

Combat Casualty Care

Development of Complement Activation Inhibitors to Limit Tissue Injury During Resuscitation

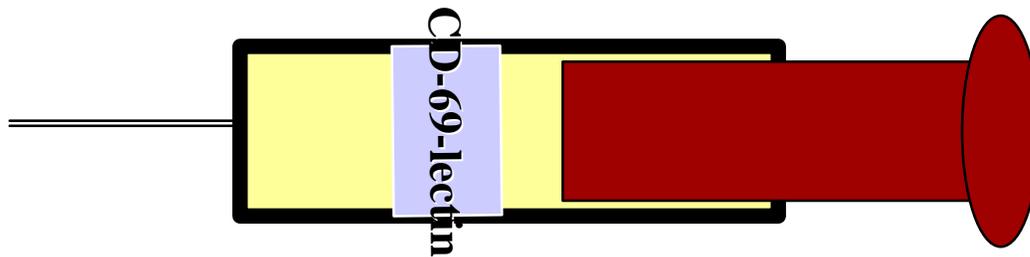
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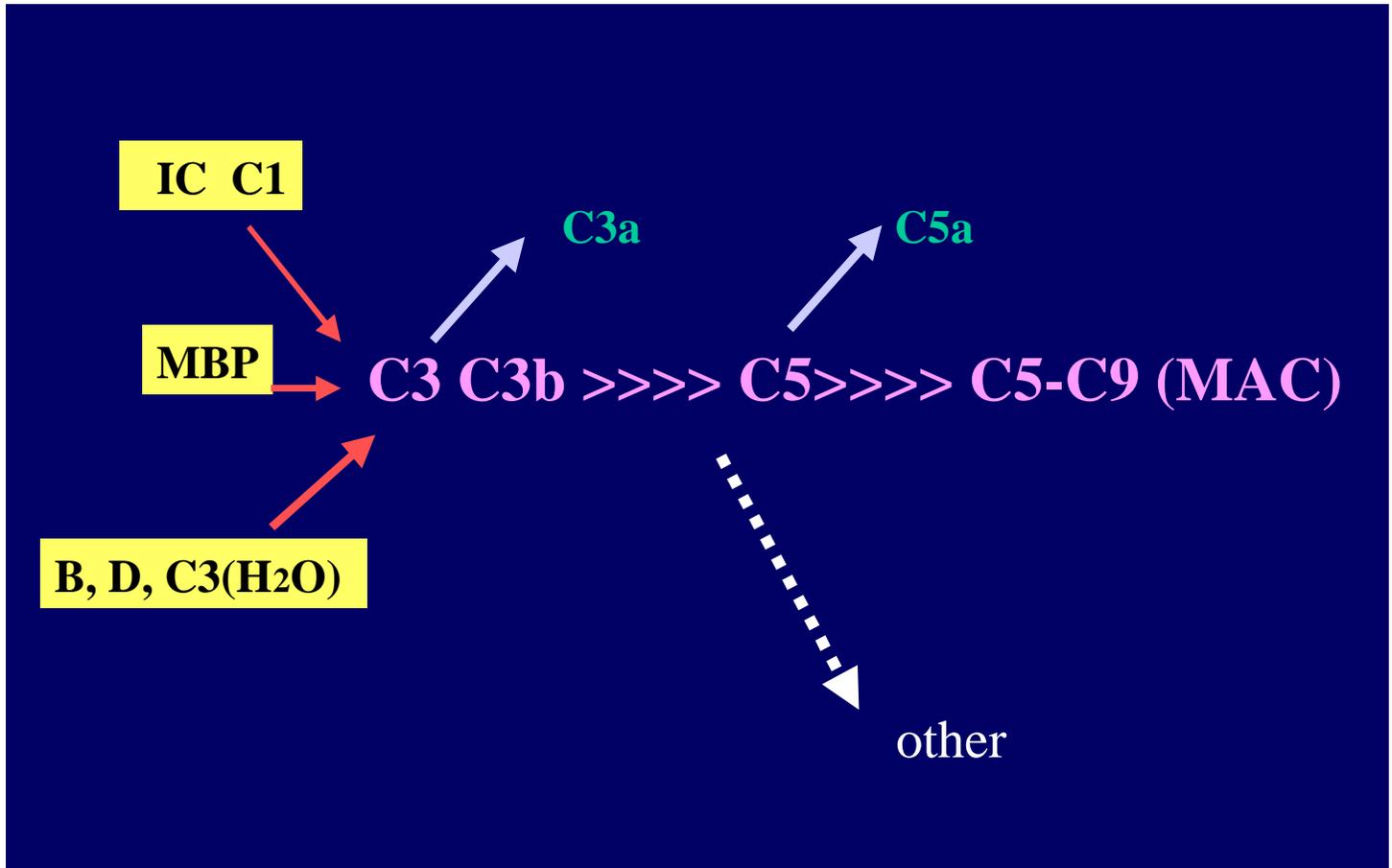
Why this program is significant?

.....**Conclusion:** for prolonged hypotensive fluid resuscitation, a minimum MAP of 60-70 is necessary, but **does not guarantee survival** even when blood is used. Additional therapies will be needed... to prolong survival,.

Report from University of Pittsburgh (2003)

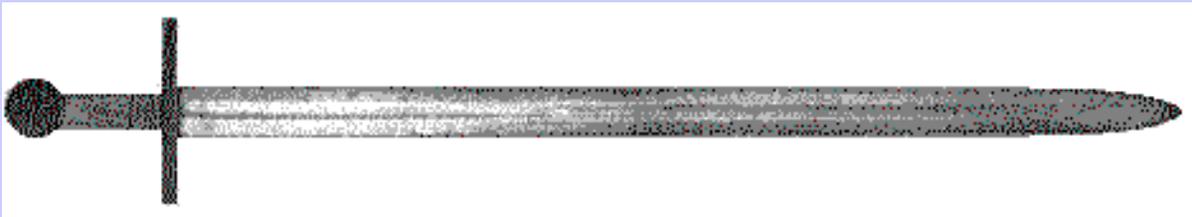


Complement activation cascade



Complement

- Promotes phagocytosis
- Supports inflammatory responses against pathogens
- Instructs adaptive immune response to select appropriate antigens for humoral response



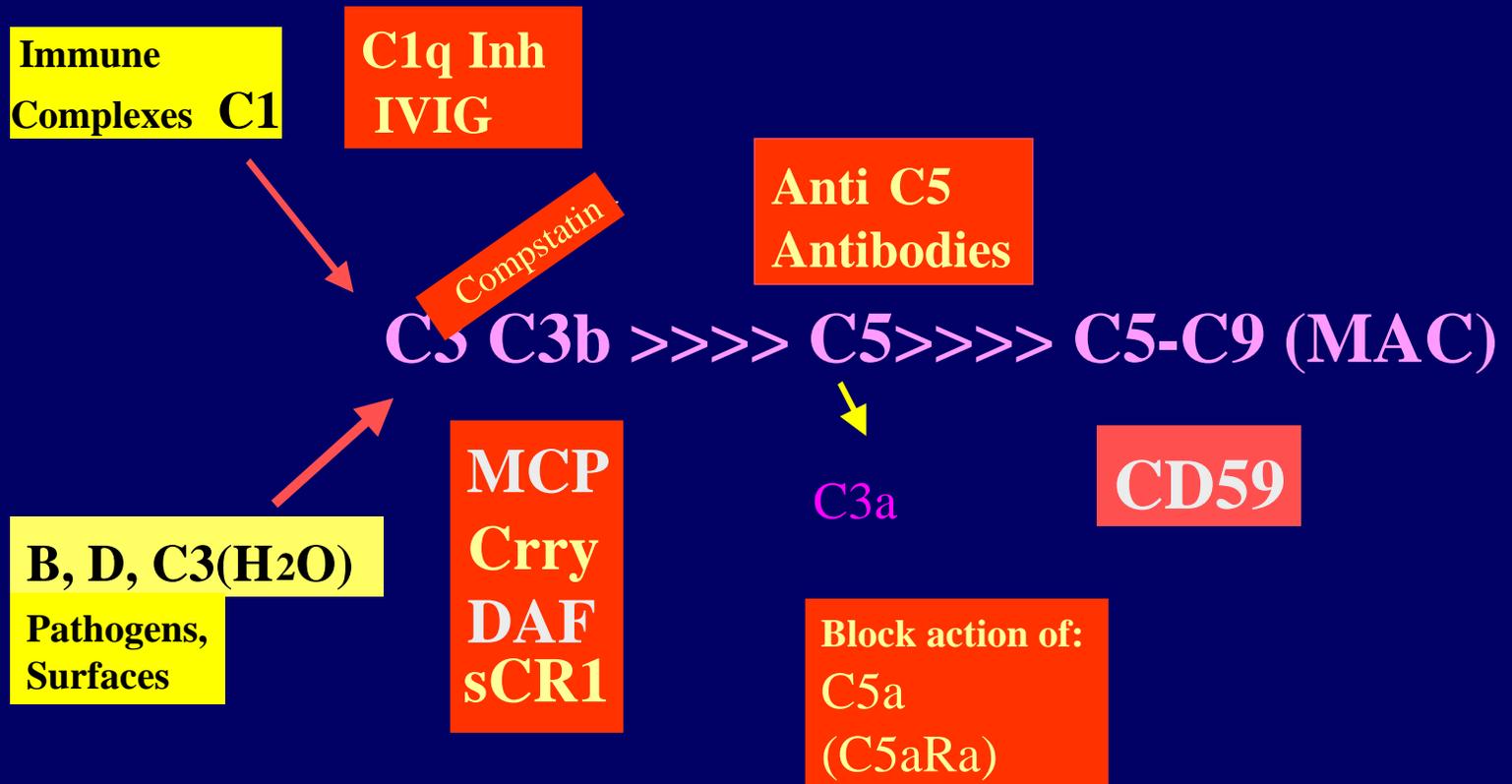
- Excessive, unwanted activation leads to host cell damage.

Complement activation mediates

- **Tissue pathology at inflammatory sites**
- **Tissue injury from ischemia or reperfusion**
- **Tissue injury following blunt trauma**
- **Tissue injury following hemorrhagic shock**
- **Tissue injury upon exposure to toxins**

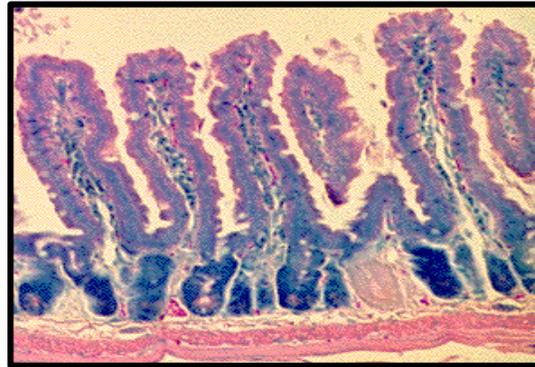
Complement activation cascade

Potential inhibitors (in red boxes)

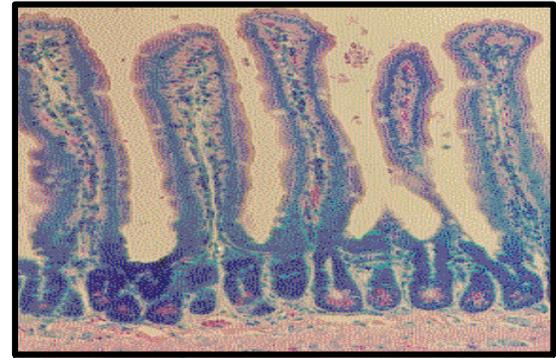


Crry-Ig prevents IR-induced mucosal damage

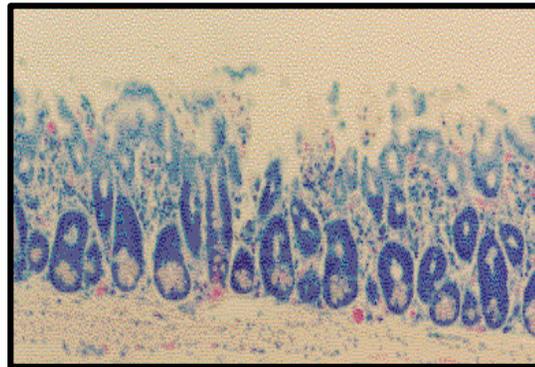
SHAM



CRRY
T-5



IR120

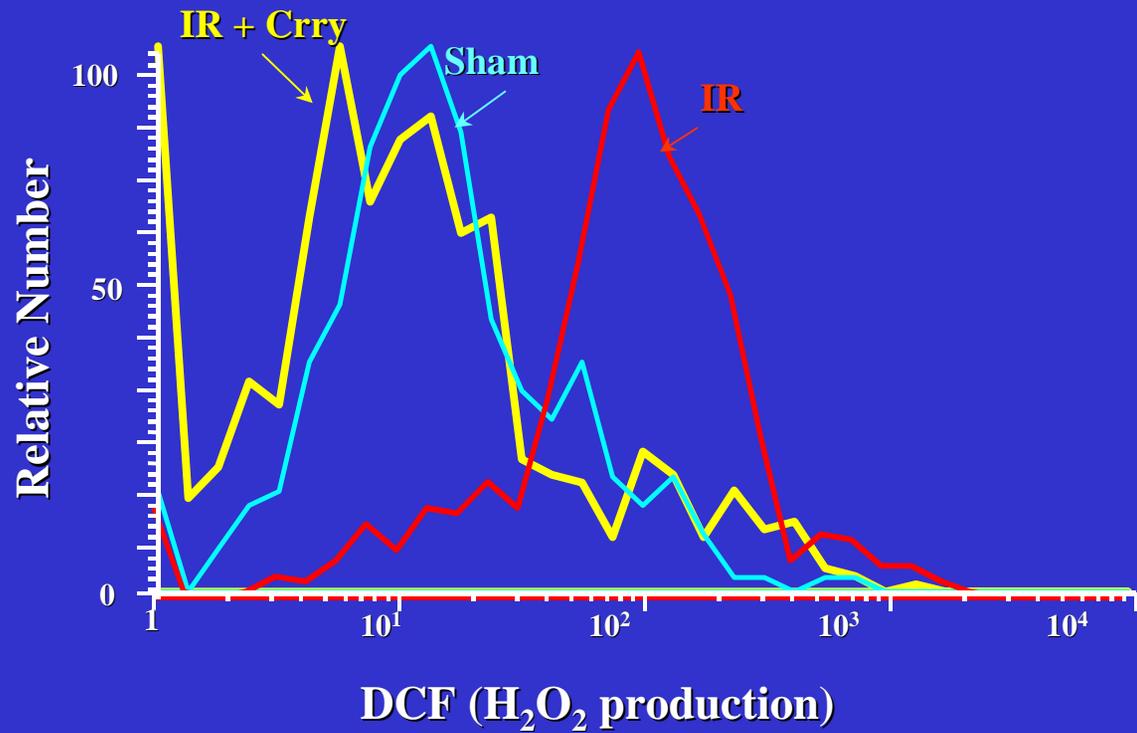


CVF

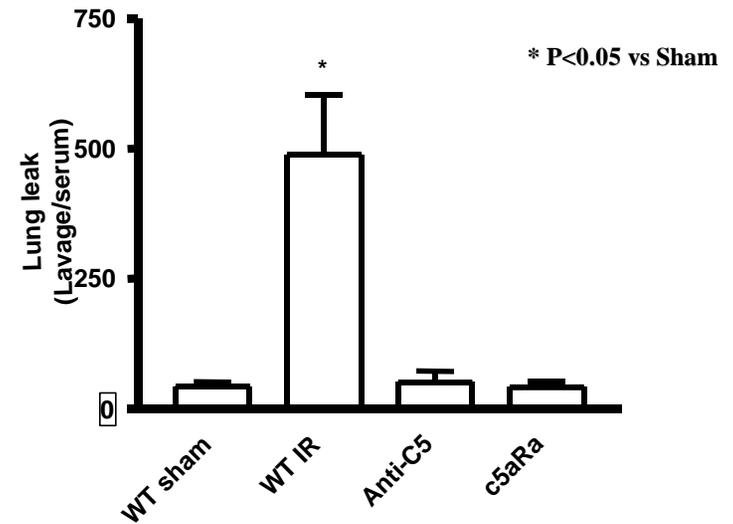
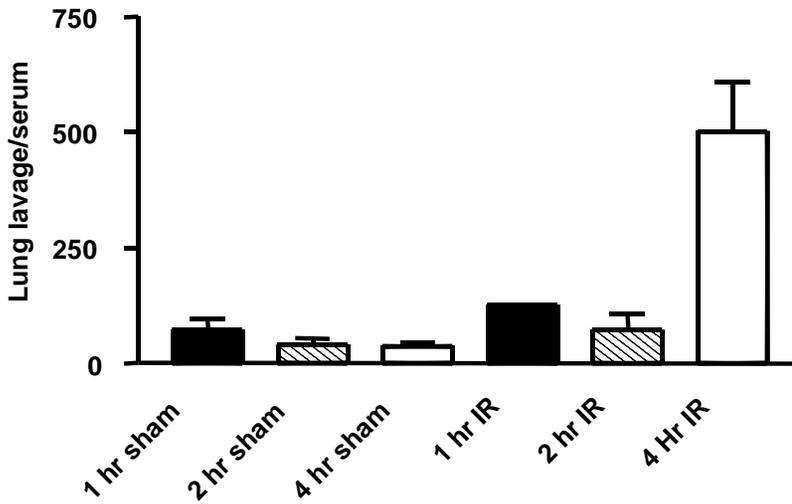


Complement activation results in PMN activation

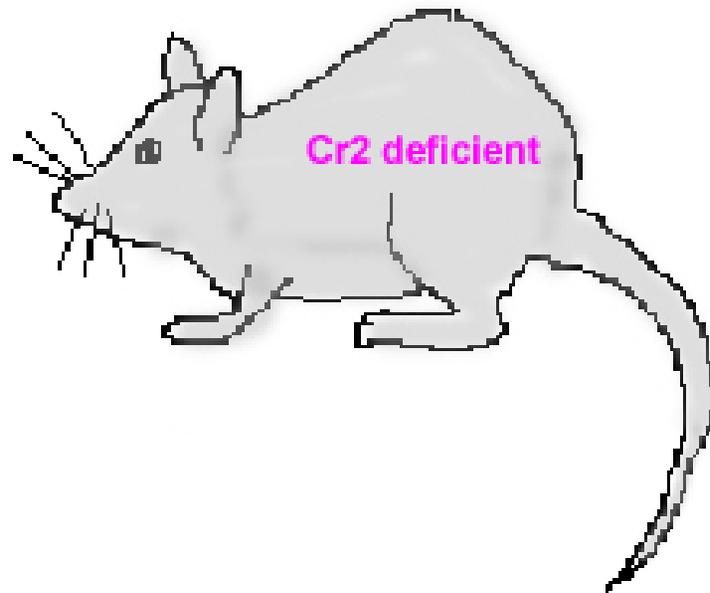
Crry Ig inhibits IR-induced PMN H₂O₂ generation



Lung damage occurs late and it can be prevented with complement activation inhibitors



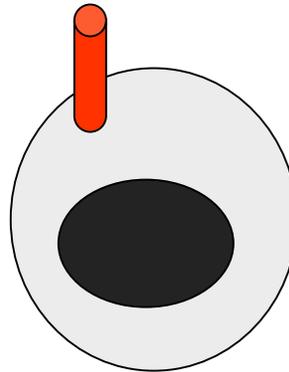
Complement receptor missing mouse



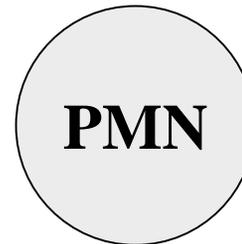
Misses certain
Natural antibodies



C5b-9



Effect of
C3a
C5a
C5b-9 (non-lytic)



Cytokines
Chemokines
other

Complement Inhibitors in Battlefield Injury (CIBI)

present and future

- **Complement activation is responsible for major part of battle-field tissue injury.**
- **Injectable products, available to the medic and/or soldier will become available.**
- **Action is expected to be prompt.**
- **Products will inhibit complement at targeted organ.**