Prequalification of therapeutic sera: a neglected public health need

Outcomes of a WHO Consultative Meeting
“Rabies and envenomings: a neglected public health issue”
(held on 10 January 2007)
Rabies

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Rabies: the global burden of human suffering

Global annual totals:
dog bites 32 millions
human rabies deaths 60,000
Human rabies in India in 2005

• 16 million bites
• 20,000 deaths
• 4 million post-exposure prophylaxis courses

Knobel DL et al. Bull WHO 2005;83:360-8
Human rabies in China in 2006

- 2,600 deaths (30% more than 2005)
- ~ 8 million post-exposure prophylaxis courses
Rabies encephalitis: incurable but eminently preventable
Rabies: the solution
modern post-exposure prophylaxis

• Wound cleaning
• Rabies immune globulin
• Active Immunisation with rabies vaccine
Rabies immunoglobulin

- Proved essential (together with wound cleaning and vaccine) for prevention of rabies after severe exposure
- Recommended by all national/international authorities (WHO Recommended, CDC, HPA etc)

**BUT** unaffordable and unavailable in most developing countries
The deficiency: current use of rabies immune globulin (% of post-exposure courses)

- Africa: 1%
- Asia: 6%

- Overall in developing countries: used in <1% of post-exposure courses
Annual Global need for rabies immune globulin (post-exposure treatments) if international guidelines were to be fully implemented

- Africa: 600,000
- Americas: 350,000
- Eastern Mediterranean: 200,000
- West Pacific (including China): 9 millions
- SE Asia (including India): 3.2 millions

Total: >13 millions

**Estimated annual global requirement: 16 million vials**
Snake bite: the global burden of human suffering

Global annual totals:
- Bites: 5 millions
- Permanent sequelae: 252,000
- Deaths: 100,000

500,000 bites
12,000 sequelae
4,000 deaths

1 million bites
60,000 sequelae
>20,000 deaths

1.2 million bites
180,000 sequelae
>60,000 deaths

5,000 bites
250 deaths
Long term complications of snake bite

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Scorpion sting in Latin America (*Tityus serrulatus*)

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Snake bites and scorpion stings: the solution

Antivenom

- The only specific antidote
- Effective in saving lives and preventing permanent complications
The deficiency: the crisis in Africa

- very few producers of antivenom
- unaffordable prices
- inappropriate products on the market
- 2 million vials needed each year but only 20,000 vials available
Estimated global requirements for antivenoms

- Snake bites 9 million vials
- Scorpion stings 1 million vials
- + guidelines and training for appropriate use
Need for antisera

• ~65% of rabies post-exposure courses require rabies immune globulin
• 50 to 75% of snake bites and scorpion stings result in envenoming that demands antivenom treatment
• These treatments are highly cost-effective: 1 patient treated = 1 life saved or 1 permanent disability prevented
Global needs for animal derived antisera

- Rabies:
  annual global requirement: **16 million vials of RIG**
- Snake bite and scorpion stings
  annual global requirement: **10 million vials of antivenom**
Conclusions

Deaths and disabilities resulting from rabies and envenomings can be prevented by:

- **Production** of animal derived sera (antisera) of assured quality and quantity
- **Distribution** of antisera according to need
- **Training** of medical staff to use the antisera according to accepted guidelines

The current shortage of antisera is a critical global public health issue

Global strategy/action should be coordinated by WHO
Key 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
• Need for affordable antisera with acceptable safety and efficacy
The Meeting urges WHO to:

- Introduce a prequalification system to increase production of antisera
- Build technical capacity and skills of local regulatory authorities and manufacturers
- Improve clinical management of these neglected diseases through adequate distribution of antisera and improved clinical guidance
- Coordinate collaborations and partnerships
Why prequalification of antisera is essential

• Millions of people live under the threat of rabies or snake or scorpion envenoming.
• Effective treatment is established but antisera are usually unavailable in the countries where they are most needed
• Many antisera are of unacceptable quality due to weakness or absence of regulatory controls
• Antisera that are affordable and of acceptable safety and efficacy are urgently needed
Expected benefits from Prequalification

- Increased availability of safe and effective treatment
- Enhanced capacity of regulatory authorities and manufacturers to ensure production of antisera of assured quality and safety
- Strengthened local production in developing countries
- Improved clinical management of rabies and envenomings contributing to optimal clinical use of antisera
- Access to effective treatment for those in need worldwide