- Cannot be used for large throughput samples
- Need not wait for batch testing
- Subjective evaluation
- No permanent record of original test results
- Cost/test may be high
- Window period – Longer duration of window period for detection of the pathogen

- **<u>Quality Control in TTI Laboratory - by Dr Wayne Dimech</u>**

Learning Objective:

- QC is a process not just testing of a sample
- QC monitors test system variation over time
- QC samples must be well selected
- QC sample level must be specific assay
- Differences between serology and clinical chemistry
- Risk of false negatives results is real but minimal

Brief Summary (approximately 500 words):

The implementation of a quality control (QC) program for infectious disease testing requires access to well-selected QC samples, a process for collecting and monitoring test results and acceptance limits to detect any abnormal variation. A QC program monitors variation overtime. There are some significant differences between clinical chemistry and

infectious disease testing. Where clinical chemistry measures "how much" analyte, infectious disease testing measures "how well" an antibody to bind to an antigen. Therefore, the approaches to QC differ between clinical chemistry and infectious disease testing. In this talk, we identify the differences and discuss how these differences effect some common concepts in QC.

- **Demonstration of Preparation and validation of QC Samples for screening of TTIs - Dr. Ambuja K**

  Learning Objectives:

  To understand

  1. Preparation of in-house weak QC samples for ELISA testing
  2. Plotting of Levy-Jennings chart
  3. Application of Westgard QC rules

  Brief summary:

  Preparation of in-house weak positive QC samples

  Internal controls are set of controls (Positive & Negative) provided along with the kit. They are supposed to be used only in those batches of kit from which they originate. They do not detect minor deterioration of kits. Hence, there is a requirement of external control. External controls are set of controls included from outside. It can continually monitor assay performance. Here borderline reactive (positive) and negative samples are used and can detect minor error in the performance.

  Strong reactive sample by ELISA shall be selected for Hepatitis B, Hepatitis C and HIV respectively for the preparation of QC sample. Also ensure the repeatability of the test and confirm the results with referral lab. AB Negative plasma which is negative for Hepatitis B, Hepatitis C and HIV shall be used for serial dilution. Then serial dilution shall be performed and cut off shall be calculated. A dilution that is double that of the cut off value or slightly more than double should be selected. Test the positive sample at the dilution chosen with the same diluents to confirm. Required volume of the controls shall be made based on the total quantity of weak positive sample. Then batch validation has to be done to rule out inter-aliquot variation. After batch validation, with proper labelling, it can be stored in the deep freezer.

  Levy Jennings chart:

  LJ chart can detect systematic variation, random variation, lot to lot variation and day to day variation. It can highlight the outliers, batch to batch variation, operator to operator variation and Changes in assay performance even when test runs are valid.

  Application of Westgard rules:

Multi-rule QC procedure uses two or more statistical tests (control rules) to evaluate the QC data, then rejects a run if any one of these statistical tests is positive. There are warning rules and rejection rules. When there is a warning rule, use other rules to inspect the control points. When there is a rejection rule, Stop testing and carefully inspect control data, identify and correct problem, repeat control, repeat testing on samples and results shall not be reported until problem is solved.

- **Documentation and Records in TTI Laboratory - Dr. Sitalakshmi S**

  Learning Objective:
  - Goals of documentation
  - Role of documentation in Quality management system
  - Document control
  - Document vs Records
  - Retention of records

  Brief Summary: Documentation and record keeping is an essential element of the Quality management system. The goal of documentation is to find information whenever required. Documents are written information about policies, processes, and procedures. The characteristics of documents are: Documents reflect the laboratory's organization and its quality management. Documents communicate information to all persons who need it including the lab staff and lab management. They need to be updated, must be changed when a policy, process, or procedure changes and formats need to be established for recording and reporting information by using standardized forms. Once the forms are used to record information, they become records. Quality manual, quality systems procedures, standard operating procedures and work desk instructions are some examples of documents. A policy is "a documented statement of overall intentions and direction" defined by those in the organization and endorsed by management. It includes a statement of the organizational mission, goals, and purpose and serves as the framework for the quality system, and should always be specified in the quality manual. Processes are the steps involved in carrying out quality policies. They are a "set of interrelated activities that transform inputs into outputs." Procedures are specific activities of a process. SOPs are written step-by step instructions that laboratory staff should follow when performing a procedure. Work instructions are shortened versions of SOPs that are displayed at the bench for easy reference on performing a procedure. Documents communicate what is done in the laboratory. Good documents are written clearly and concisely, using a standard format, written explicitly reflecting all implemented measures, responsibilities, and procedures and maintained to ensure that it is always up to date. A document control system provides procedures for formatting and maintaining documents and should assure that the current version of any document is in use, ensure the availability and ease of use and provide for the appropriate archiving of documents. A document control system provides a method for formatting documents to be easily managed and sets up processes for maintaining the inventory of documents. This requires a uniform format that includes a numbering system, to identify the version (date) of the document. It also includes a process for

formal approval of each new document, a distribution list, and a procedure for revision. A master log of all documents is necessary. Stored documents and records must be protected from unauthorized changes, inadvertent destruction, damage (fire, water, rodents), unauthorized viewing (confidential information) and inadvertent loss of data (overwriting, system crashes) Records are the collected information produced by the laboratory in the process of performing and reporting a laboratory test. They are permanent and not revised. They should be complete and legible and easily retrieved. Example: LJ charts, sample logs, temperature log, QC data Records are required for continuous monitoring, tracking of samples, evaluating problems and serve as important management tool. Retention times for records are determined based on the length of time the laboratory will need to have access to its records, government requirements or standards and the time interval between the laboratory's assessments. Electronic data serve as backup data, stored in an off-site location and secured to prevent unauthorized access.

- **Equipment Management in TTI Laboratory - Dr. Nova Hippy**

  Learning Objectives:

  ● To Develop an understanding of how to manage the TTI test equipment

  ● To identify the documents needed to improve the equipment management

  Summary:

  Before understanding equipment management in TTI laboratory, we have to understand the importance of the quality management system and its various aspects starting from the organisation in which a laboratory is set up, the lab personnel involved, equipment used, purchasing and inventory to process control. We also have to look into how the information pertaining to how lab is managed, how documents and records are maintained, how different incidents are assessed and how we can improve processes in order to provide good customer service keeping in mind the facilities provided and ensuring safety.

  Benefits of quality management system results in high performance level of the equipment, decline in cost for repair, lengthens the lifespan, less variations in test results.

  Once we select an equipment for a laboratory, we have to look into the performance characteristics, cost, the reagents required, ease in handling the equipment, language, warranty, safety and space for placement of the equipment.

  Certain set of documents are necessary during the selection and acquisition of the equipment which includes the product specification, documents related to possession of equipment, bid invitation, evaluation of bid, vendor's responsibilities and trial period.

One must ensure that the equipment is installed by the manufacturer after meeting the qualification requirements, and authorization of the equipment is mandatory. After installation, a standard operating procedure has to be finalized, approved and lab personnel must be trained appropriately.

Evaluation of the performance with respect to precision and accuracy of the equipment is required followed by ability of the test to detect the disease in terms of sensitivity, specificity, positive and negative predictive value has to be done. Instrument should also be monitored by performing periodic function checks to ensure quality and safety of the test.

Maintenance of the equipment after procurement is essential in order for better functioning and durability by routine cleaning, replacement of equipment parts in case damage. Quality of the test has to be maintained by preventing inaccurate test result, delay in reporting results and low productivity.

Management of trouble shooting firstly by repeating maintenance procedure, following the process and manufacturer's instructions by verification of procedures being followed. Defective equipment should be taken out of service and clearly labelled for the same. We must follow up by checking the function of the equipment once repaired. Equipment operators training on trouble shooting should be done and interruption of routine flow of work has to be avoided at all costs to maintain quality by arranging an alternative.

Retiring or disposition of equipment is done when the equipment is not functioning, or outdated must be replaced with a new equipment. Salvage of useful parts and following safety protocols of potential biohazards is required during disposal. All elements of equipment management demand proper documentation which reflects on the quality, efficiency and safety of a laboratory.

- **External Quality Assessment Scheme and Proficiency Testing - by Dr Gajendra Gupta**

Learning Objectives

To understand

1. The concept of proficiency testing in Blood Transfusion services
2. Benefit and role of proficiency testing in improving quality

Brief summary

Introduction

Quality Control refers to the measures that must be included during each assay run to verify that the test is working properly. It includes Internal quality control and external quality control. Internal Quality Control monitors the quality of a single laboratory and is necessary for daily monitoring of precision and accuracy. External Quality Control monitors comparison of performance of many laboratories and is required for long term accuracy of the analytical method. External quality assurance or proficiency testing is a quality monitoring scheme to challenge a laboratory's routine methods and procedures. Additionally, it accesses the overall ability and performance of a group of laboratories. It helps to investigate factors in performance and act as an educational stimulus to improvement in performance.

EQAS in transfusion medicine:

In transfusion medicine, the entire testing process including quality of results generated by the laboratory is assessed using samples of known but undisclosed content. It Includes comparison against other laboratories. It monitors whether the samples are handled correctly, assays are performed accurately and results are recorded appropriately. Role of the organizer blood center is to prepare specimens, analyze results and prepare reports while the role of the participant blood center is to examine specimens, report results, and evaluate the report. Processes of EQAS are in the order of pilot study, registration of participants, preparation of test panels, distribution of panels, collection of data, analysis of data, and final report generation. Three types of EQA are proficiency testing, rechecking or retesting and onsite evaluation.

Benefits:

Benefits of EQAS to participating blood centres are comparison with performance of other participating labs, identification of problems relating to laboratory processes, techniques and reagents, provision of information & education to improve performance, encouragement of best practice, enhanced credibility of the laboratory and access to a network of labs for exchange of information. Benefits of EQAS in regulatory authorities involves establishment of a network of blood transfusion laboratories with a known standard of performance, provision of useful information to assist in setting standards, reviewing testing strategies and technologies, effective utilisation of resources, and improvement of public confidence in the blood transfusion service.

Limitations: Proficiency testing cannot act as a substitute for Internal Quality Control. It is not meant for training individual analysts. It also cannot validate analytical methods. It also does not provide diagnostics to help solve the problem. It is indicative of proficiency in only selected analytes.

- **Root Cause Analysis and Process Improvement in TTI Laboratory - Dr. Shamee Shastry**

Root cause analysis is an important part of the quality assurance system. It is a team approach. The main reason to perform RCA is that problems can be a result of multiple factors so it is important to find the cause and effect relationship to address it effectively. Root cause, Cause that if addressed, will prevent or minimize the chances of an incident recurring.

Root cause analysis : Root cause analysis is a structured investigation that aims to identify the true cause of a problem, and the actions necessary to eliminate it.

Scope:

Identify and describe the problem clearly
Distinguish between the root cause and other causal factors
Establish a causal graph between the root cause and the problem
Six Main Activities of RCA:

1. Defining the Problem
2. Gathering the Data
3. Mapping the Information
4. Analyzing problems for contributory factors
5. Identifying and agreeing the root causes
6. Making recommendations and Reporting

The commonly used tools for analysing the problem

- Brainstorming
- Retrospective Why?
- Fish-Bone Diagram
- Barrier analysis

Benifits of RCA are:

- Provides a structured and consistent approach
- Shifting the focus away from individuals
- Open and fair culture, Increases awareness
    - Demonstrating the benefits of reporting incident
    - Development of recommendations based on the the root cause(s) of an incident
    - Prevention or reduction of recurrences of problem

Process improvement is a systematic and periodic approach to improve laboratory quality and the inputs and outputs. The Deming Plan-Do-Check-Act (PDCA) cycle shows how to achieve continual improvement in any process. RCA will help us in initiating the Corrective action and take preventive action CAPA. CAPA will lead to the process improvement in the system.

- **<u>Recent Advances: Nucleic Acid testing for TTI screening - Dr.Rahul Katharia</u>**

Learning Objectives:

- To familiarize the concept of NAT and its importance in reducing the residual risk.

Key points:

- Magnitude of problem TTI seroprevalence
- Trigger: NAT as an additional safety layer

- Progression: Current scenario across globe & INDIA
- Implementation: Balance cost versus benefits
- Recommendations

Summary:

The main objective of blood centres is to provide safe blood to the patients. Even with improvement in technologies, 16 million HBV infections, 5 million HCV infections, and 1,60,000 cases of HIV infections. 5 to 10% of HIV infections worldwide are transfusion associated. In some countries the routine testing of HIV, HBV, HCV is still not done. The prevalence of Transfusion transmitted infections is higher in low- and middle-income countries in comparison with high income countries.

In India, approximately 11.6 million blood donations happen annually. The structure of blood banking is Heterogeneous (Government / Private / NGO / Stand Alone), due to which there is lack of standardization of screening procedures. Risk of TTI is high in India (1-2/ 1000 recipients) due to high prevalence in population and high percentage of replacement blood donors. Currently many measures have been put in place to improve blood safety like- voluntary blood donor, proper donor screening and improved blood testing.

Window period is defined as time from infection to lab detection of organism. The window period reduces significantly with Nucleic acid amplification test (NAT) when compared to ELISA. NAT is a molecular technique for screening to reduce the risk of TTI. Different technologies involved in NAT include a. extraction of nucleic acid, amplification, and detection. It was Introduced in the developed countries in the early 2000's.

Benefits of NAT include, it narrows the window period, it can detect the viruses with genetic variation that may be missed by serological assay, and detection of occult HBV virus infection where serology markers are absent. NAT has been implemented by blood centers in most of the developed countries. In India the implementation is scattered (~10%). The need for NAT implementation in India is higher as the prevalence of HIV, HBV is high among blood donors, and prevalence of TTI is high in multiply transfused patients. In a pilot study done on NAT in India, involving 12,224 donors from 8 centers very high NAT yield was observed (1 in 1528) for all three viruses. Even though the cost of implementation of NAT is higher initially, it will play an important role in reduction of infection by reducing the window period.

- **<u>Recent advances: Pathogen inactivation - Dr.C.K.Lee</u>**

Learning objectives:

· Learn the concept of blood safety in transfusion medicine
· Learn the measures in protecting blood safety
· Learn the latest development in pathogen inactivation
· Learn the benefit and current limitations in pathogen inactivation

Summary:

Blood transfusion is a lifesaving procedure in many patients' management. It happens every second, everywhere around the world. Blood transfusion is only possible when there is sufficient and safe blood donation. Blood supply should be obtained from VNRBD and screened by infectious disease markers before use in clinical transfusion. The transfusion chain starts from the blood donor. After successful blood donation, blood components are separated and stored in blood banks, which are then transfused to patients when needed.

Blood transfusion is a vein-to-vein procedure starting from donor to patient. Blood donors can hide some of their information and this can make the patient susceptible to infections, which can be nothing to life-threatening or even causing death. Adverse events from blood transfusions are classified into infectious and non-infectious. The measures to secure blood and transfusion safety include VNRBD as far as possible, screening for infectious diseases, SOP and Quality Standards at Blood Centers to ensure quality and safety as far as possible, appropriateness in transfusion indications, proper storage and handling in hospitals, surveillance, and monitoring (haemovigilance).

Mandatory infectious disease screening includes HIV, HBV, HCV, and Syphilis. Developed countries include both serologic and molecular tests. Other infectious diseases like HTLV, Zika, West Nile virus, Trypanosoma cruci are screened based on local epidemiology. Emerging infections are also a major threat to blood safety.

Pathogen inactivation has been shown to enhance blood safety, as an adjunct to current blood safety measures used in blood establishment. After donation screening, the addition of pathogen inactivation technology to blood components, could theoretically and substantially enhance blood safety. The addition of certain chemicals could chelate and damage the DNA/RNA of pathogens to achieve a significant reduction of pathogen load by up to 105 difference. The concerns are the safety of the chemical and the quantity, quality, and outcome of existing blood components.

The two approaches include the inactivation of lipids and damaging of nucleic acid and preventing normal replication of a wide array of microorganisms. Amotosalen, methylene blue, riboflavin, theraflex are used for pathogen inactivation. The addition of these compounds causes intercalation of pathogen DNA/RNA, which on UV light illumination forms permanent crosslinking. Benefits of pathogen inactivation are reduced infectious organisms, the extended shelf life of platelets to 7 days, CMV safe, and prevention of transfusion-associated GVHD (blood irradiation not required in cellular products).

Currently, pathogen inactivation is available for plasma, platelets, and whole blood. Limitations include incomplete inactivation, inability to inactivate prions, cost, the potential for damaging or depleting plasma proteins, the potential for damaging cellular components, and manpower. Ideal pathogen inactivation covers as many pathogens as possible can apply to whole blood; once treated, can process to component separation, minimal residual, minimal alternations in blood components quantity and quality, and semi-automated.

Further advances will be able to make pathogen inactivation in red cells a reality. Blood safety can be further enhanced with the use of pathogen inactivation.

- **<u>Donor Notification & Counselling - Dr.Nusret Nuri Solaz</u>**

  Learning Objective: The objective of this text is improving capacity of Blood Center staffs who will be able to perform proper donor notification and counselling that a. will avoid or minimize blood donation complications b. will provide safe blood for transfusion c. will avoid or minimize mis-deferral of blood donor d. will protect Blood Center staffs from TTI contamination by keeping high risk blood out of Blood Center

  Brief Summary: The population of World is increasing while percentage of blood donation eligible people is shrinking elderly people percentage is increasing. This hardens to provide sufficient safe blood for Transfusion. Blood donor is the “basic” of SAFE TRANSFUSION

who should be handled with extreme care scientifically, officially, and socially.Blood donor counselling is corner stone to reach safe blood donor which is a confidential dialogue between a blood donor and a trained counsellor about issues related to the donor's health and the donation process; it is done before, during and after blood donation. Although screening technologies are highly developed, and results are more accurate than before still there is a risk of non-detectable period for TTI agents; window – phase. Donor counselling is an important chance to get rid of TTI risks "Donor notification" is informing the blood donor about blood donation and related topics both verbally and by written consent. "Donor counselling" is learning about the actual health status of blood donor candidate via specially prepared Donor Evaluation Form. Capable staff, private area, sufficient technical and physical infrastructure are the main requirements for counselling and notification. Donor Notification & Counselling should be based on; 1. Guidelines which is issued by National and/or international authorized organizations; 1.a. contents necessary medical information to save donor's life and protect patients from transfusion complications 1.b. standardizes donor N & C at national and / or international level 1.c. is accepted as a reference at administrative and legal conflicts 1.d. translated Guidelines should be adopted to the specific conditions of the country 2. Specifically trained counsellor; 2.a. can be either a medical doctor or other medical staff such as nurse, paramedic, etc. 2.b. should have a special training on donor N & C although the counselor is a medical doctor or other medical staff. Even the contents are different; training program and certificate should be approved by official bodies 2.c. non-certified medical staff should not be allowed for donor N & C 3. Proper infrastructure and tools; blood donor counselling is a confidential dialogue between a blood donor and a trained counsellor. This can be provided by different requirements such as; 3.a. private and proper place for confidential dialogue 3.b. efficient and safe IT infrastructure (equipment, software, etc.) for proper archiving the confidential files 3.c. Donor Form is the essential tool of blood donor notification and counselling in medical, official, and legal aspects. Medical history, life style, vital signs, contact information of blood donor are documented at this form 4. Sufficient and sustainable financial, official, and political support are essential. Otherwise, the system might be failed or interrupted. Donor Notification & Counselling has 3 main steps; before donation, during donation, and after donation. Evaluating the eligibility of donor candidate is the main purpose of predonation counselling. During blood donation counselling donor is followed up against any complication. Informing the donor about the screening test results and further guidance in case of abnormal results are the functions of after donation counselling. Knowledge is science, service is an art. Donor Notification & Counselling is both an artistic and scientific action at Blood Service for reaching SAFE BLOOD.

- **<u>Waste management in transfusion centres - Dr.Nabajyothi Choudhury</u>**

Learning Objectives:
To have an understanding of:
· How to implement an effective system for waste management in Blood Transfusion Services (BTS)
· How to manage the waste management process in BTS
· Guidelines to staff for waste classification, storage, segregation, transportation
· Providing guidelines to treatment and disposal

Summary:
Biomedical waste generated in the diagnosis, treatment and, immunization of human beings or animals in research or the production and testing of biological products needs proper disposal because of its infectious and hazardous characteristics.
BMW can be hazardous waste that poses a substantial or potential threat to human health or the environment. The threat may be due to the quantity or concentration of the waste, or to its physical, chemical, radioactive, genotoxic or, infectious characteristics. About 15-25% of HCW generated in an HCF is likely to be hazardous.
BMW is categorized into 10 categories depending on the nature of waste which helps in proper handling and disposal of it. Poor management of BMW

Details on the pilot webinar series:

Registration - Details of the participants (Annexure -3)

Feedback received - (Annexure 6)

Documents submitted:

1. Annexure 1- Program Brochure
2. Annexure 2 - Final Program schedule
3. Annexure 3 - Registration details
4. Annexure 4- Powerpoint presentations
5. Annexure 5- Video recording of lectures (one drive folder)
6. Annexure 6 - Feedback