GUJTRANSCON 2022
3rd & 4th September, 2022
Agrasen Foundation Hall
Shela, Ahmedabad

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Tackling window period: Best available option

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Transfusion Transmissible Infections – *Historical Perspective*

- 1867: English surgeon Joseph Lister uses antiseptics to control infection during transfusions
- 1915: The first known case of syphilis through blood transfusion was reported by Fordyce
- 1943: P. Beeson gave the classic description of transfusion-transmitted hepatitis

Journal of the American Medical Association- 1945

July 28, 1945

HEPATITIS FOLLOWING BLOOD OR PLASMA TRANSFUSIONS

OBSERVATIONS IN THIRTY-THREE CASES

EMANUEL M. RAPPAPORT

JAMA. 1945;128(13):932-939. doi:10.1001/jama.1945.02860300022005

Abstract

Hepatitis due to inoculation with homologous serum has received considerable prominence in medical literature during the past few years owing to its widespread incidence following inoculation of troops with normal human serum employed as a vehicle for the yellow fever virus. While the pathogenesis of this disease has not been definitely established, the result of considerable investigation in both this country and England suggests that the icterogenic agent is a virus which retains its virulence after storage for long periods in a dried state. Hepatitis has been produced experimentally in human volunteers by parenteral injection,[1] by feeding[2] and by nasal inoculation[3] of material containing the infective agent.

Similar sequelae following whole blood or plasma transfusions were reported in 9 cases by Morgan and Williamson[4] and in 5 cases by Steiner.[5] Beeson,[6] in describing the occurrence of jaundice in 7 cases following the use of

The second part of the story- how to prevent TTIs

With blood-transfusion now being an essential factor in medical management of diverse clinical conditions, the prevention of transfusion-transmitted infectious (TTIs) has become a major area of interest in the transfusion medicine fraternity.

The most important TTIs being human immunodeficiency virus (HIV), Hepatitis B and C viruses (HBV and HCV respectively).

Over the past 50-60 years, scientists have been coming up with various strategies to prevents TTIs

Blood can never be 100% safe, but its our moral responsibility to adopt strategies to make it as safe as possible

Prevention of TTIs- Global Timeline

- **1971** Hepatitis B surface antigen testing of donated blood begins.
- **1981** First Acquired Immune Deficiency Syndrome (AIDS) case reported.
- **1984** Human Immunodeficiency Virus (HIV) identified as cause of AIDS
- **1985** The first blood-screening test to detect HIV is started
- **1987** Hepatitis B core antibody & alanine aminotransferase test (ALT) test started
- **1992** Testing for anti-HIV-1 & anti-HIV-2 is implemented.
- **1996** HIV p24 antigen testing of donated blood begins..
- **1998** HCV lookback campaign —alert people exposed to HCV by blood transfusions
- **1999** Blood Banks begin implementation of Nucleic Acid Amplification Testing (NAT)
- **2002** NAT for HIV and HCV licensed by the Food and Drug Administration in the US.
- **2014** US FDA approved pathogen reduction system for platelets
- **2020** US FDA approved pathogen reduction system for plasma

Need for newer technologies –

Due to the limitations of detection in older ones

The French Fiasco

France Convicts 3 in Case of H.I.V.-Tainted Blood

A French court convicted three health officials on charges of distributing tainted blood that resulted in infection of more than 1,250 patients with the AIDS virus. Already 273 of them have died.

The case showed that senior health officials had ordered the continued use of the blood-clotting factor that hemophiliacs need even though the officials knew it to be contaminated **at a time when procedures to detect and eliminate the virus were already available.**

BBC NEWS

Tuesday, February 9, 1999 Published at 12:15 GMT

Europe : French Aids blood trial opens

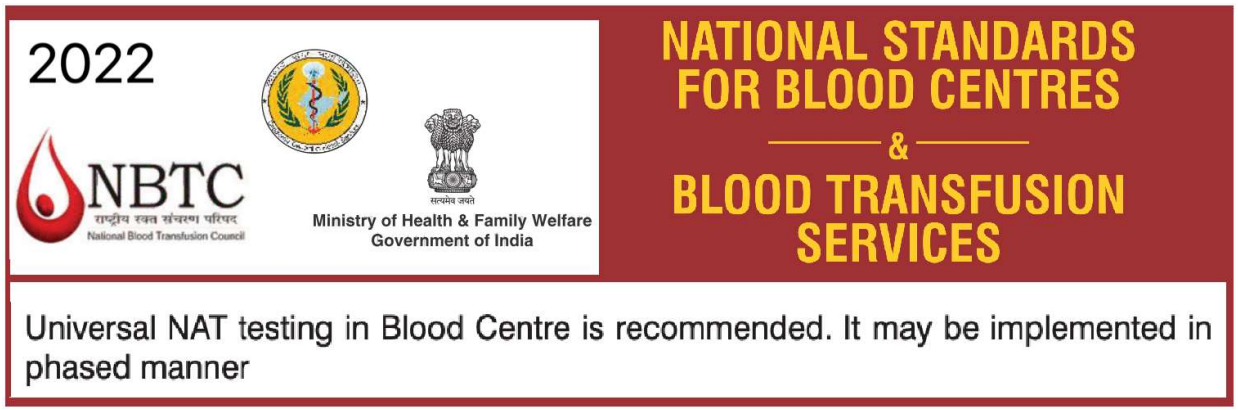
Parents who lost two sons to Aids after transfusions ar

for the trial

A former French Prime Minister and tw
fellow ministers have gone on trial accu
the manslaughter of five people who di
receiving transfusions of tainted blood.
Laurent Fabius, Socialist Prime Ministe
1984 to 1986, and his colleagues are a
of being responsible for seven people
contracting Aids from blood transfusion

Prevention of TTIs- India Timeline

- The Govt of India mandates testing all donated blood for **HIV, Hepatitis B, Hepatitis C, Syphillis and Malaria.**
- Blood Banks governed by Drugs & Cosmetic Act in India, according to which only blood tested non reactive for above infections can be transfused
- **- 1989** - HIV testing mandatory for blood banks.
- **- 1999** - Hepatitis B surface antigen, Malaria and Syphilis testing made mandatory.
- **- 2001** - Hepatitis C virus and test for antibody to Hepatitis C made mandatory.



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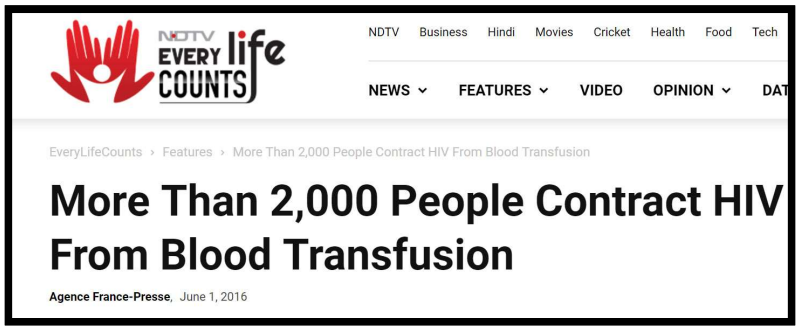
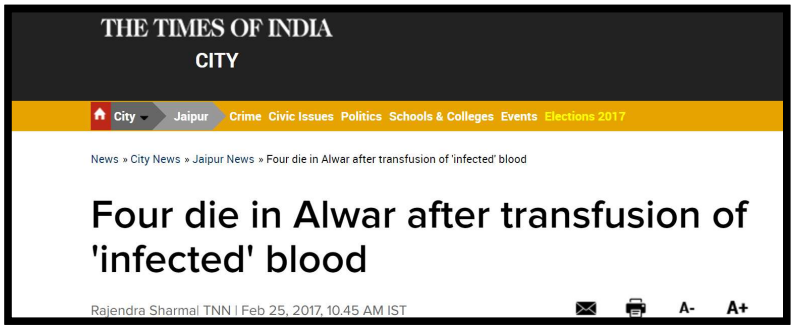
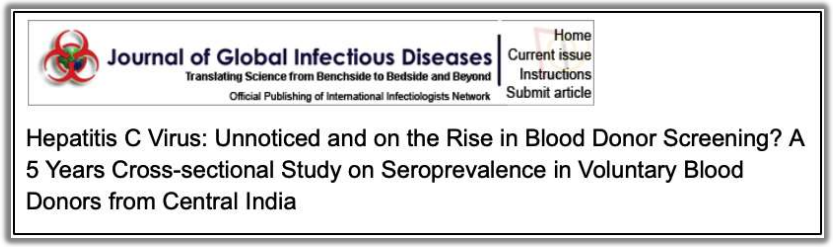
Outcome of not adopting newer technologies in India

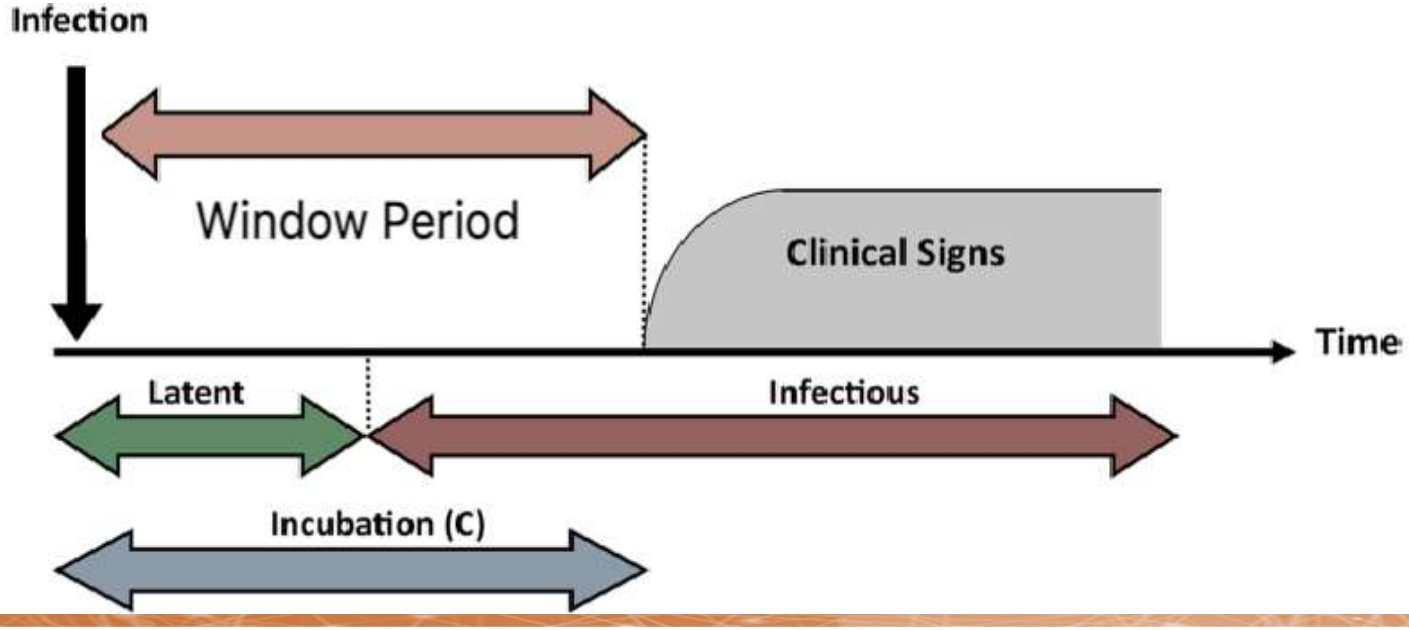






That brings us to the issue of Window Period

- **Latent period** -the time interval between when an individual is infected by a pathogen and when they become infectious
- **Incubation period** -the period between exposure to an infection and the appearance of the first symptoms.
- **Window period** - In blood banking, the **window period** for a test/intervention designed to detect a disease is the time between first infection and when the test can reliably detect that infection



Window period- available options

- The time between HIV exposure and when a test can detect HIV.
- The window period depends on the type of HIV test used-i.e the Technology

Nucleic Acid Test (NAT)*
window period
5-15 days

Antigen/Antibody Lab Test*
window period
18-45 days

Rapid Antigen/Antibody Test†
window period
18-90 days

Antibody Test‡
window period
23-90 days

Donor selection process

Thorough donor education (**a confidential dialogue)** and history leading to donor deferral

- Pre-donation information
- Pre-donation counselling
- **Donor history questionnaire**
- **Donor awareness**

Not always ideal specially because

- Donors are not well educated/aware
- Do not want to self defer when donating in a group
- Non voluntary-replacement donors

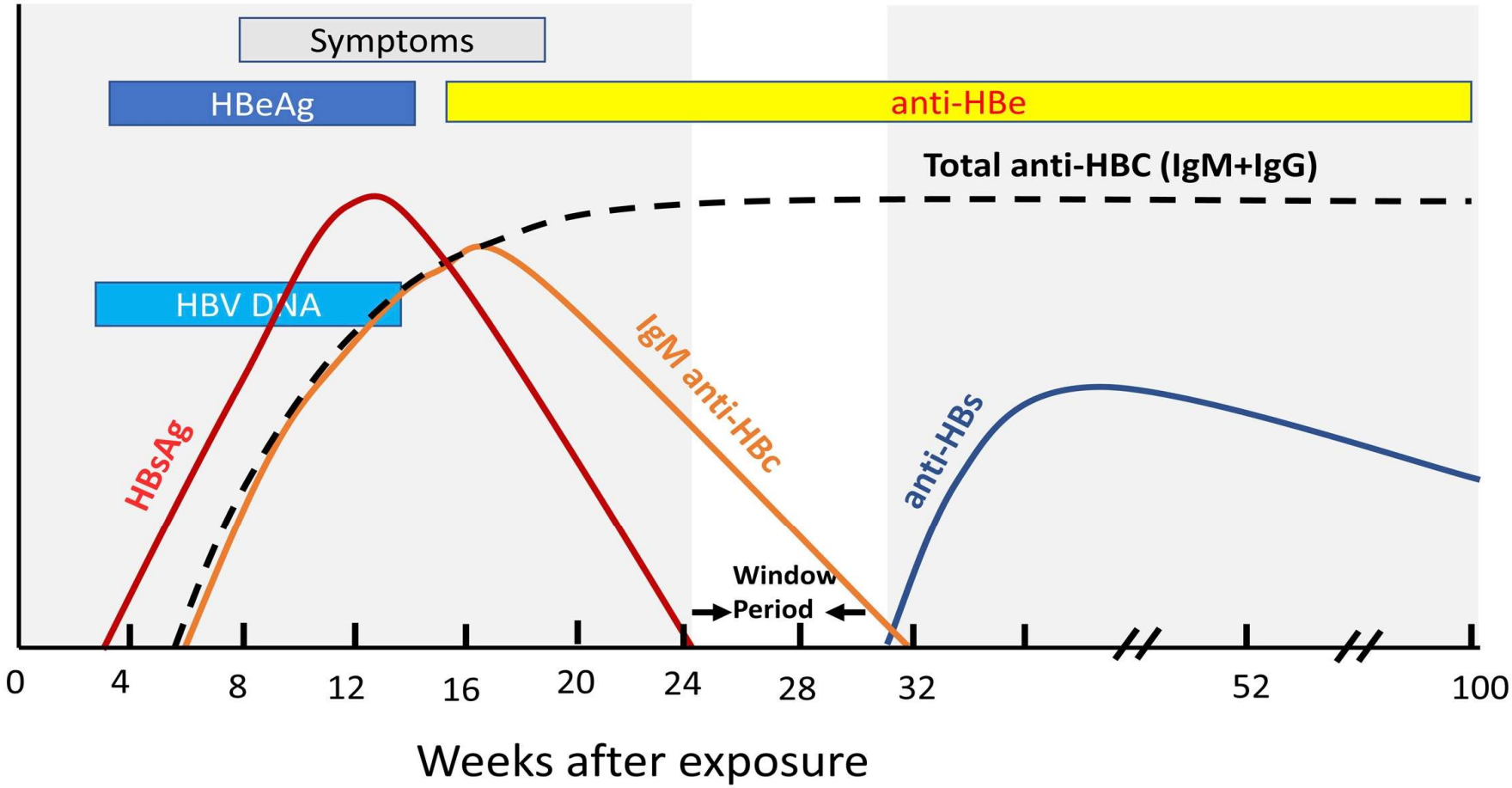
Testing to screen for infections

In India, blood screening for HBV, HIV and HCV is done by

- Rapid test
    - Less sensitive/accurate
    - Subjective variation
    - No automation
    - Not allowed* as per the D & C act
    - Doesn't detect infection in window period/chronic cases

- ELISA & Chemiluminescence (CLIA) & Enzyme Immunoassay (EIA)
    - Better sensitivity
    - Can be automated
    - No subjective variation
    - Used in most blood banks
    - Doesn't detect infection in window period/chronic cases

Testing to screen for infections- drawbacks of serology

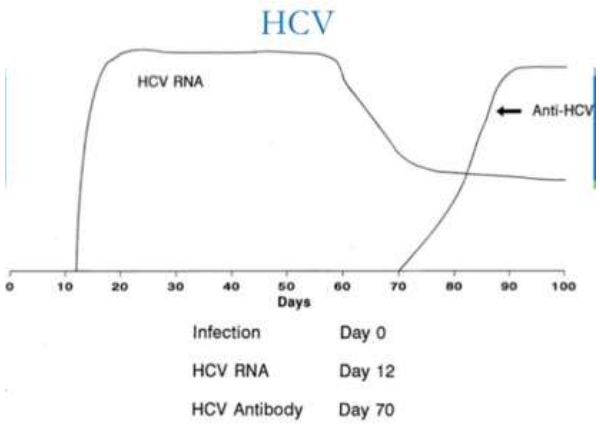


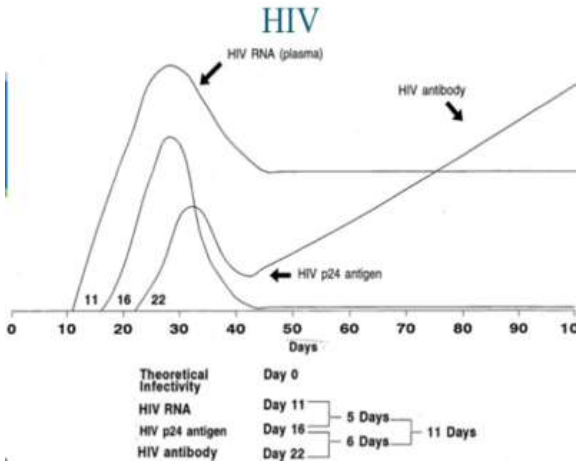
Prevalence of infections in blood donors in India- very high

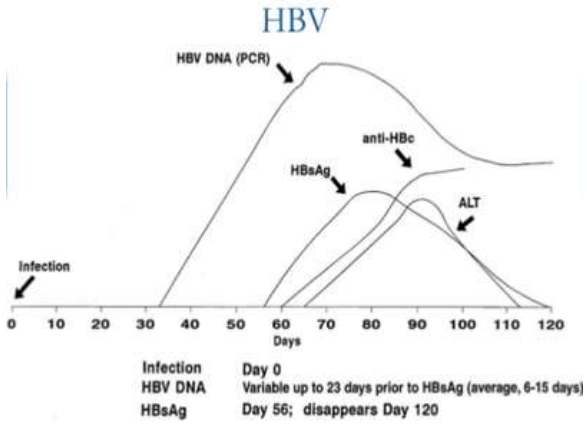
India : Blood donation and TTI +ve data

Financial Year	Total Collection (in Millions)	Collection in NACO supported BB (in millions)	Voluntary Blood Donation in NACO supported BB (%)	HIV (%)	HBsAg (%)	HCV (%)	MP (%)	VDRL (%)	Component Separation in NACO supported BCSU
2012-13	9.8	5.48	84	0.2	1.1	0.4	0.1	0.2	
2013-14	9.95	5.76	84	0.2	1	0.4	0.1	0.2	58.7%
2014-15	10.83	6.64	84	0.14	0.85	0.33	0.08	0.18	61.6%
2015-16	10.8	6.3	79	0.14	0.86	0.34	0.07	0.15	69%
2016-17	11.09	6.6	77	0.12	0.92	0.30	0.05	0.21	68%
2017-18	11.45	7.8	78	0.13	0.89	0.29	0.07	0.18	71%

Genetic material vs proteins/antibodies







- The genomic material appears first, much before proteins and antibodies
- The genomic material can be amplified by PCR (not antigenic proteins)

Nucleic acid amplification test (NAT) NAT

- A nucleic acid test (NAT) or nucleic acid amplification test (NAAT) is a technique utilized to detect a particular nucleic acid, virus, or bacteria which acts as a pathogen in blood, tissue, urine, etc.
- Since it is looking for the DNA/RNA, it is detected at an early stage
- Since it involves a step of amplification, even very low amount of virus/pathogen can be detected

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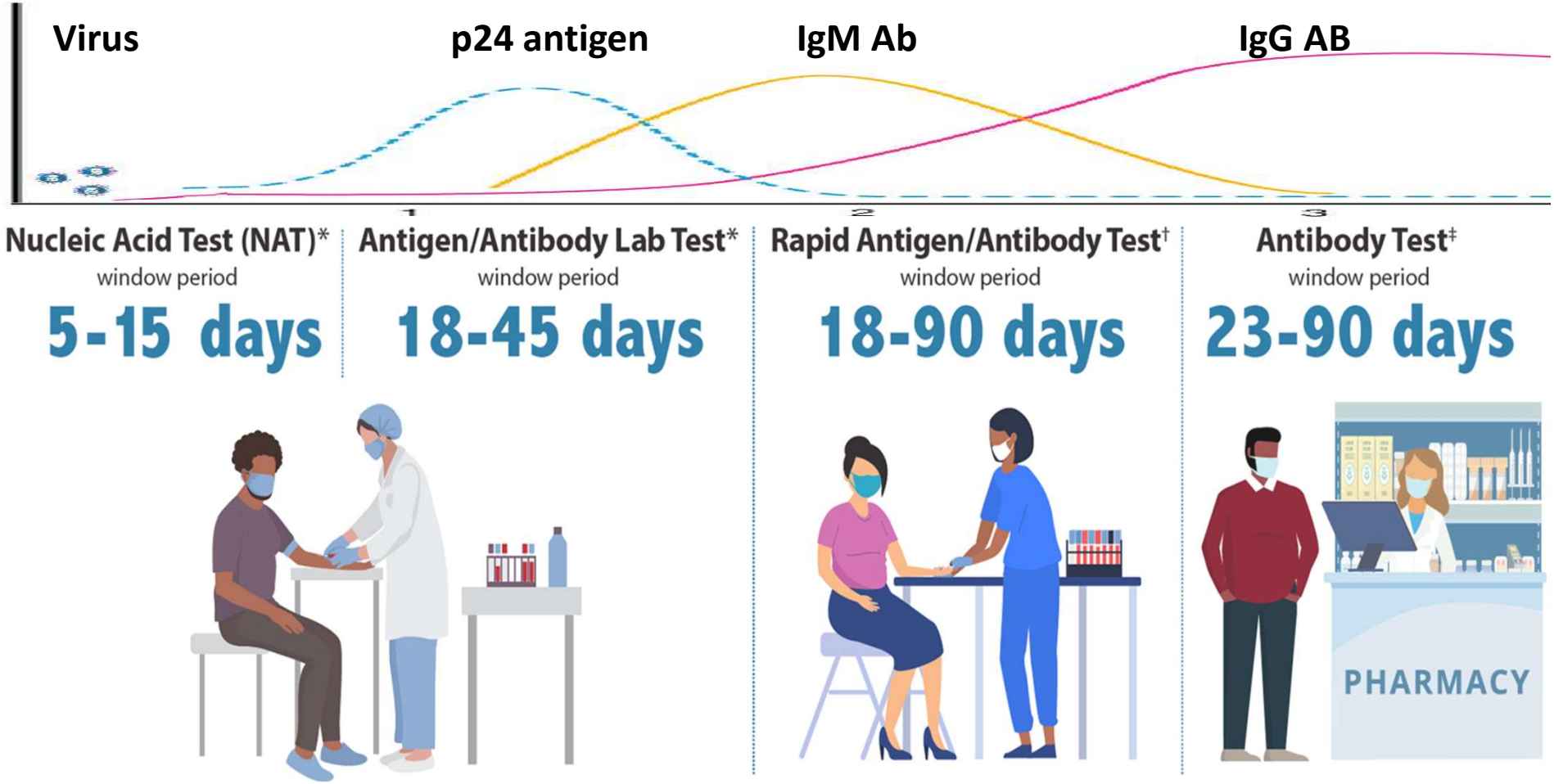
Tackling window period- Technology makes a difference



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NAT - best tool to tackle window period- Indian scenario

Current Scenario

Unmet need for reliable blood infection testing in blood banks

~4 %

out of 3000+ blood banks in India use NAT*

NAT has been available in India For nearly 18 years now!

Our Vision

Safe, NAT tested, blood is the right of every recipient in India

100 %

Blood centers in the West carrying out NAT

The elitist tag associated with NAT tested blood needs to go

Blood Donor Screening using Nucleic Acid Testing (NAT)

Since late 1990s usage of Nucleic Acid Amplification Acid Test (NAT) for screening for the following pathogens has become routine in most countries of world

- Human immunodeficiency virus (HIV)-1, HIV-2
- Hepatitis C virus (HCV)
- Hepatitis B virus (HBV)

However, NAT is not done routinely in India because

- High equipment capital
- High cost to set up the NAT screening lab
- High running cost due to imported reagents/kits
- Fragment blood banking system in India
- Many small blood banks with lower workload
- Patient pressure groups not very strong (eg. Thalassemia association)
- Was no India-specific solution until 2-3 years back

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NATSpert - Simplifying the NAT Lab in Blood Bank

	Traditional Lab	Lab with Compact XL
Instrument needed for molecular Lab	 ...and many more	
Lab consumables needed		
Lab Rooms required	3 - 4  1000 to 1500 sqft area	1  100 sqft area
Workflow	Manual workflow	Sample to RTPCR
Manpower required	 Skilled molecular biologists	 Lab Technician
Turnaround time	3 to 4 hours	Less than 2 Hrs
Errors	Multiple manual Errors	Error Free
Throughput per 24 hrs	100 to 150 samples	750+ samples
Economy	High Capex, High Opex	Low Capex, Low Opex

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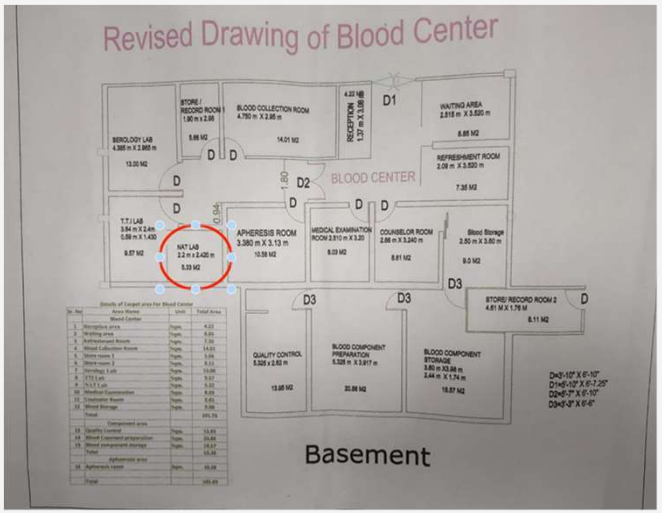
Solution for small to high throughput blood bank

Process minimum 18-20 samples per day



Scaling of **1 to 1000 Samples**

Pathogen Reduction Technologies

The major pathogen reduction methods currently available for plasma involve the use of a

- solvent/detergent (SD)
- methylene blue (MB)
- amotosalen (A) or riboflavin (R) based photochemical process

PRT offers a departure from the traditional paradigm of targeted testing as these allow for global treatment of blood products, rendering them safe from spreading the infection by making the pathogens (Bacteria, protozoa or Virus) incapable of replication.

- While the individual PRTs vary, a key limitations is the absence of the technology for red cells and whole blood and high cost.

Risk-based decision making to tackle window period

Risk-based decision making is increasingly recognized as key to support national blood policy makers concerning the implementation of safety interventions, especially to address emerging infectious threats and new technology opportunities.

There is an urgent need for practical decision support tools, especially for low- and middle-income countries.

WHO supported the development of such a tool for blood safety. The tool enables users to perform both a quantitative Multi-Criteria Decision Assessment and a novel step-by-step qualitative assessment..

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Thank You

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