



Centers for Medical Countermeasures Against Radiation

Paul Okunieff, MD

CMCR Steering Committee Chair

CBARMFI (Rochester) Principal Investigator

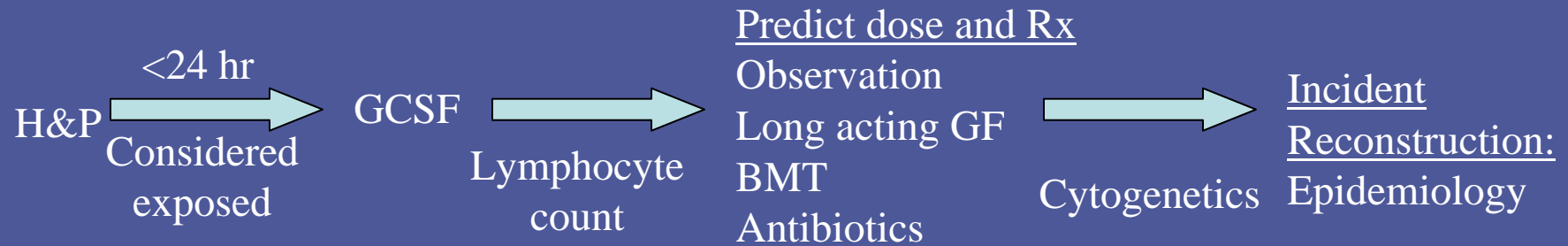
CMCR Locations

Columbia • Dana Farber/Harvard • Duke • Medical College of Wisconsin • Pittsburgh • Rochester • Seattle • UCLA



Global Plan

Standard of Care



Critical Need ↑

Critical Need ↑

Critical Need ↑

↑

Critical Need ↑

High throughput screen for exposure v worried well

Bone marrow mitigator that produces better than a mere 10% modification

Biodosimeter that MEASURES dose and distinguishes neutron dose, lung dose, genotoxicity...

Most toxicity in long-term survivors will not be bone marrow and much acute toxicity will not be bone marrow. Current transplant technology poor

Triage

Mitigators

Dosimetry

Mitigation and Rx for heme and non-hematologic

Currently Available Treatments:

Potassium Iodide (KI): *Only for Iodine-131, and only if taken before exposure*

Prussian Blue: *Only for Cs-137 or Thallium, and Only if taken at time of ingestion*

DTPA: *Only for Americium, Plutonium, Californium, Curium, and Berkelium ingestion*

Amifostine: Must be taken before and during exposure. Causes hypotension and neuropathy. Insufficient dose modification.

Cytokines: G-CSF, pegG-CSF, GM-CSF

*“No data showing increased survival”; pre-clinical data in radiation models has produced mixed results; **limited quantities available***

Transfusions and Bone Marrow Transplantation: *“The outcomes of patients undergoing BMT after radiation accidents have been **very poor**”*

-Flynn DF, Goans RE. Nuclear Terrorism: Triage and Medical Management of Radiation and Combined-Injury Casualties. Surg Clin N Am 86:601-636 (2006).

-Centers for Disease Control: Radiation Emergencies (<http://www.bt.cdc.gov/radiation/>) Accessed September 2006.

If the most likely scenarios will yield between 10-1000 casualties (with an estimated 41% receiving >3 Gy), these interventions and their availability are **completely insufficient**.

State of funded Researchers in USA:

Before 2005

- Number of active R01 grants on normal tissue effects of ionizing radiation funded by NCI was under 3 per year
- A similar number of extramural grants were funded by DOD and NASA
 - RERF (Radiation Effects Research Foundation) closed
 - AFRRRI (Armed Forces Radiation Research Institute) at risk
 - Decreased perceived career growth for new scientists

2006

- Double grant numbers DOD, NASA, & NIAID
 - NIAID U19's (\$28M) represent over half of all scientists involved in normal tissue radiation effects research

MAIN POINTS OF CRITICAL NEED

- The volume of science in the field is far too small but rapidly growing (need to keep the momentum in the Strategic Plan)
- Incentives for radiobiological scientists to enter the field are needed

State of CMCR Mission:

MAIN POINT OF STRATEGIC NEED

1. There are many very promising translational research projects in development for agents and instruments to deal with radiological events including: (1) Triage, (2) Biodosimetry, (3) mitigation, and (4) treatment.
2. There are 8 centers, a few government research groups, and a few independent scientists now funded to develop the critically needed products.
3. The Stockpile does not yet have any fully satisfactory agents or instruments for radiological threats.
4. The range and number of critical products in development requires Centers with substantial multidisciplinary skills (biology, physics, pharmacology, chemistry, engineering, molecular bio...).