

A Global Perspective on Blood Safety and Availability

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26th IPFA/PEI Workshop on Surveillance
and Screening of Blood Borne Pathogens
22 May 2019, Krakow, Poland

A Global Perspective on Blood Safety and Availability

- Findings of the 2015 WHO Global Database on Blood Safety
- Challenges in low and medium income countries
- World Health Assembly Resolutions on blood systems and blood regulation
- Blood safety in Africa
- Summary

Findings of the 2015 WHO Global Database on Blood Safety (GDBS) - I

- The 2015 GDBS contains reports from 173/194 Member States of whom 80% provided data for 2015 or 2014 (respectively 139 and 17 countries). Data obtained in 2013 was included for another 17 countries.
- Findings of the 2015 GDBS will be published in the 2019 Global Status Report on Blood Safety and Availability. The GDBS data summarized in this presentation were kindly provided by the WHO Blood Transfusion Safety Programme.
- Findings of the 2013 GDBS were published in the WHO 2016 Global Status Report on Blood Safety and Availability (apps.who.int/iris/bitstream/10665/254987/1/9789241565431-eng.pdf)

Findings of the 2015 WHO Global Database on Blood Safety - II

INADEQUACY AND MALDISTRIBUTION OF GLOBAL BLOOD SUPPLIES

- Of an estimated 117.4 million global blood collections ~42% were collected in high income countries (HIC), home to only 16% of the world population.
- In low income countries (LIC) ~42% of blood transfusions were given to children under age 5y, whereas in HIC ~68% of transfusions were in patients over age 60y
- The median annual blood donation rate was ~7 times higher in HIC (32.6 per 1,000 population) than in LIC (4.4 per 1000 population). Sixty-six countries collected less than 10 units per 1000 population including 37/45 (82%) in the WHO African Region
- Component separation was performed in 58.1% of collections in LIC compared with 90.8% in HIC
- Only 55/157 (35%) of reporting countries distributed locally collected plasma for fractionation

WHO has not estimated the global unmet need for blood, but others suggest this may be up to 50%. (There is no validated model for estimating national blood need.)

Findings of the 2015 WHO Global Database on Blood Safety - III

DEFICIENCIES IN BLOOD DONATION SCREENING

- WHO recommends that all blood donations should be screened for HIV, HBV, HCV and syphilis, however:
 - 12/172 countries were unable to test collected blood for one or more infections with coverage of 95.3-99.8% for HIV, 71.6-99% for HBV, 58.5-98% for HCV and 31.7-99.5% for syphilis for units collected in those countries.
 - Testing for syphilis was discontinued in Denmark, Finland and Iceland
- Quality of laboratory testing was assessed by reporting on use of standard operating procedures and participation in an external quality assurance program.
 - Among 120 reporting countries the percent of quality assured procedures was 99.8% in HIC, 99.96% in upper middle income countries (UMIC), 83.2% in lower middle income countries (LMIC) and 76.2% in LIC
- 25/173 countries reported exclusive (7 countries) or partial use of rapid tests

Findings of the 2015 WHO Global Database on Blood Safety - IV

DEFICIENCIES IN BLOOD POLICY, GOVERNANCE AND FUNDING

- 134/165 (81%) reported a responsible unit in the Health Ministry
- 123/155 (79%) reported a national blood policy
- 109/161 (68%) reported publication of an annual report
- 104/155 (67%) reported legislation for quality and safety of blood products
- 97/154 (63%) reported a multi-year strategic plan for blood safety
- 98/162 (60%) reported a national blood committee
- 80/173 (46%) reported a national hemovigilance system

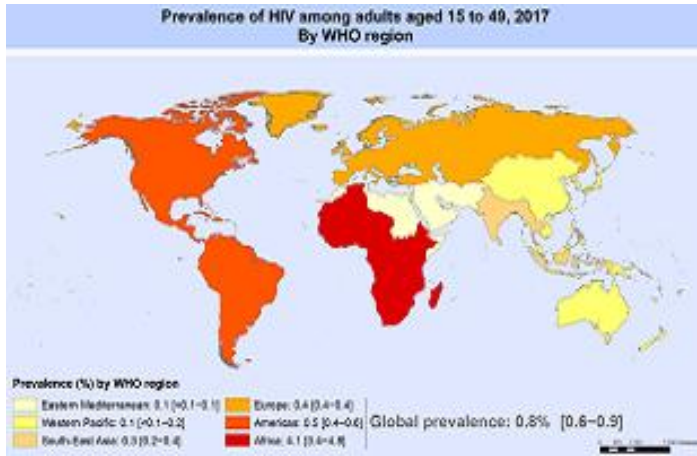
Among 173 countries, 35 (20%) reported absence of government funding and/or cost recovery for the blood service

Major Findings of the 2015 WHO Global Database on Blood Safety - V

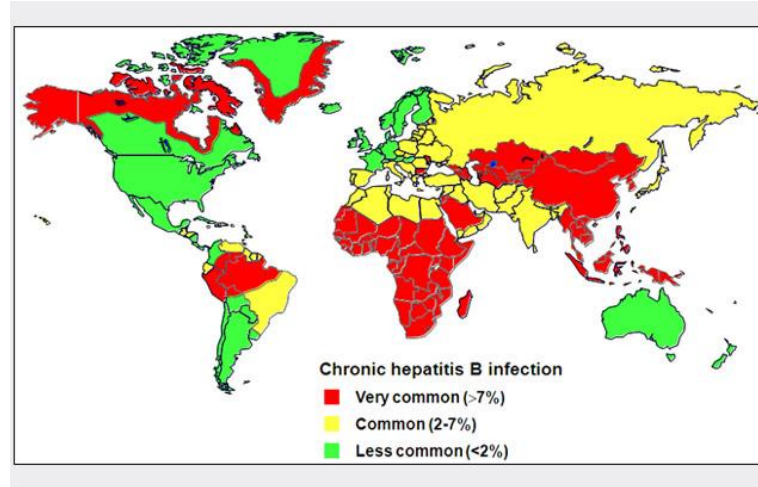
MEDIAN PERCENT OF POSITIVE/REACTIVE DONOR SCREENING TESTS

	HIV	HBV	HCV	Syphilis
HIC	0.002	0.016	0.015	0.02
UMIC	0.10	0.36	0.24	0.44
LMIC	0.14	2.27	0.39	0.70
LIC	0.86	3.64	0.93	0.62

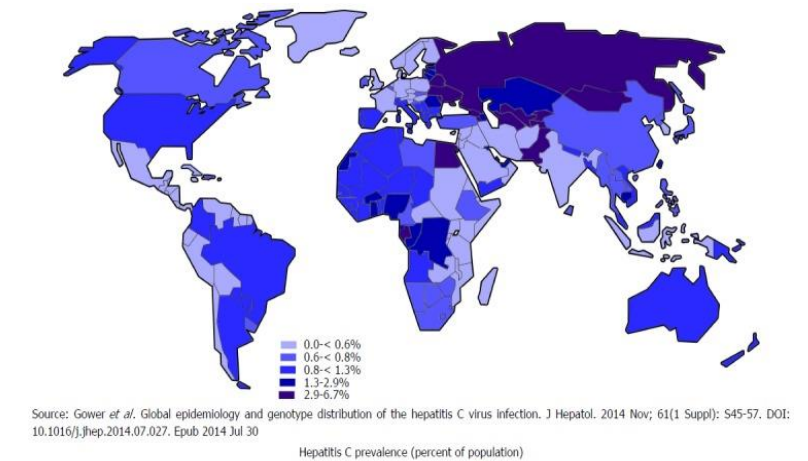
Global Distribution of Chronic HIV, HBV and HCV



HIV- 37million



HBV – 350 million



HCV – 71 million

- The WHO African region is the most severely affected by HIV accounting for nearly two-thirds of infected people worldwide and prevalence of ~4%.
- HBV prevalence is highest in the WHO Western Pacific Region and the WHO African Region, where ~6% of the adult population is infected.
- The areas most affected by HCV are the WHO Eastern Mediterranean and European Regions, with prevalence of 2.3% and 1.5% respectively.

Major Findings of the 2015 WHO Global Database on Blood Safety - VI

METHODS OF DONATION TESTING

Virus (No. reports)	Method in use (Number of Countries)
HIV (167)	Ab only (26); Ab+Ag (91); Ab+NAT (24); Ab+Ag+NAT (26)
HBV (172)	HBsAg only (87); HBsAg+anti-HBc (31); HBsAg+anti-HBc+NAT (18); HBsAg+NAT (25); [Selective use of anti-HBc (3) or NAT (8)]
HCV (169)	Ab only (84); Ab+Ag (32); Ab+NAT (45); Ab+Ag+NAT (8)

Major Findings of the 2015 WHO Global Database on Blood Safety - VII

ADDITIONAL TESTING FOR TRANSFUSION TRANSMISSIBLE AGENTS

Malaria:

- Testing is reported in 50 countries: 18 test all donations (5 in AFR, 5 in SEAR, 3 in EMR, 2 in AMR, 2 in WPR, 1 in EUR);
- Test methods include blood smear (29), antigen (17) and antibody (15)

HTLV-I/II:

- A policy to test all collections exists in 37 countries (28 in AMR, 5 in EUR, 4 in EMR,) and selective testing (geographic exposure, new donor, no previous test) is done in 11 countries
- Three provinces of China require testing of all donations and the government requires surveillance testing of 10% of collections in all provinces

T. Cruzi:

- 20 countries (18 in Latin America, 1 in EUR, 1 in SEAR) test all collections
- 10 countries have selective testing (travel to at-risk areas, defined risk factors)

Challenges to Blood Systems in Low and Medium Income Countries

Challenges to blood availability and safety in low- and middle-income countries were identified at an NHLBI/NIH workshop in April 2017 (Transfusion 2018;58:1307-1317)

- Blood availability is an overriding concern with low donation rates, high donor deferrals rates, and lack of access particularly in rural areas
- Insufficient and poor quality testing for transmissible infections compromises blood safety, particularly in settings of paid donation
- Assurance of blood quality is limited by fragmented systems and deficiencies in infrastructure resources, regulatory and professional oversight, quality systems, and hemovigilance monitoring of donors and recipients
- Overall progress is limited by insufficient government commitments, unstable financing and unmet needs for education and training

WHA Resolutions on Blood Systems and Blood Regulation - I

- The World Health Assembly (WHA) is the forum through which the WHO is governed by its 194 Member States. It is the world's highest level health policy setting body and is composed of health ministers from the Member States. The WHA is convened annually.
- **WHA 28.72 (1975) first established globally the principle of nationally supported, managed and coordinated blood systems as an essential part of the health system**
 - WHA 28.72 prompted many national and regional efforts to enhance blood safety and availability
 - Subsequent Executive Board and WHA resolutions strengthened the recommendations of WHA 28.72

WHA Resolutions on Blood Systems and Blood Regulation - II

- The goal to assure access to safe blood for all patients requiring transfusion was endorsed in resolution **WHA 58.13 (2005), which established World Blood Donor Day**
 - Under WHA 58.13, Member States are urged to support implementation of well-organized, nationally coordinated and sustainable blood programs with appropriate regulatory systems
 - World Blood Donor Day, on 14 June, is celebrated by countries around the world to raise awareness of the need for safe blood and blood products and to thank blood donors for their life-saving gifts of blood

WHA Resolutions on Blood Systems and Blood Regulation - III

- **WHA 63.12 (2010)** recognized that “stringent regulatory control is vital in assuring the quality and safety of blood products...” and urged Member States to “update their national regulations ... in order to ensure that regulatory control in the area of quality and safety of blood products across the entire transfusion chain meets internationally recognized standards.”

WHA 63.12 (2010) may be found at website

http://apps.who.int/gb/or/e/e_wha63r1.html

(Open WHA63/2010/REC/1, then scroll to pages 19-22)

WHO Assessment Criteria for National Blood Regulatory Systems

- In 2012, WHO published Assessment Criteria for National Blood Regulatory Systems to provide a tool to assist capacity building of National Regulatory Authorities (NRAs) for blood and blood products (www.who.int/entity/bloodproducts/NationalBloodRegSystems.pdf)
 - For both developed and developing countries, an internal or external assessment process provides international benchmarking and highlights strengths of the NRA while identifying gaps or areas for future development
 - Global assessment criteria promote international standardization which may reduce burdens to product developers

Blood Components as Essential Medicines

- The WHO Model List of Essential Medicines contains the medications considered to be most effective and safe to meet the most important needs in a health system
 - The WHO list is frequently used by countries to help develop their own lists of essential medicines
- In 2013, WHO added whole blood, red blood cells, platelets and fresh-frozen plasma to the Model List of Essential Medicines
 - Recognition of blood and blood components as essential medicines draws attention to the need to maintain an adequate supply and the need to assure product quality and safety through regulation
- In 2017 WHO published a Guideline on Management of Blood and Blood Components as Essential Medicines

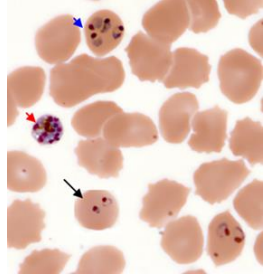
<http://apps.who.int/medicinedocs/documents/s23322en/s23322en.pdf>

WHA Resolutions on Blood Systems and Blood Regulation - IV

- **WHA 67.20 (2014)** requested the WHO Director General to “support Member States upon their request in the area of regulatory system strengthening, including, as appropriate, by continuing to: evaluate national regulatory systems; apply WHO evaluation tools; generate and analyze evidence of regulatory system performance; facilitate the formulation and implementation of institutional development plans; and provide technical support to national regulatory authorities and governments”
- Consistent with this resolution, WHO is incorporating its “Assessment Criteria for National Blood Regulatory Systems” into its “Global Benchmarking Tool” for national regulatory authorities

Blood Availability and Safety in Africa

- Demand for blood is driven by malaria (especially in children under 5 years), obstetrical hemorrhage, traffic accidents, armed conflicts, sickle cell disease, HIV, parasitic infections, and anemia from malnutrition
- Approximately 6 million blood donations account for 5% of all global collections serving 14% of the world population
- Transfusion-transmitted infections are a great concern due to high prevalence in the population, variable acceptance of high risk donors, inconsistent availability of test kits, and sub-optimal quality assurance of test kits and laboratory testing
- Safety monitoring of transfusions is limited



Blood Safety in sub-Saharan Africa - I

- Challenges to blood safety were documented in a review of publications from January 2009 through March 2018 (Transfusion 2019; 59:412-427)
- Consistent with the WHO GDBS, critical systemic deficiencies were identified in policy and its implementation, extent and quality of donation testing, inappropriate transfusions and absence of hemovigilance data collection
- Major international funding (~\$2.1B from 2000 to 2015) resulted in expanded testing for TTIDs and increased voluntary non-remunerated donation (VNRD)
 - Blood shortages persist despite overall increases in donation
 - TTID rates in donations remain high despite increased VNRD
 - High costs of blood safety interventions remain significant barriers (VNRD recruitment, high performance serologic tests, NAT, pathogen reduction technology, QA systems and hemovigilance reporting)
- The overall pace of progress was not sustained when external support decreased since 2009, but regional capacity has improved and gains in education, training and accreditation are strong and ongoing

Blood Safety in sub-Saharan Africa - II

- The rate of transfusion transmitted HIV remains unknown. Near universal reliance on serologic testing without NAT allows uncontrolled risk from recent (window period) donor infections. Test quality varies.
- Occult HBV (presence of DNA with negative HBsAg) is unaddressed in the absence of testing by NAT or anti-HBc. Sensitivity of rapid diagnostic tests (RDT) for HBsAg is low (average of ~47% in 12 countries)
- Testing for malaria by microscopy and RDT is insensitive. A study in Ghana of pathogen reduced whole blood showed reduction of malaria transmission (4% from treated versus 22% from untreated blood), but is cost prohibitive
- Prevalence of HCV has increased in some countries
- Few countries test for HTLV-I/II despite high seroprevalence in some areas.
- Testing is not done for CMV, HEV or arboviruses (dengue and Zika)
- Risk of bacterial contamination is not controlled

Pilot Assessments of African Blood Regulatory Systems

- In response to the 2015 Ebola crisis in Africa, the German Ministry of Health established a Global Health Protection Program with two Modules, “BloodTrain” and “VaccTrain” implemented by the Paul Ehrlich Institut (PEI)
- Under the BloodTrain, benchmarking exercises were undertaken in ten selected countries of Africa using a prototype of the WHO Global Benchmarking Tool incorporating indicators of the “WHO Assessment Criteria for National Blood Regulatory Systems”
- The outcomes of these assessments was used to identify gaps as a basis for institutional development with targeted technical assistance from the PEI



Path Towards an African Blood Regulators Forum

- WHO convened training workshops in Africa in 2013, 2015, 2016 and 2018 at which medicines regulators met with blood operators to discuss blood standards and blood regulation
- An outcome of the 2018 workshop was a consensus by delegates of 19 African regulatory agencies to establish an African Blood Regulators Forum as a Technical Working Group under the African Medicines Regulatory Harmonization (AMRH) initiative of the African Union. This concept was supported by the AMRH Steering Committee in September 2018
- Draft Terms of Reference for the Forum were developed in November 2018 and amended after review by the AMRH Steering Committee
- An initial meeting of the Forum is anticipated in October 2019

Summary

- A 1975 WHA Resolution called for establishment of national blood systems, yet access to safe blood for transfusion remains inadequate in many low and medium income countries (LMIC)
 - Challenges to progress in LMIC are recognized (e.g. deficiencies in governance and funding, technology limitations) but difficult to address without external support
- Awareness has increased with World Blood Donor Day since 2005
- WHA Resolutions in 2010 and 2014 focused attention on blood regulation as a core strategy to advance national and regional blood systems
 - An effort is ongoing to strengthen and harmonize blood regulation in Africa

WHO is developing a comprehensive plan to promote access to quality and safe blood components, and plasma-derived medicinal products...

Thank You!

FDA