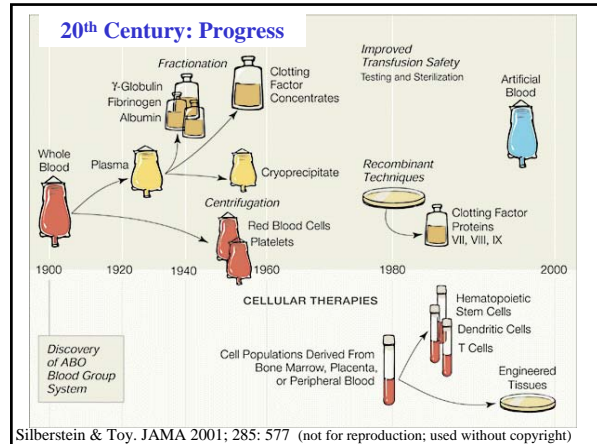


Transfusion Medicine: Looking into the Crystal Ball 2008 - 2018

Walter H. Dzik, MD
Co-Director, Blood Transfusion Service
Massachusetts General Hospital
Associate Professor of Pathology and Medicine
Harvard Medical School, Boston, MA USA



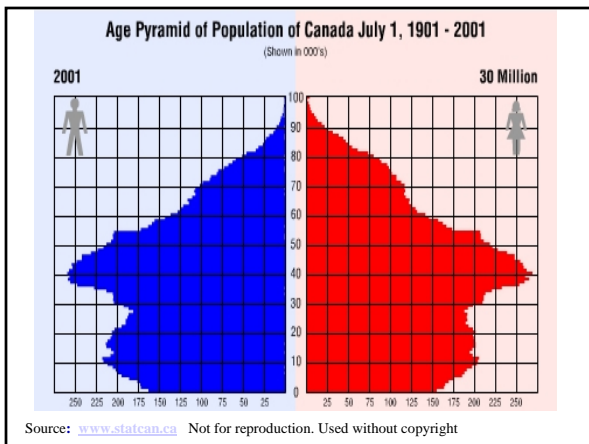
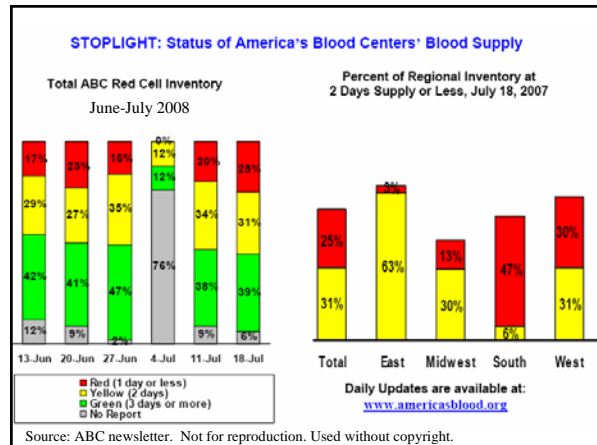
NIH Building



Silberstein & Toy. JAMA 2001; 285: 577 (not for reproduction; used without copyright)

What will the future bring...?

	Donor Services	Infectious hazards	Non-infectious hazards	Diagnostics	Therapy
Recent years			2000 - 2008		
Next 5 years			2009 - 2014		
Beyond			after 2015		



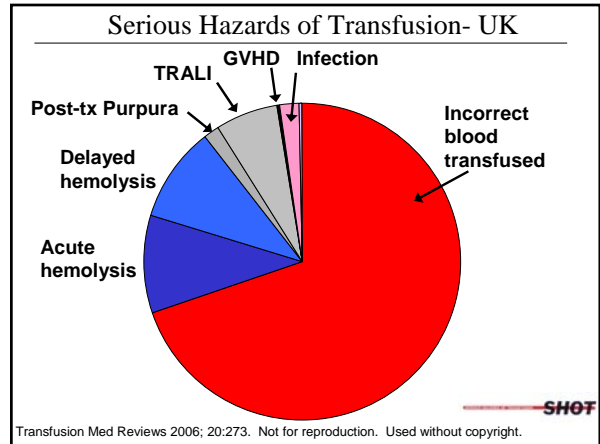
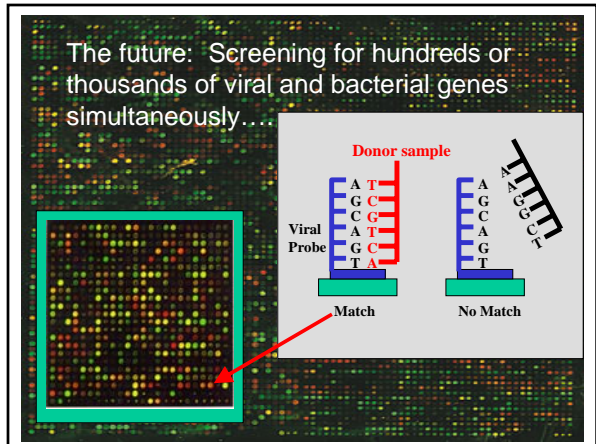
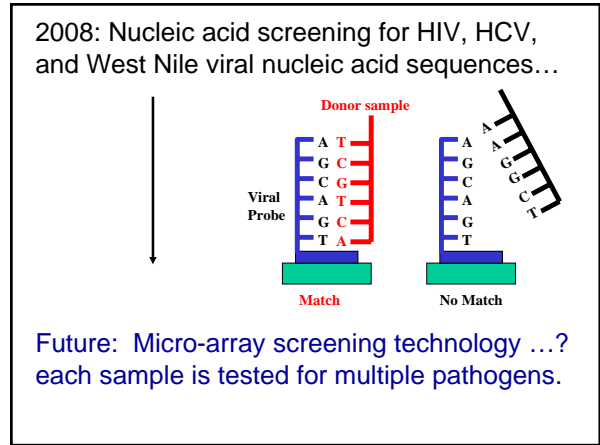
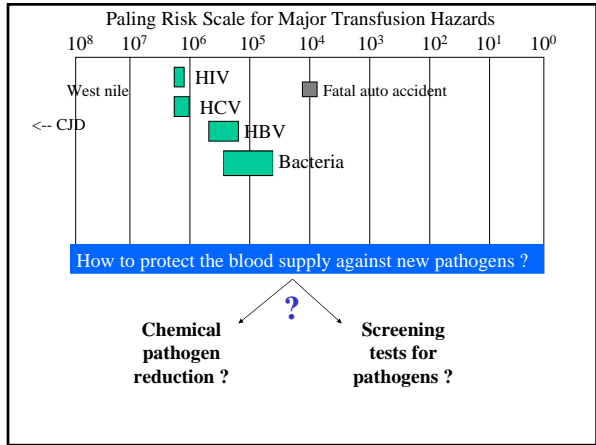
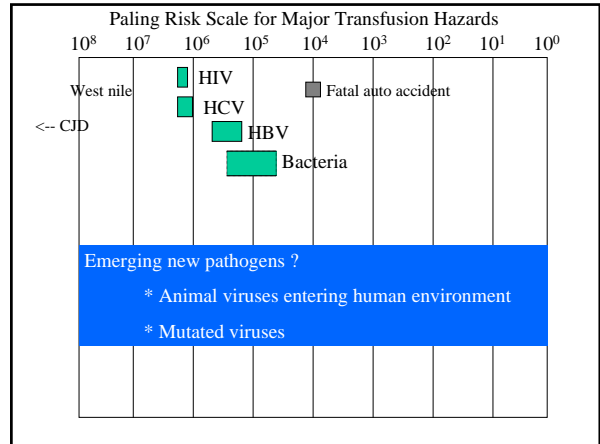
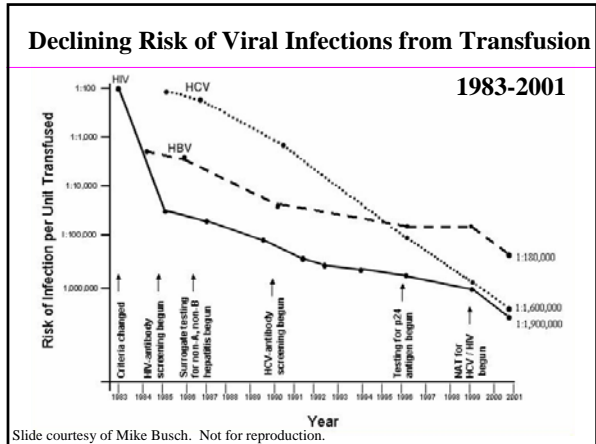
2015 and beyond... Blood Donation Services: Professional Donors... ?

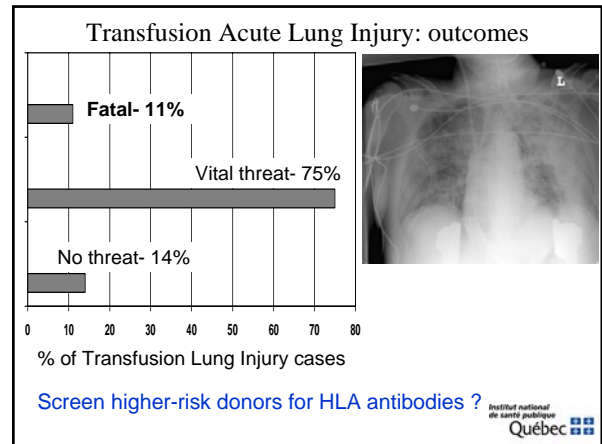
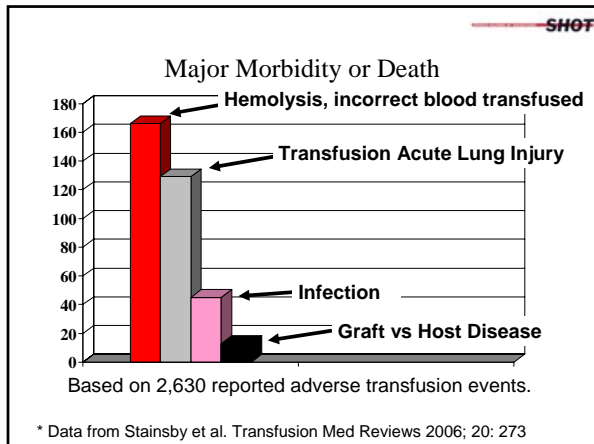
National Blood Donor

Name/nom: Dzik, Walter
Reg Number: 1234567
Viral testing history:
Jan 12, 2015: PCR-neg
March 3, 2015: PCR-neg
May 10, 2015: PCR-neg
Blood Group: A1; D+C+c=-,E+,e+...

"I hereby agree to repeat viral testing and registration in a national data bank..."

- Paid, professional blood donors
- Be required to undergo routine surveillance viral testing
- Registered with government
- DNA, phenotype, HLA data
- Legal responsibility for truthfulness on blood donor questionnaire





Preventing Errors in Blood Administration

* Machine-readable I.D. technology is used in nearly every facet of society-- except healthcare !

- Credit card (retail)
- ATM (cash machine)
- Library
- Toll booth
- Supermarket
- Parking garage

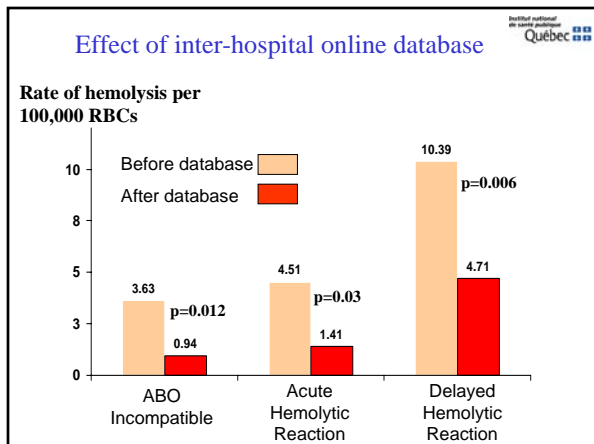
Photo Courtesy of Michael Murphy, MD. Not for reproduction.

Preventing Hemolytic Transfusion Reactions....

HDN - Sommaire transfusionnel

Prénom, Nom	S	M	Né
CHARLES XXXX	M	M	19XXXX

Date	ABO/Rh	RAI	Anticorps	Phénotype(s)
2003/04/24	A POSITIF	Positif	Anti-E Anti-K	C+ c+ E- K+ k+
Directive(s) SANG K-, SANG E-				
Date	ABO/Rh	RAI	Anticorps	Phénotype(s)
2002/11/27	A POSITIF 1ère Diète	Positif	Anti-Jka Anti-K	



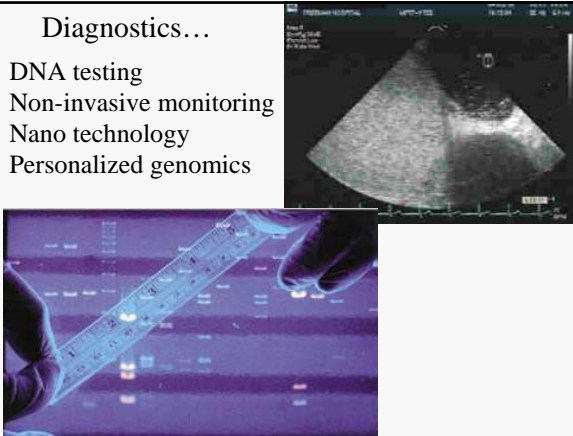
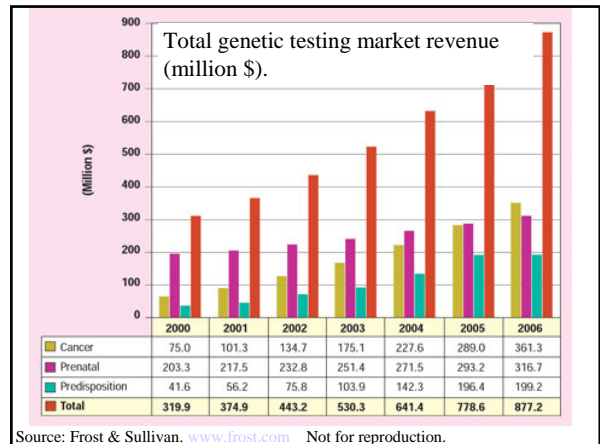
Where will the future lead us...?

	Donor Services	Infectious hazards	Non-infectious hazards	Diagnostics	Therapy
Recent years	Apheresis	PCR for HCV, HIV; Bacterial screening	WBC reduction		
Next 5 years	Shortages	DNA methods Research	TRALI risk reduction		
Beyond 2015	Professional donors	Chemical pathogen reduction or Micro-array technology	Mis-transfusion risk reduction		


Hemovigilance

Diagnostics...

- DNA testing
- Non-invasive monitoring
- Nano technology
- Personalized genomics

Non-invasive readout of Hemoglobin




12.5 g/dL

STEP 1: APPLY SENSOR

RESULTS DISPLAYED IMMEDIATELY

Photo courtesy of Masimo Corp. Not for reproduction.

Nanotechnology Sensors ?



“Doctor, probe # 258 in the patient’s cerebellum is reporting very low local levels of oxygen...”

A spherical chip: data sent to an external recorder

Applications include implantable vital signs sensors.

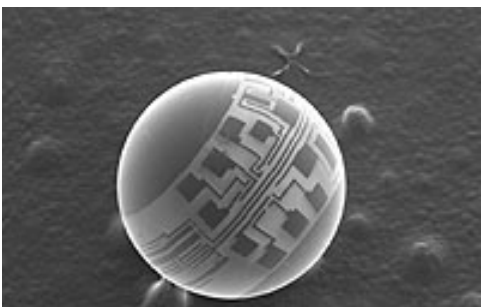
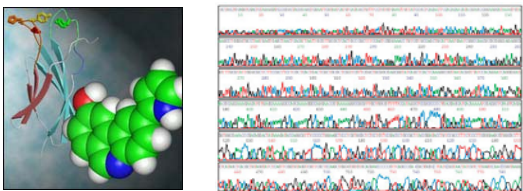


Photo courtesy of Ball Semiconductors Inc, 2000 Not for reproduction.

Clinico-genomics: why are we now on the threshold of “new medicine” ?

Two technologies have converged:

1. High throughput DNA sequencing
2. Informatics (computer processing)

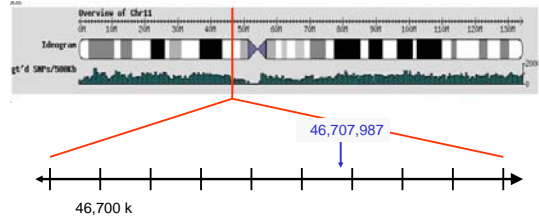


Single nucleotide polymorphisms (SNPs):
Well known to Transfusion Medicine !

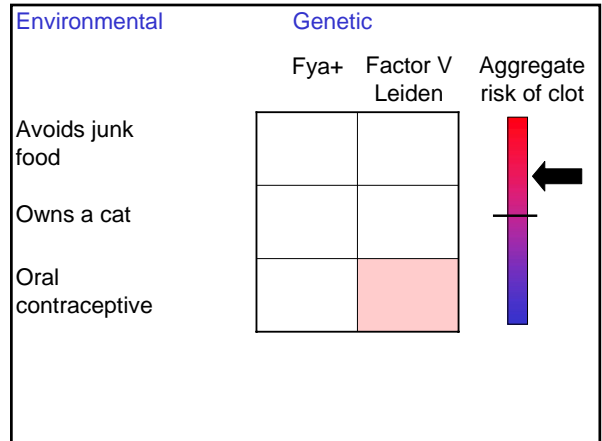
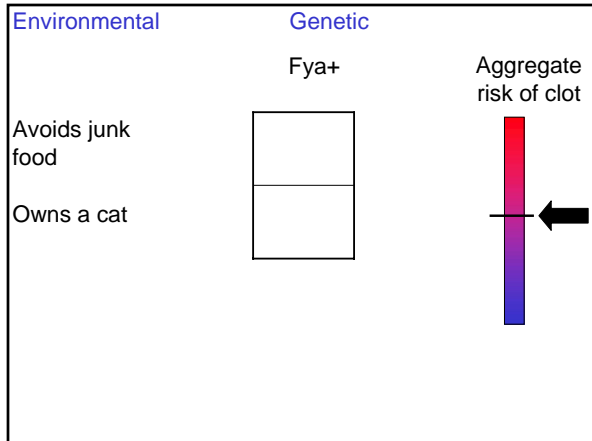
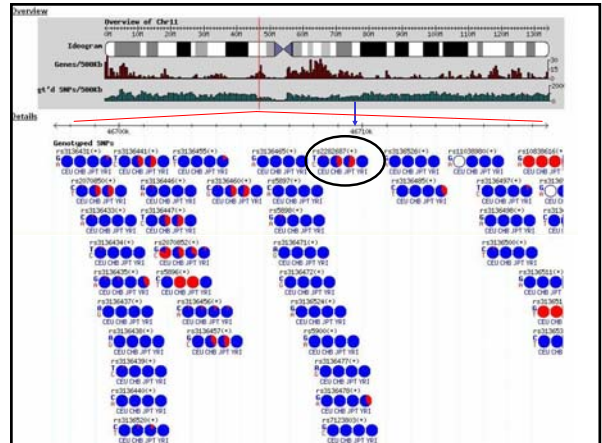
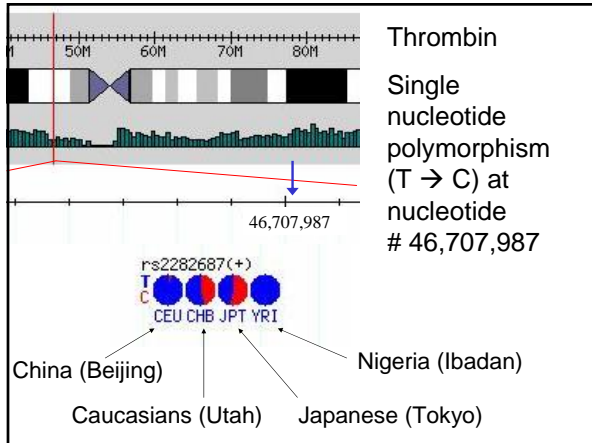
Antigen	Aminoacid	DNA code	Chromo
S	Methionine	...ATG...	4q28
s	Threonine	...ACG...	
HPA-1a PL ^{A1}	Leucine	...CTG... 196	17q21
HPA-1b PL ^{A2}	Proline	...CCG... 196	

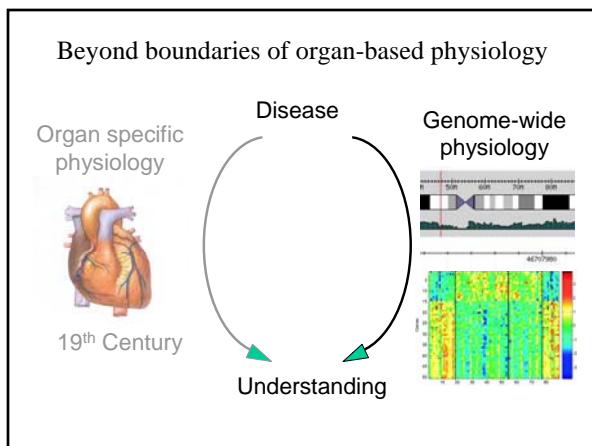
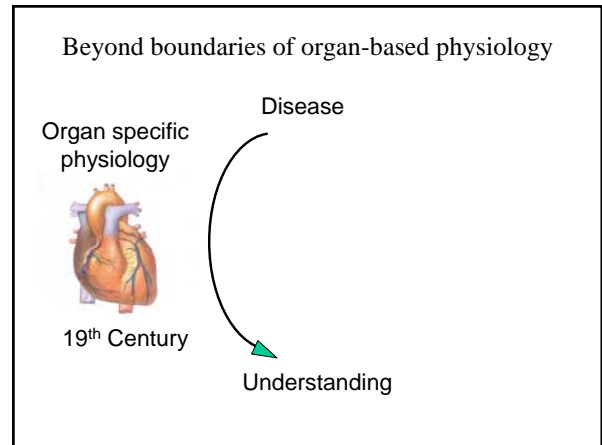
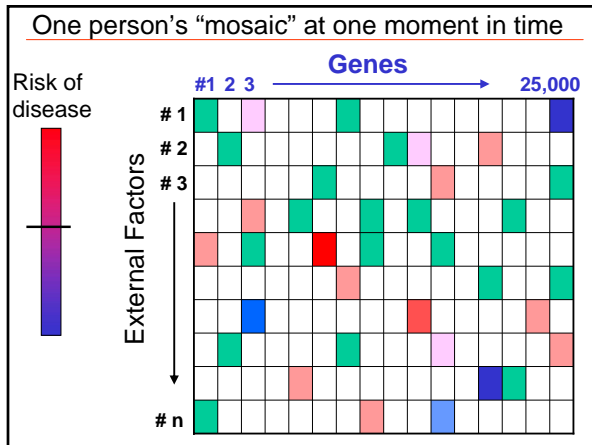
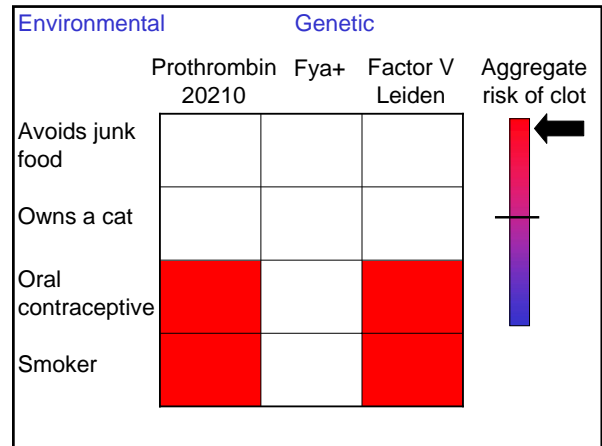
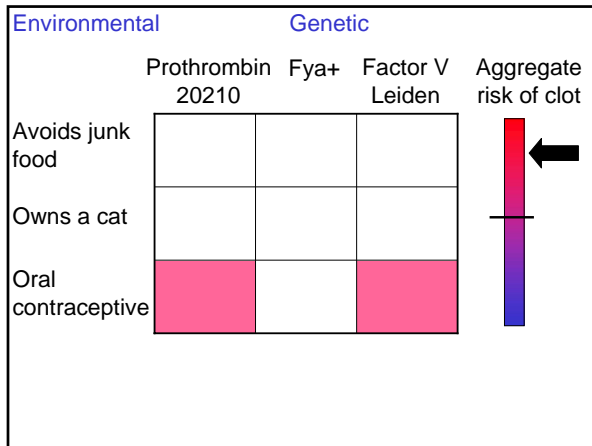
The International "Hap Map" Project
www.hapmap.org

Thrombin: Chromosome 11



Showing 20,300 base pairs on chromo 11;
positions 46,697,330 to 46,717,630





- Diagnostic Medicine:**
Opportunities in the future...
- To analyze each patient's full genome (DNA throughput).
 - To understand the intersection of your genetic susceptibility and your actual exposure to disease (informatics).
 - To reassert *the individual* as the center of diagnosis and treatment.

Therapeutics...

rVIIa; Rituxan; CD34 stem cell transplants

Fresh blood vs stored blood

RBC substitutes

Gene therapy

Immunology drugs

Pro-coagulants →

Anti-coagulants

Rituximab RITUXAN™

rVIIa

Hirudin

Activated prot C

Fondaparinux

Recent advances: CD34 stem cell transplants

- * Allow high dose chemotherapy
- * Simpler than bone marrow harvest
- * Excellent engraftment

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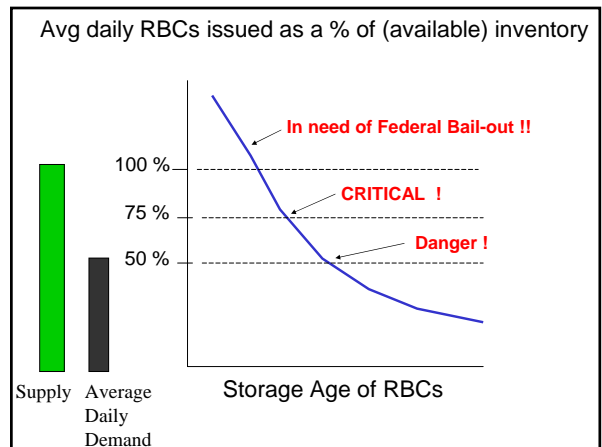
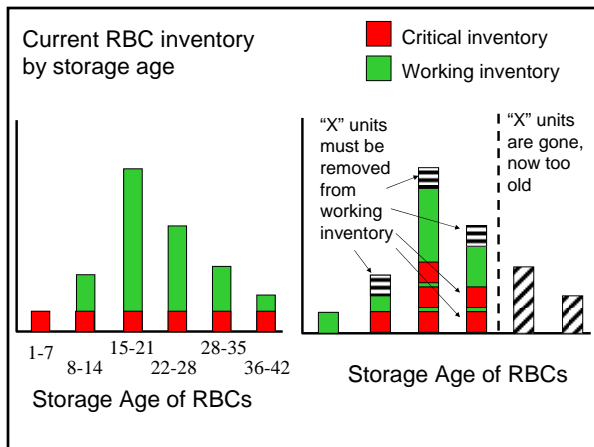
RBC shape changes during blood storage

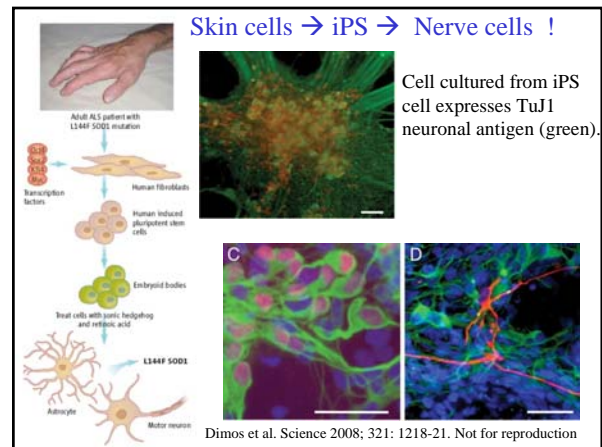
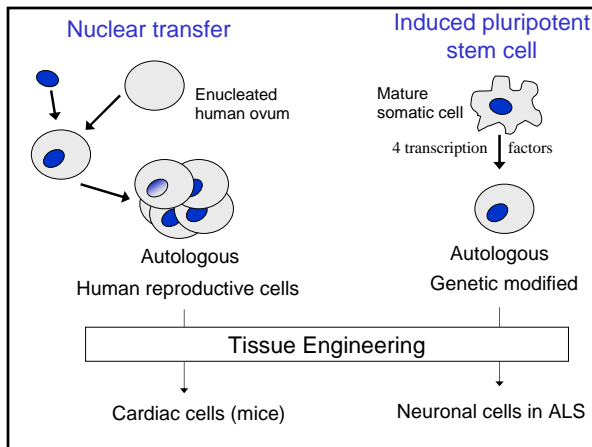
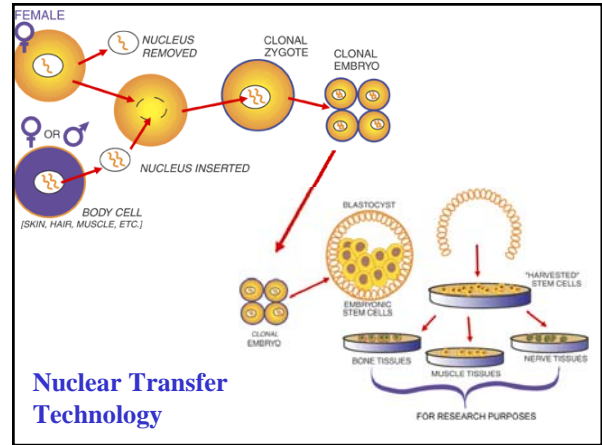
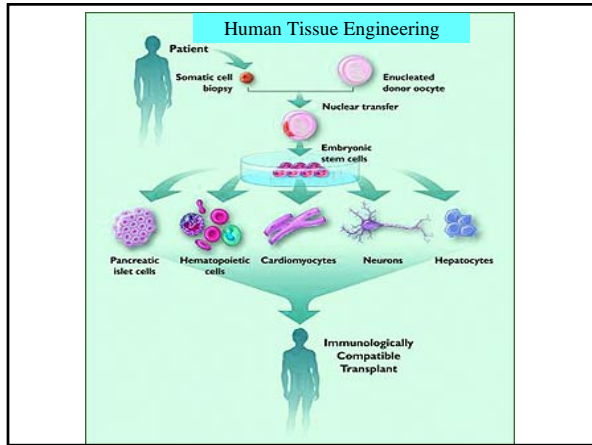
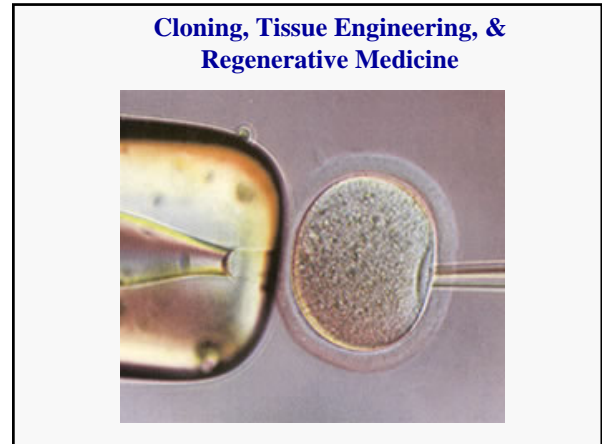
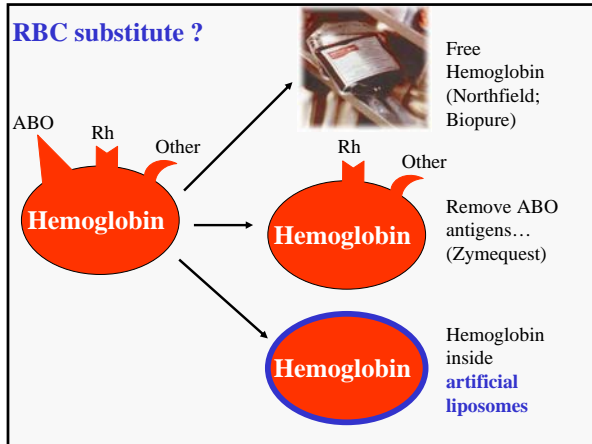
Figs A through D are reversible. E & F do not reverse post-transfusion.

2,3 DPG declines during first 14 days.

ATP levels decline and Na+/K+ pump fails.

Gradual hemolysis occurs.





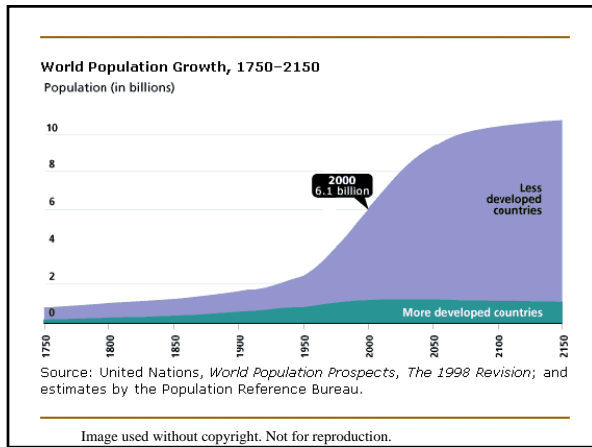
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Next 5 years	Shortages	DNA methods Research	TRALI risk reduction	Microarrays Non-invasive monitoring	Fresh blood controversy; PCC's;
Beyond 2015	Professional donors	Chemical pathogen reduction or Micro-array technology	Mis-transfusion risk reduction	Nano technology; Personalized genomics	Hb carriers; Gene Rx & Regenerative medicine

Hemovigilance Randomized clinical trials

New opportunity brings new challenges

- Develop and adopt new technology wisely
- Finance the application of new biotech
- Remain educated to new developments



Our challenges for the future...

- To balance technology with humanism.

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- To define our success not by the achievements of the most wealthy, but by the condition of the most poor.
- To temper zeal for discovery with compassion for the sick.
- To advance not only our biological selves, but our spiritual selves as well.

