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Better health through laboratory medicine.

PEARLS OF LABORATORY MEDICINE

Biobanking

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CCTC Clinical Chemistry Trainee Council

Definitions

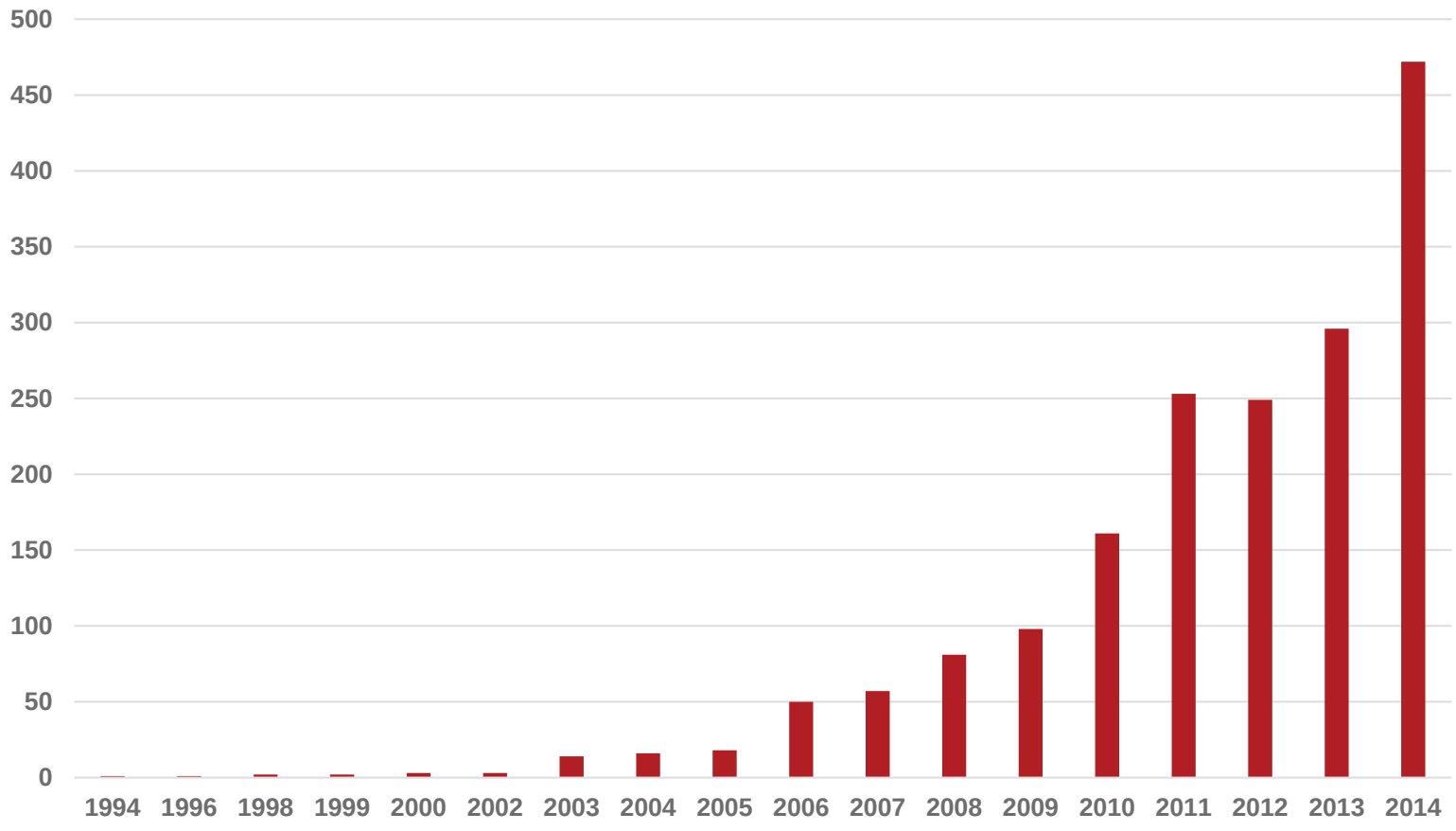
- **Biobank or Biorepository**[1]: *an entity that receives, stores, processes and/or distributes specimens, as needed. It encompasses the physical location as well as the full range of activities associated with its operation.*

- **Biospecimens**: *Samples of material, such as urine, blood, tissue, cells, DNA, RNA, and protein from humans, animals, or plants.*

[1]International Society for Biological and Environmental Repositories. Best Practices for Repositories: Collection, Storage, Retrieval and Distribution of Biological Materials for Research. 3rd edition (2011) www.isber.org

Publication Trajectory

Number of publications per year with the entry word “biobank” or “biorepository” in PubMed



Types of Biospecimens

Invasive	Less-Invasive	Non-Invasive
Whole blood	Dried blood spot	Urine
Plasma	Dried serum spot	Saliva
Serum	Cord blood	Buccal cells
Tissue	Placenta	Feces
Pathological		Hair
Normal around pathological		Nail
Normal		Breast milk
Cerebrospinal fluid		Nasal secretions
Amniotic fluid		Tears
Bronco-alveolar lavage		Sweat
Stem cells		Cervico-vaginal excretions
		Semen
		Oocytes

Risk: High → Moderate → Minimal

Advantages and Disadvantages of Biospecimen Types

Risk	Example of Biospecimen Type	Advantages	Disadvantages
Invasive/High	Blood	Many analyses possible depending on tube type, additive, etc.	Patient-rest Staff competency required Painful collection Prone to pre-analytical variation Processing required
Less invasive/ Moderate	Dried blood spot	Less painful No processing requirement Room temperature storage Easy transport Small blood volume Pediatric collections Saves space Cost efficient	Risk of disposal due to poor collection technique Low or high hematocrit Inadequate blood volume collected
Non-invasive/Low	Urine	Easy collection Patient self-collection Pediatric collections	Must be kept on ice until long-term storage Contamination

Pre-Analytical Variability

Pre-analytical: any part of the process which occurs before analytical analysis of the biospecimen

- Fluid specimen collection variables
  - Ordering (forgotten)
  - Consent (restricted, lost, forgotten)
  - Anatomical location of collection
  - Posture (supine, sitting, standing)
  - Tourniquet time
  - Collection (forgotten, incorrect, duplicate, insufficient volume, contamination)
  - Order of draw
  - Labeling (improper, mislabeled, no label, destroyed label)
  - Processing time
  - Transport conditions
- Tissue specimen collection variables
  - Time to fixation
  - Fixative

Biological Variability

- Age
- Sex
- Ethnicity
- Menstrual cycle, pregnancy, lactation
- Diet
- Alcohol
- Smoking
- Physical activity
- Medication
- Caffeine
- Smoking
- Diurnal variation
- Hydration
- Fever
- Disease

Environmental Variability

- Seasonal changes
- Temperature
- Humidity
- Moisture
- Geographical location
- Altitude
- Sunlight

Impact of Long-Term Storage on Biospecimens

- Aggregation
- Precipitation
- Degradation
- Ice damage
- Dehydration; increased salt concentration resulting in osmotic damage
- Water crystals
- Recrystallization
- Toxicity from cryoprotectants and lyoprotectants

Recommendation: perform pilot studies and literature searches *before* conducting analyses on stored biospecimens

Long-Term Biospecimen Storage Facilities

- Liquid nitrogen freezers
- Mechanical freezers
- Refrigerators
- Walk-in environmental storage systems
- Fully automated entry and retrieval systems
- Ambient temperature storage

Potential Biobank Disasters

- **Natural**
  - Storms, hurricanes
  - Extreme heat or cold
  - Flooding, earthquake
  - Epidemic
- **Man-made**
  - Theft, sabotage
  - Accidental damage
  - Chemical spill
  - Contamination
- **Technical**
  - Fire
  - Freezer breakdown
  - Water damage
  - Air conditioner failure
  - Power outage
  - Explosion
  - Vehicle accident during transport
  - Server breakdown of data storage

Potential Consequences to Biospecimens Following a Disaster

- Concentration differences due to water or evaporation
- Oxidation
- Degradation
- Evaporation
- Desiccation
- Moisture
- Sunlight (strand breaks in DNA)
- Encapsulation in ice after re-freezing
- Microbiological contamination: yeast, mold, fungus, bacteria, and virus causing biological hazards
- Barcodes damaged or destroyed

Security Systems and Emergency Planning

- Redundant alert and monitoring systems remote and in near proximity
- Duplicate and split collections
- Redundant freezers in near and remote proximity
- Maintain service contracts; check equipment at fixed intervals
- Emergency lighting
- Uninterruptible power supply and emergency generators
- Access control
- Fire preparation
- SOPs for emergency response

Biobank Administration and Oversight

- Accreditation or certification
- Staff and staff training
- Laboratory information management system (LIMS) *(Slide 14)*
- Data annotation *(Slide 15)*
- Publication standards
- Costs
- Sustainability

Laboratory Information Management System (LIMS) Features and Benefits Specific for Biobanks

- **Monitors and Records**
  - Pre-pre-analytical variables
  - Analytical variables
  - Post-analytical variables
  - Data management
- **Benefits**
  - Improves productivity and workflow efficiency
  - Data reliability and accuracy by elimination of manual error-prone processes
  - Simple administration, organization, and management
  - Complete and accurate biospecimen traceability
  - Regulatory compliance
  - Clinical data annotation
  - Quality control
  - Statistics and reports

Examples of Clinical Data Annotation

- **Disease Endpoints**
  - ICD diagnoses and disease staging, surgical procedures
- **Questionnaire Data**
  - Lifestyle
  - Socioeconomic
- **Laboratory Data**
  - Clinical chemistry measurements
  - Genotypes
  - Microbiological
  - Pathology
- **Phenotypic Data**
  - Blood pressure, ECG
  - Anthropometric measures: e.g. weight, height
  - Spirometry

Biobankonomics

- **Expenses**
  - Capital investment
    - Location, equipment, IT logistics
  - Operating costs
    - Equipment, salary, LIMS system, inventory, accounting, insurance, communication/marketing, utensils
- **Funding Sources**
  - Governmental
  - Hospital
  - Private
  - Public
  - Biobank activities
  - Patient associations

ELSI (Ethical, Legal and Social Implications)

- Consent
- Privacy
- Return of results
- Public trust
- Commercialization
- Governance
- Data sharing and exchange
- Ownership

Examples of Content in Access Agreements between Biobanks and Researchers

- Biospecimen Details
  - Type and volume
  - Criteria for use, transport/shipment, storage, and handling
  - Return/destruction of used biospecimens
  - Date of return/project end
- Data
  - Transfer; access
  - Prohibition of transfer of data to third parties
  - Date of return/project end
- Costs (administration fees)
- Roles and responsibilities of the biobank and researchers
- Code of conduct
- Pre-publication criteria
- Return of results from project to biobank for future research use
- Project description
- Approvals

Reasons for Culling of Collections

- Storage space constraints
- Control costs
- Consent issues
- Regulatory changes
- Protocol modifications
- Scientific goals have been met
- Compromised specimen integrity
- All identifying information has been lost
- Lack of use
- Potential biohazards associated with the specimens
- When the status of a participant changes from “eligible to ineligible” or their case/control status changes

Summary Statistics of Biobanks (% of Biobanks)

- **Year of Establishment:**
  - After the year 2000: ~50%
  - Before 1980: 7%
- **Primary Reason for Establishment:**
  - Research on a particular disease or type of disease
- **Biobank Specimen Types:**
  - Serum or plasma: ~ 80%
  - Tissue: ~ 70%
  - ~ 50% store more than 4 specimen types
- **Number of Specimens in Storage:**
  - > 10,000 samples: ~50%
- **Percentage of Biobanks Obtain Specimens From:**
  - Direct consent from individuals: 75%
  - Residual specimens: ~60%
- **Organizational Structure:**
  - Academic institution: 78%
  - Hospital or health care organization: 27%

Henderson et al. Genome Medicine 2013; 5:3
http://genomemedicine.com/content/5/1/3

Summary

- Collection, processing, storage, and retrieval of biospecimens
- Security measures, disaster preparation, and response
- Quality management, accreditation and certification, staff education
- Annotation of data
- Cost and sustainability
- Ethical, legal, and social issues
- Governance and ownership
- Access criteria

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Disclosures/Potential Conflicts of Interest

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