

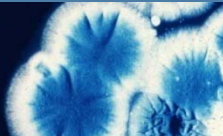
# ASTEC

ASPERGILLUS TECHNOLOGY CONSORTIUM

## The AsTeC Repository

John Wingard, MD  
AsTeC Principal Investigator

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INVASIVE ASPERGILLOSIS ANIMAL MODELS

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- ◆ Population under surveillance & sampling strategies
- ◆ Types of samples collected
- ◆ Types of clinical information to annotate samples

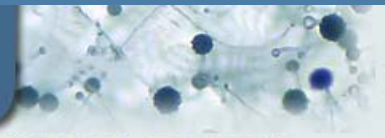
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# Collection Sites

Dr John Wingard  
Principal Investigator  
  
Dr. Barbara Alexander  
Co-Principal Investigator

Clinical Sample Repository  
  
Dr. Wingard

Laboratory Testing  
  
Dr. Alexander

University of Florida  
Wingard

Duke University  
Alexander

Brigham & Womens  
Baden



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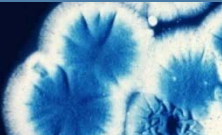
# Specimen and Clinical Data Repository

## Targeted Annual Enrollment

- In order to collect 30-50 cases of proven IA per year
- Anticipate enrolling approximately
  - 500 HSCT Recipients
  - 400 Acute Leukemics
  - 225 Lung Transplant Recipients

Assumption: 6-15% of subjects will develop IA,  
30-40% of which will be "proven"

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# Patients at our collection sites

Types of Patients	University of Florida	Duke University	Brigham/Dana Farber	Totals (yr)
HSCT patients*	150	268	315	733
- allogeneic**	80	158	175	413
Adult				297
Peds				116
Cord blood				77
-autologous	70	110	140	320
Other at risk patients*	478	1,895	1,510	3,883
- Acute leukemia	75	175	130	380
- Liver transplant	98	43	0	141
- Lung/heart-lung transplant	82	86	50	218
- Other solid organ transplant				
- HIV/AIDS	160	191	103	454
	63***	1,400	1,227	2,690

\*Children represent 28% of HSCT pts and 10% of all pts

\*\*66% of pediatric HSCT are cord blood grafts

\*\*\*Hospitalized only



# How many IA cases we can collect

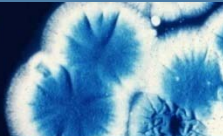
Types of Patients	Nos. of pts at risk	Estimated rate of IA (%)	Total no. of IA cases	Nos. of <u>Proven</u> IA Cases* (% of pts at risk)	Nos. of <u>Probable</u> IA Cases*
HSCT patients*	733	15%	75	29 (4%)	46
- allogeneic**	413		62	24 (5%)	38
Adult	297	4%	13	5 (2%)	8
Peds	116				
Cord blood	77				
-autologous	320				
Other at risk patients	3,883		84	31 (2%)	53
- Acute leukemia	380	9%	34	13 (3%)	21
- Liver transplants	141	4%	6	2 (1%)	4
- Lung transplants**	218	6%	13	5 (2%)	8
- Other transplants	454	1%	4	1 (<1%)	3
- HIV/AIDS	2,690	1%	27	10 (<1%)	17
Totals	4,616		159	60	99

\*We estimate that 39% of total IA cases are proven, the remainder probable

\*\*Includes heart-lung transplants

\*\*\*hospitalized only

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# Our patients and how many IA cases we estimate we can collect

Types of Patients	Nos. pts. at risk	Est. rate of IA (%)	Total no. of IA cases	Nos. of <u>Proven</u> IA Cases* (% of pts at risk)	Nos. of <u>Probable</u> IA Cases*
<b>HSCT patients</b>	<b>733</b>		<b>75</b>	<b>29 (4%)</b>	<b>46</b>
- allogeneic	413	15%	62	24 (5%)	38
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<b>Other at risk patients</b>	<b>3,883</b>		<b>84</b>	<b>31 (2%)</b>	<b>53</b>
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\*We estimate that 39% of total IA cases are proven, the remainder probable

\*\*Includes heart-lung transplants

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# Sampling Plan: Two strategies

## ■ GROUP 1

Longitudinal collection of samples from those at highest risk

Sampling is driven by occurrence of clinical factors that put pt at risk for IA

- Allogeneic BMT
- Acute leukemia
- Lung transplant
  - **Pros:** Baseline samples before onset IA
  - **Cons:** Very inefficient

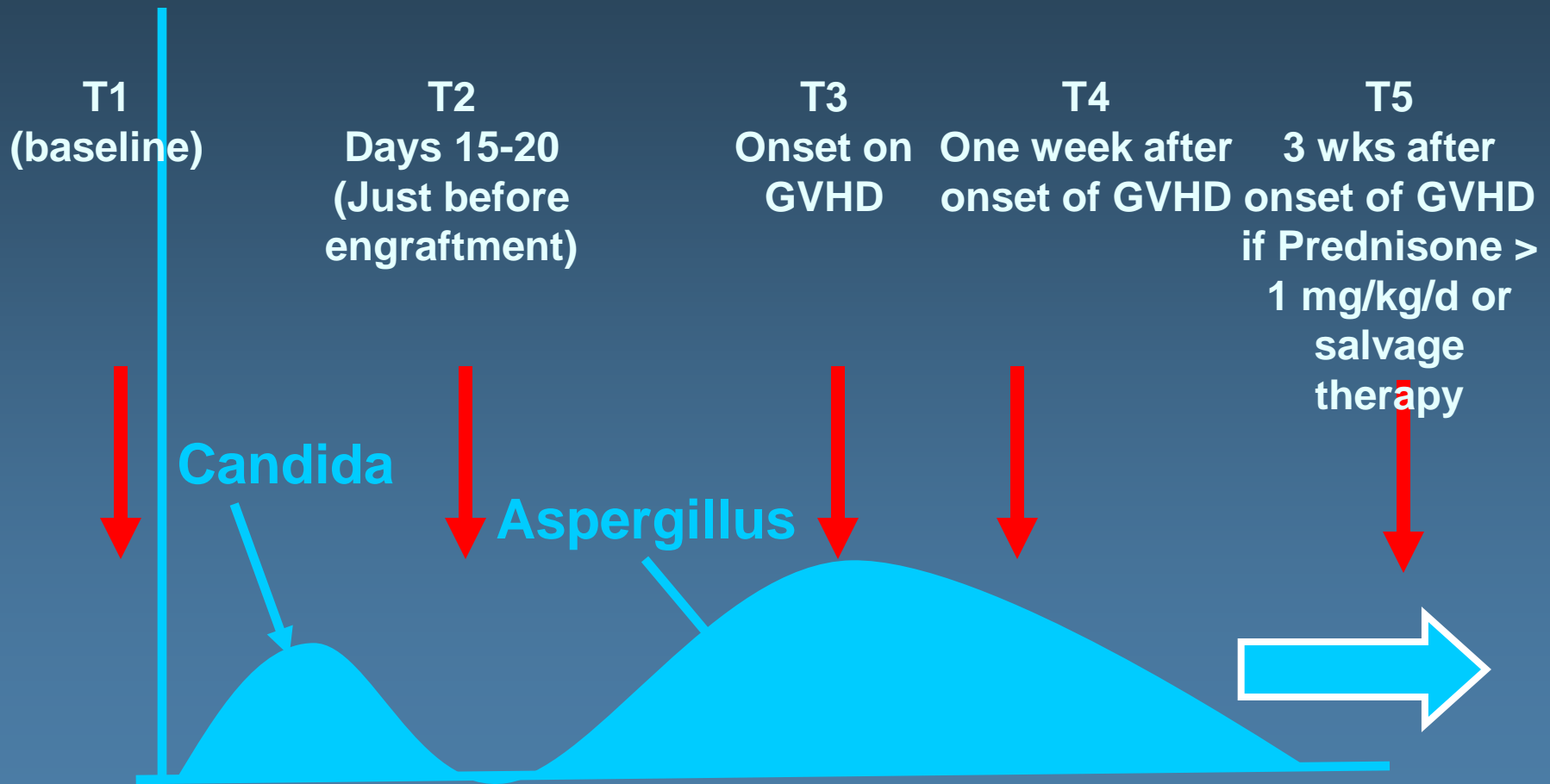
## ■ GROUP 2

Collection of samples from pts with suspected IA

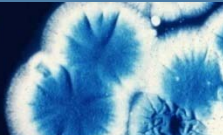
- Any pt group
  - **Pros:** More efficient; data from other pt groups
  - **Cons:** No baseline uninfected samples



# Collection timeline for adult Allogeneic BMT (Group 1)



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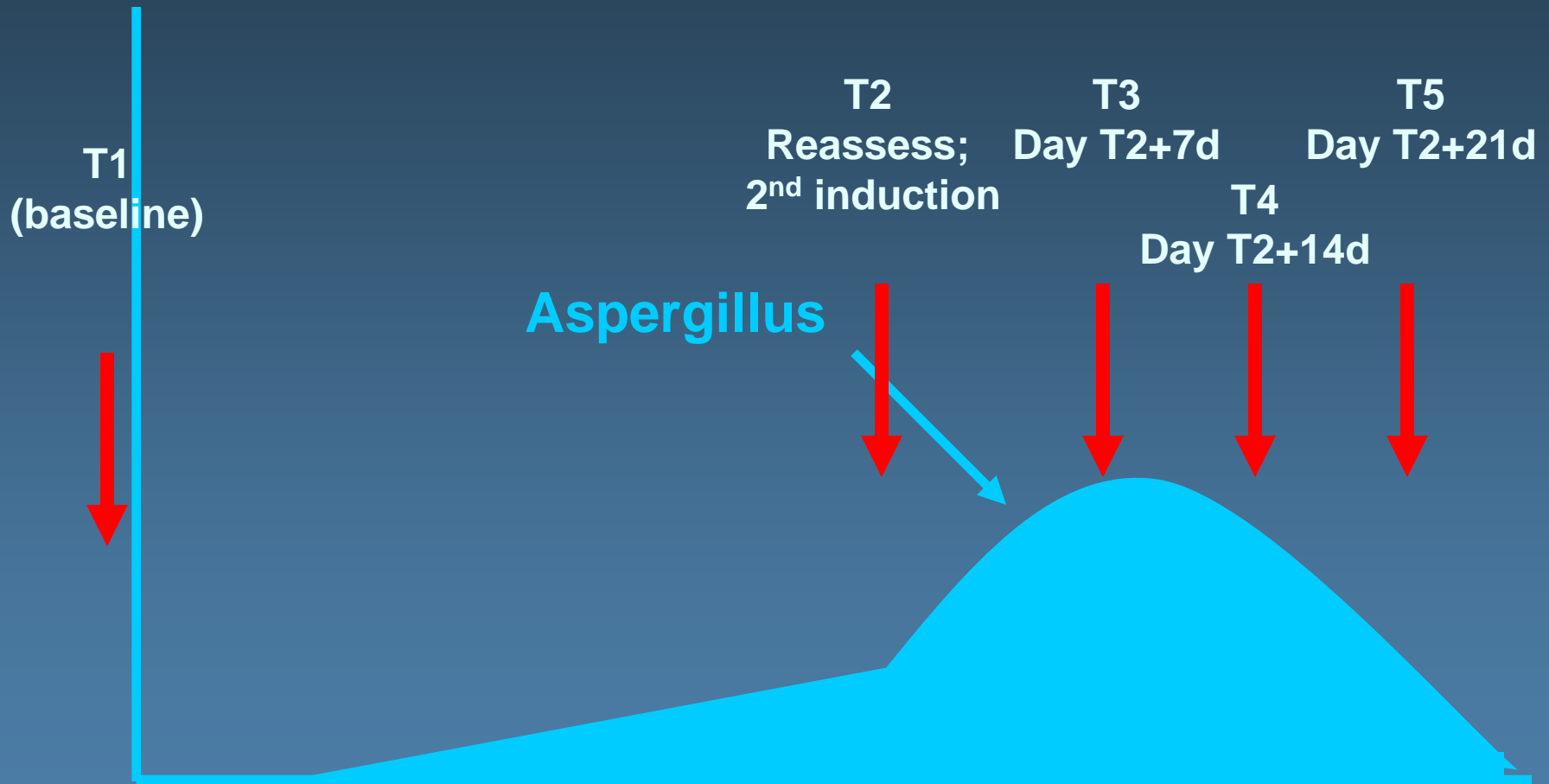


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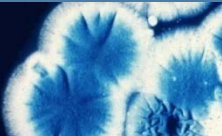
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# Collection timeline for AML patients (Group 1)



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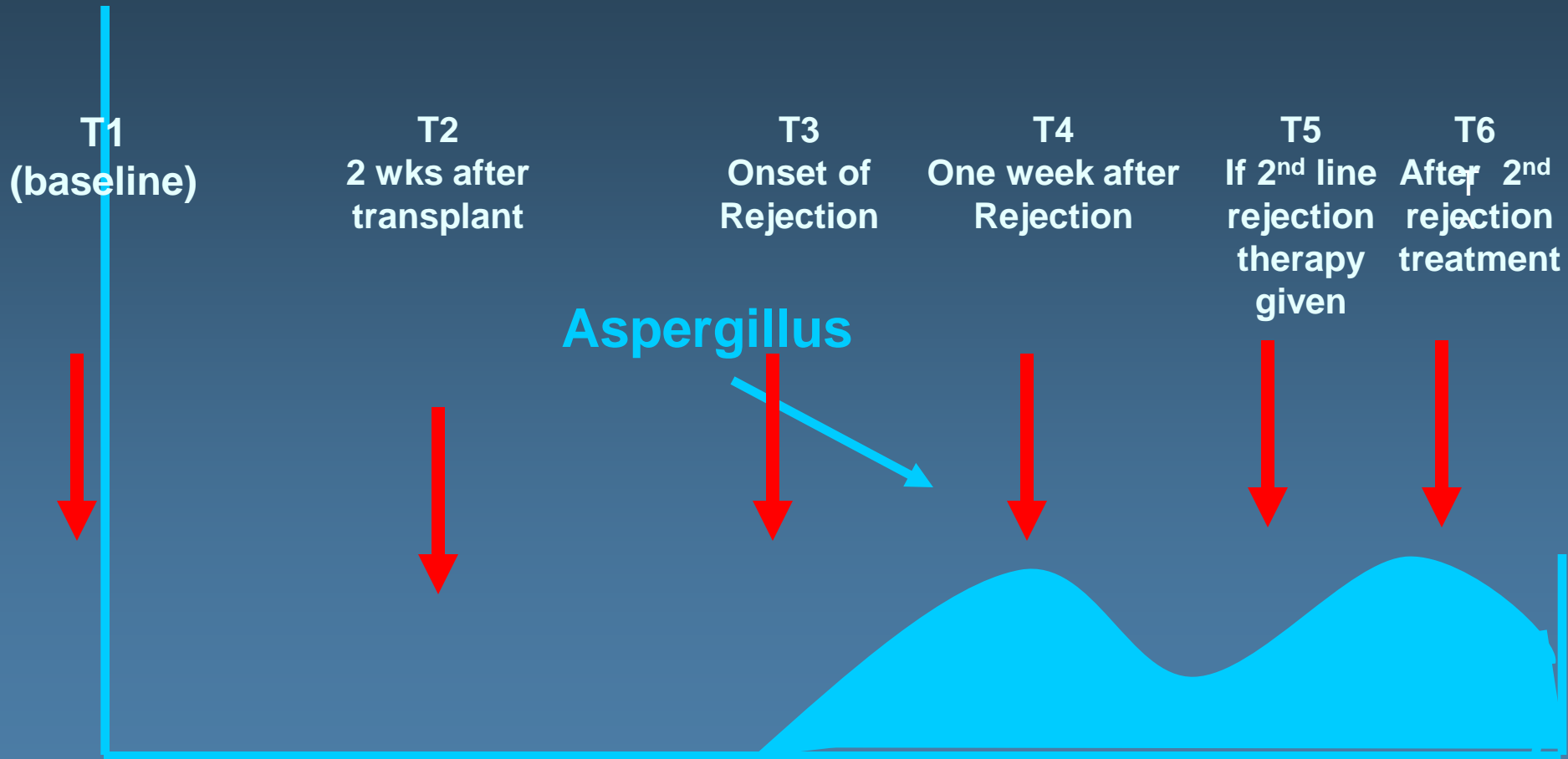
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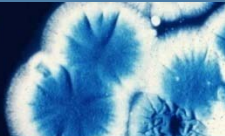
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# Collection timeline for Lung Transplant (Group 1)



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# What we expect to get from longitudinal sampling (Group 1)

- Longitudinal samples from 42 pts with proven IA/yr
- Longitudinal samples from 67 pts with probable IA/yr
- Baseline samples from 902 pts at risk for but not infected/yr
- Follow-up sampling is driven by the occurrence of clinical factors that put pt at risk for IA
  - about 30-40% of pts enrolled at baseline

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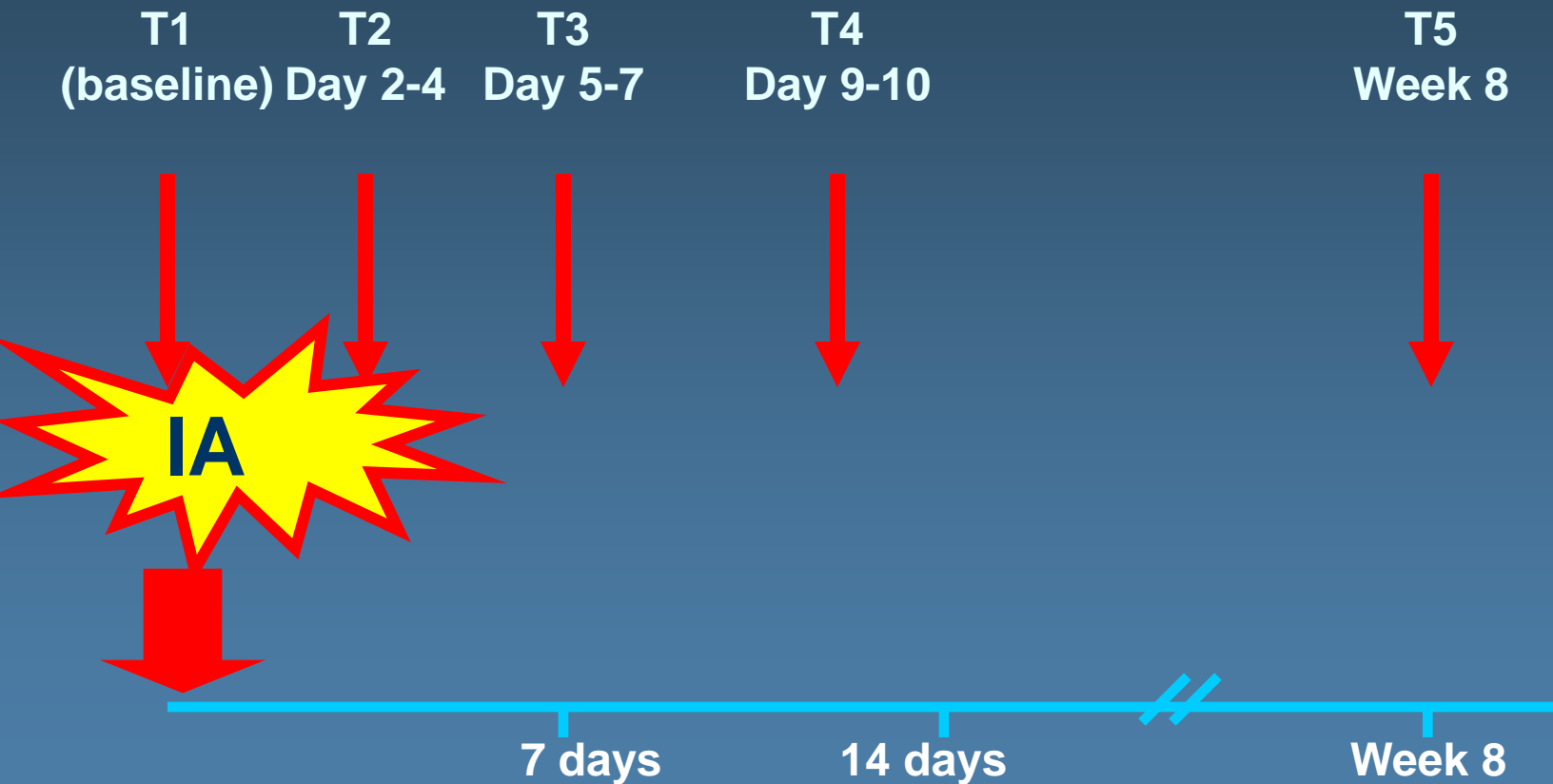
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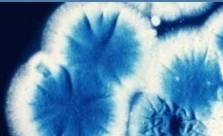
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# Group 2 Collection timeline...

When an IA infection occurs (Group 2, Group 1 --> 2)



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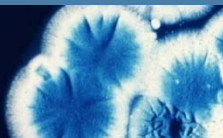
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# What we expect to get from sampling patients suspected to have IA (Group 2)

- Pts with suspected IA/yr
- 30-40% will have documented IA
- Of IA cases 30-40% will have proven IA (the rest probable)
- To collect a target of 30-50 pts with proven IA, we will collect samples from 188-556 pts with suspected IA

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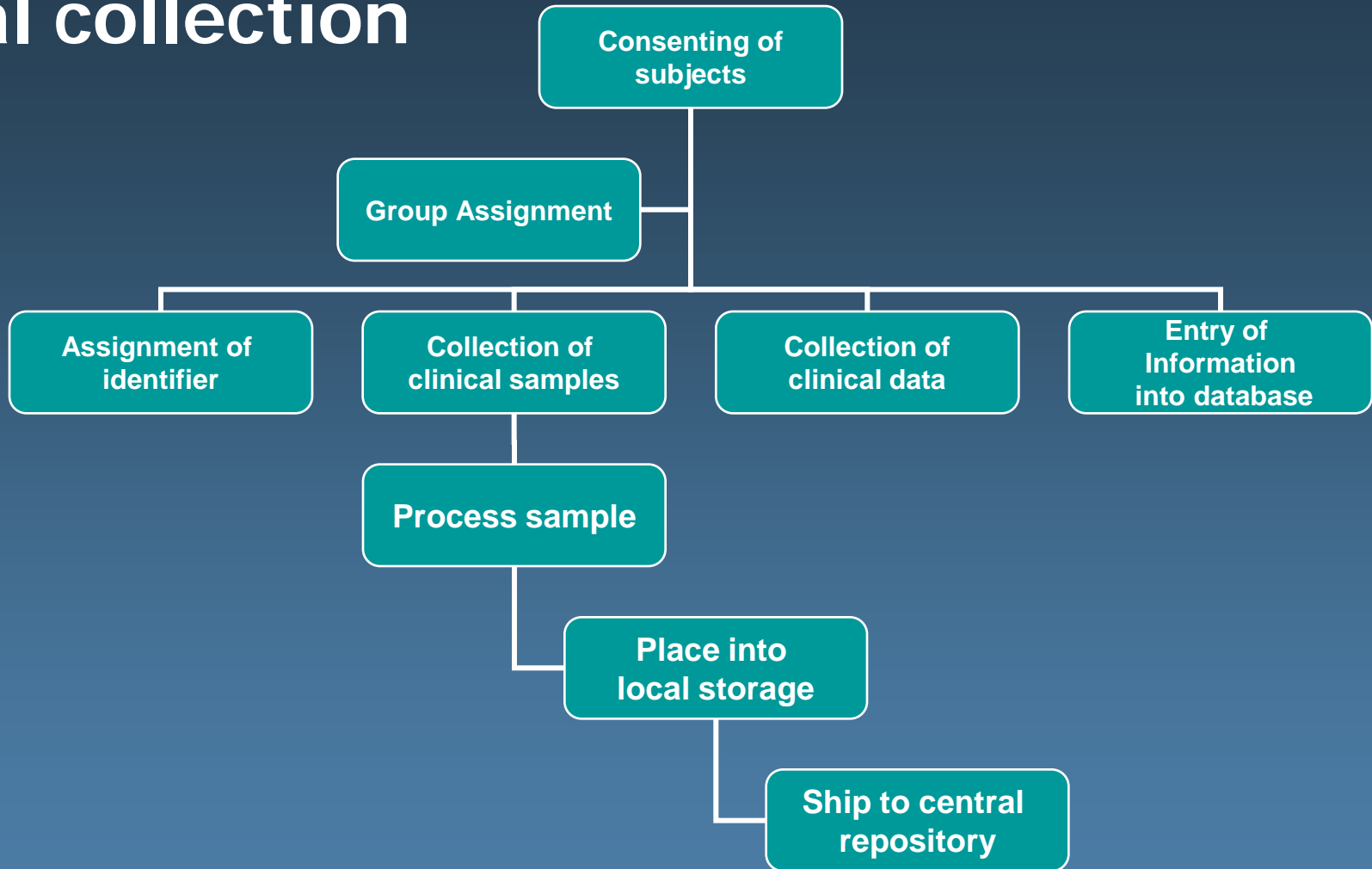


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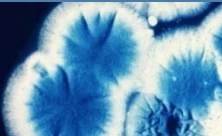
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# Procedures at local collection site



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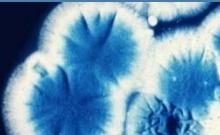


# Samples to be Collected

- **Blood**
  - **Whole Blood** – Fungal DNA / RNA
  - **White Blood Cells** – Host genetic markers for risk
  - **Intracellular RNA** – Host response; sequential gene expression profiles
  - **Serum** – Antigens, antibodies, metabolites
  - **Plasma** – Proteomics
- **Urine**
- **Bronchoalveolar Lavage\***
- **Tissue\***
- **Infecting fungal isolate**

\*If procedure is performed for clinical reasons or autopsy

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# Blood Volumes

Vacutainer type	No. of tubes per collection	Blood component	Tube volume	Aliquot size	No. of aliquots anticipated at each sampling
Serum	1	Serum	6 mL	0.5 mL	6-8
Cell Preparation Tube (CPT)	1	Plasma	4 mL	0.5 mL	2-4
		Leukocytes		Buffy coat pellet	1
EDTA	3	Whole blood	6 mL	3 mL	5
				1.8 mL (1mL+2.6mL RNAlater)	2
				1 mL (For BOOM tubes)	2
PAXgene™ Blood RNA	3	RNA	2.5 mL	2.5 ml (6 µg RNA)	3

**ADULTS:** 35.5 mls per draw; **CHILDREN:** 11.5 mls per draw

- In no case will more than 550 ml in 8 weeks for adults and no more than the lesser of 50 ml or 3ml/kg will be drawn for children over an 8 week period.
- Pts weighing < 16kg are ineligible for the study.
- Samplings will be omitted if next collection would exceed 8 week limit.



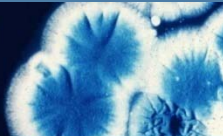
# Clinical data collected

- **Demographic information**
- **Underlying disease**
- **Disease/transplant Treatments**
- **Concomitant medications**
- **Transfusions**

- **Goal:**

- **Determine pre-test probability of infection**
- **Potentially interfering medical conditions**

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# Next steps...

- We expect sufficient samples to be available for testing summer/fall 2009
- Initial sampling strategy will be reassessed after 1-2 years

