Improving access to life-saving medicines

Improving safety and availability of animal derived sera for therapeutic use

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Summary

• Deaths or disability resulting from rabies and envenomings can be avoided if sufficient supply of animal derived sera (antisera) of controlled and assessed quality was ensured, logistics and distribution improved and education on clinical use and management of the disease provided

• The shortage of antisera, a critical public health issue at global level

• Global strategy/action coordinated by WHO
The products: Animal derived hyperimmune sera

- Anti-venoms (e.g. snake, scorpions)
- Anti-rabies
- Anti-tetanus
- Anti-diphtheria
- Anti-botulism
Snake envenomings: A silent killer….

Antivenom Sera (IgS):
The only effective specific treatment
Envenomations: Figures for Africa*

*As a model for calculation of needs and worldwide concern
Treatment needs: Sub-Saharan Africa

• 50 to 75% of snake bites lead to an envenomation necessitating antivenom therapy: e.g. 500,000 cases/year

• Treatment needs only in Sub-Saharan Africa would be in the order of 2 000 000 doses

• 100% cost-effective treatment
  – 1 patient treated = 1 life saved or 1 severe sequelae avoided

Global demand would be 7 to 11 million vials per year
Envenomations: Health economics

- Currently large majority of envenomings are not treated adequately, leading to
  - Death: 20,000 / year
  - Harms vital sectors of a community: farmers & children
  - Children account for 20-40% of cases
  - Lifelong Sequelae: 5 – 10 % (?) out of 500,000 envenomings
  - Long hospitalization time: 2 or 3 fold more than treated patient

Significant Human and Social Impact and Cost
Coordinated approach

- Efficiency of snake bites/dog bites treatment campaign
  - Epidemiological data updated
  - Availability of antivenom-sera: large unmet needs
  - Quality of antivenom sera (efficacy, adapted to local species)
  - Adequate cold chain & supply system to remote areas
  - Health workers training: clinical management

- Financial support mechanisms to countries that cannot afford 100% of the treatment cost
WHO Proposals to support access to safe products

Development of a global strategy
PRODUCTION OF ANTIVENOM SERA:
Technology in the public domain (not protected by intellectual property)
The issues:

• Decreasing number of producers

• Fragility of production systems in developing world

• Poor regulatory control and need for clinical trials: antivenoms inappropriately marketed in countries

• Costly production: need for affordable antisera with acceptable safety & efficacy
Component 1: Global Quality Assurance Guidance

- Development of WHO Guidelines on the Production, Control and Regulation of animal plasma-derived antisera (encompassing e.g. control of starting materials and large-scale implementation of manufacturing steps critical to viral safety)

- Development of WHO Guidelines on GMP for the production, control and regulation of antisera

- Elaborated in parallel to, and as a result of, technical workshops
Component 2: Technical capacity - Workshops

- Target audience: local NRA and local manufacturers currently producing animal origin immunoglobulins
- Organized at regional/inter-regional level to facilitate networks
- Focus: Good Manufacturing practices of antisera (GMP inspectors)
  - Good animal husbandry practices
  - Collection practices of animal plasma
  - Characterization of venoms
  - Correct implementation of existing manufacturing steps possibly contributing to viral safety (e.g. caprylyc acid precipitation, low pH treatment), efficacy (e.g. IG specificity and activity) and absence of side reactions (e.g. anaphylactic reactions)
Safety issues:

- Potential risk of transmission of animal viruses to humans, (but no cases recorded)
  - Need to help identify dedicated VI/VR steps
  - Current manufacturing steps have VI/VR potentials but may not be considered as such by manufacturers (manufacturing practices must be adjusted)

- Regulatory controls in developing world are poor

VI: viral inactivation; VR: viral removal
Promote technological cooperation

- Transfer of technology
- Production arrangements
- Technical cooperation in specific issues (validation of viral inactivation steps, stability, preclinical and clinical testing)
Component 3: Pre-Qualification

- Establish pre-qualification system for antisera, as based on WHO systems, including:
  - Procedures for Expression of interest
  - WHO norms and standards
  - Documentation
  - Inspection procedures
  - Role of local NRAs
- Based on existing WHO experience in pre-qualification of other medicinal products
Component 4: Clinical management

- Development of guidance and training materials on the prevention, diagnosis and management of diseases treatable by antisera (esp. envenomations, rabies)
- Promote development of local epidemiological data
Component 5: Distribution logistics

• Foster/identify the collaboration of other International Organizations using already established channels & strategies to assure appropriate distribution, storage and use of immunoglobulins
Component 6: Financial support mechanisms

• Foster/identify the collaboration of other International Organizations to support financial mechanisms to countries that cannot afford 100% of the treatment cost
Expected benefits for public health at global level

• Increased availability of safe animal-derived sera
• Enhancement capacity of MRAs and manufacturers to ensure production of antisera of assured quality and safety
• Improved clinical management of rabies and envenomings contributing to optimal clinical use of antisera
• Access to effective treatment for those in need world wide