detection and diagnosis and the treatment of those exposed with drugs that would be beneficial in all stages of disease. Monoclonal antibodies, preferably from human origin to prevent severe complications, which neutralize or block the pathological effects of biological agents, are the optimal candidates to be deployed in case of biological warfare or a bioterrorist event. Recent research has shown that a combination of monoclonal human antibodies against the protective antigen (PA) and lethal factor (LF) of the anthrax toxin even after application 48 hours after the infection is therapeutically effective. This new development offers a safe therapy that can start several days after bioterrorist victims are possibly infected with anthrax spores.

Study Design & Production Process: The human body is one of the better and most suitably equipped places for the generation of monoclonal antibodies that can be used effectively in humans for treatment. Such antibodies will be of optimal physiological specificity, affinity, and pharmacological properties. In addition, the chances of severe adverse effects and cross-reactivity with human tissues will be slim. Therefore, the human immune response has been used by the Dutch company IQ Therapeutics, a spin-off of the Groningen University and financially supported by the Dutch Armed Forces, as a basis for selecting the antibodies. People, immunized against or infected with the agent in question, donate blood cells voluntarily, which are used to generate fully human monoclonal antibodies.

The antibody-based part of the human immune response, which, by selection, is found in the blood of the donors is preserved by processing the antibody producing B lymphocytes according to a novel human adaptation of Köhler and Millstein's mouse hybridoma technology. The antibody producing genes are transferred to the human PER.C6 cell line (licence from Crucell), which produces up to 3.5 g/l therapeutic antibody; but the culture of this human cell line also can be done in an XD™ (eXtreme Density) process to get higher yields.

In this way, effective therapeutic class IgG1 antibodies, with an affinity typically better than 10-10 against the protective antigen (PA) and lethal factor (LF) toxin components of Bacillus anthracis are developed. Currently antibodies against orthopox viruses are generated as well from donors, which have been immunized with vaccinia. Other projects are the development of therapeutic antibodies for antibiotic-resistant *Staphylococcus aureus*, and *Enterococcus spp.*

Results: Both human antibodies against the anthrax toxin components are efficacious in vitro and in pre- and post-exposure settings in mice and rabbits (inhalation). The anti-LF IgG1 (k-light chain) antibody against domain 1 of the anthrax lethal antigen has been tested in a phase I clinical trial in Q3 of 2009. GMP-testing material already is available. The anti-PA antibody is in a pre-clinical stage, as are the other antibodies mentioned.

A remarkable result is that we have seen a strong synergistic effect in the treatment of anthrax infections when both anti-LF and anti-PA are used simultaneously. Studies have shown that a sub-optimal concentration of anti-PA can be supplemented with anti-LF to obtain 100% survival of the rabbits infected with a lethal dose of anthrax by inhalation.

The animal experiments indicated that with the use of dual (anti-LF and Anti-PA) antibodies, the window of treatment can be extended as well. While the onset of disease in the rabbit anthrax inhalation studies is in 25–29 hours, the lifesaving treatment of the animals with a normal dose has proven to be still effective when the treatment starts 32 hours after the lethal dose is given.

Conclusions: The Dutch company IQ Therapeutics has successfully generated and developed a fully human monoclonal antibody against the lethal factor of *Bacillus anthracis*. The same technology can be used to generate antibodies for passive immunization after (suspected) exposure to other biological threat agents. As such, antibodies are effective immediately after application, the scientists have termed them Instant Immunity™ antibodies. There is a strong synergetic effect of human antibodies directed against LF and PA epitopes of anthrax, which leads to higher therapy rate, lower dose, and wider window of treatment.

Keywords: anthrax; bioterrorism threat; monkey pox; MRSA; orthopox; smallpox; toxin
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Feasibility of Use of ROTEM to Manage the Coagulopathy of Military Trauma in a Deployed Setting

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Introduction: Hemostatic resuscitation; the rapid, proactive treatment of the coagulopathy associated with major trauma, is an accepted part of combat casualty care. Thromboelastography offers timely and convenient monitoring of the coagulation state when compared to standard laboratory tests; ROTEM® is one method to do this. This paper describes the evaluation of use of the ROTEM into a deployed setting, and how it has been used to optimize management of trauma patients.

Methods: Over a seven-week period from January to March 2009, ROTEM was used prospectively to gain information on trauma patients who underwent immediate transfusion when admitted to the Role2E facility. Analysis also was undertaken of admission physiology, injuries, blood product use, and outcome. In patients who underwent massive transfusion, further ROTEM were preformed to monitor product use.

Results: Thirty-one patients were tested with ROTEM; 20 were enrolled onto the massive transfusion protocol (MTP). 15% of the MTP group (3/20) had an abnormal PT/APTT on arrival, whereas 60% (12/20) had an abnormal initial ROTEM trace. In these patients, the initial average results were; temp = 34.8°C; pH = 7.24; Base excess = 6.42; and total blood product (units) use was 168 P RBC; 121 FFP; 13CRYO; 16PLT. Specific cases clearly demonstrated the machine's benefit in guiding management.

Conclusions: ROTEM can be used successfully in a deployed setting, and has shown its value in both monitoring and guiding patients who have a massive transfusion situation.

Keywords: coagulopathy; deployed setting; massive transfusion; ROTEM®; trauma
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