Plasma Medical and Healthcare Opportunities in the Developing World

David B. Graves

University of California, Berkeley

Third International Conference on Plasma Medicine

September 19-23 , 2010

Ambient Gas Plasma: A sustainable and viable tool for infection control in the developing world

Sustainable Products and Solutions Program
Blum Center for Developing Economies
at the University of California at Berkeley

Yuki Sakiyama, UCB
Matt Pavlovitch, UCB
Zhi Chen, UCB
Doug Clark, UCB
Lee Riley, UCB
Hiroshi Nikaido, UCB
Vivek Sharma, UCB
Santhi Hariprasad, UCB
"Missing postdoc" UCB

Greg Morfill, MPI
Mark Kushner, U Michigan
Greg Fridman, Drexel
Gary Friedman, Drexel
Others…

One Major Thrust for Plasma Medicine: Infection Control

- **Global factors promoting spread of infectious disease**
- **Hospital-acquired infections**
- **Growing challenge of antimicrobial resistance**

Special challenges of infection control in the developing world.

Opportunity for plasma technology to have significant impact:

CHEAP, SIMPLE, EFFECTIVE

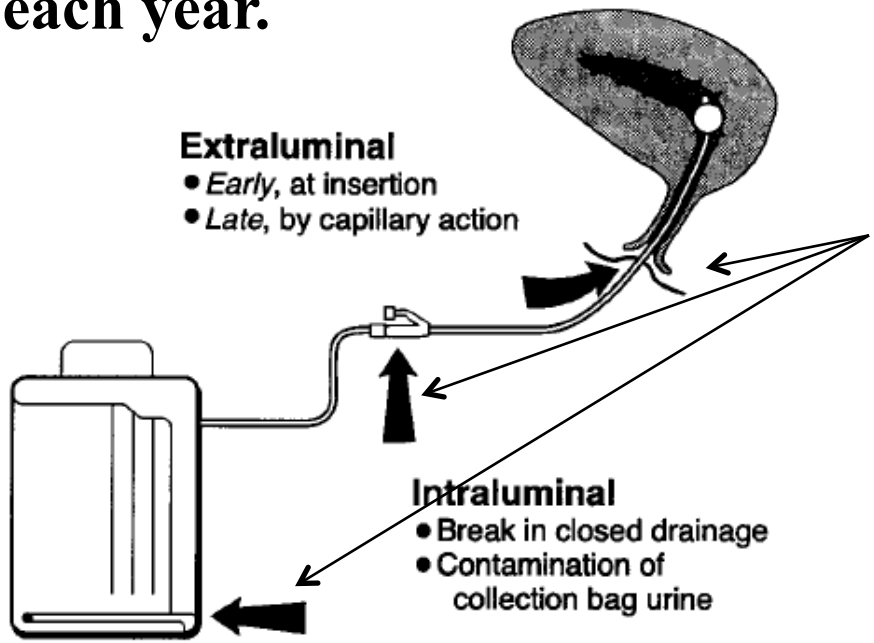
Global Factors Promoting Spread of Infectious Disease

- **globalization: rapid movement of people, food, microbes**
- **explosive population growth, rise of large cities, coupled with poverty, urban migration and limited public health facilities**
- **intensive/concentrated livestock industry**
- **global climate change disrupting ecosystems**
- **antimicrobial resistance: inexorable rise in number of resistant microbes limits use of traditional infection control (e.g. antibiotics)**
- **emerging threat of bioterrorism**

Major Problem: Hospital-Acquired Infections: HAI, or 'Nosocomial' Infections

2002 in US: 1.7 million HAIs & 99,000 deaths

***Catheter-associated urinary tract infections*. CAUTI is a common nosocomial infection, with an estimated 1 million cases in the US each year.**



Routes of entry of pathogens to catheterized urinary tract

Maki, et al, 2001

Major Problem: Hospital-Acquired Infections: HAI, or 'Nosocomial' Infections

2002 in US: 1.7 million HAIs & 99,000 deaths

***Catheter-related bloodstream infections*. CRBSI occurs about 250,000 times per year in US hospitals.**

***Surgical site infections*. This accounts for a significant number of HAIs.**

***Ventilator-associated pneumonia* (VAP). VAP is thought to occur on up to 25% of all people who are on mechanical ventilation for at least 48 hours. Of these, morbidity rates are among the highest of all forms of HAI.**

Infectious Disease Control: Context of Emerging Antimicrobial Resistance (WHO, 2002)

- **Since 1940's, antibiotics substantially reduced threat of infectious diseases.**

- **They have also contributed to the major gains in life expectancy experienced during the latter part of the 20th century.**

Infectious Disease Control: Context of Emerging Antimicrobial Resistance (WHO, 2002)

- **This progress is threatened by emergence and spread of microbes that are resistant to cheap and effective first-choice, or "first-line" drugs.**

- **Microbial resistance is most evident for: diarrheal diseases, respiratory tract infections, meningitis, sexually transmitted infections, and hospital-acquired infections.**

Infectious Disease Control: Context of Emerging Antimicrobial Resistance (WHO, 2002)

- **Resistance to first-line antimicrobials requires treatment with second- or third-line drugs: much more expensive and sometimes more toxic as well**

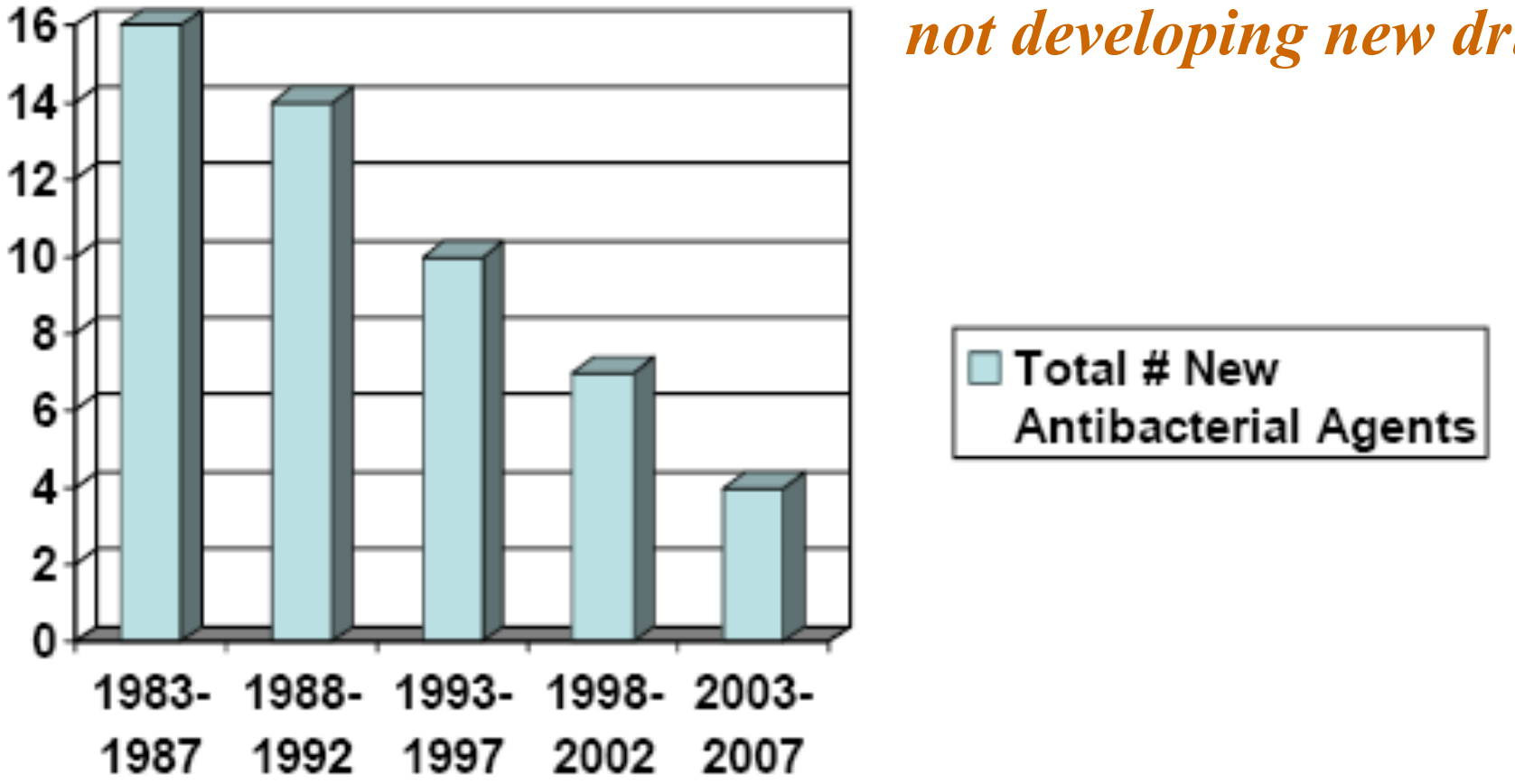
- **e.g., drugs needed to treat multidrug-resistant forms of tuberculosis are over 100 times more expensive than the first-line drugs used to treat non-resistant forms.**

Infectious Disease Control: Context of Emerging Antimicrobial Resistance (WHO, 2002)

- **In some diseases, resistance is developing for virtually all currently available drugs: *a post-antibiotic era may be coming!***

But modern medicine *relies on invasive procedures*, and antimicrobials are essential in current practice to avoid subsequent, often inevitable infections

Total Approved Antibacterials: US



Pharmaceutical companies not developing new drugs!

Spellberg, et. al., *CID* May 1 2004, Modified

Elements of *Plasma-Assisted Infection Control*

1. Plasma used to sterilize/disinfect environment

- **air and/or aerosol-based microbes**
- **water-based microbes**
- **microbes on objects/surfaces ('fomites')**

2. Plasma used to sterilize/disinfect in/on devices

- **medical device surface (e.g. surgical)**
- **catheter extra-luminal or intra-luminal (e.g. vs. biofilm)**
- **implant device sterilization**

3. Plasma on skin/wounds/burns or during invasive procedure

- **hand hygiene; pre-/post-invasive procedure**
- **coupled with immune system/wound repair**
- ***key role of reactive oxygen/nitrogen species ROS/RNS***

Special Challenges of HAIs in LRCs

L. Raca, J. Hospital Infec, 2009; V. Rosenthal et al., AJIC, 2008

- **12 million ID deaths occur globally: 95% in LRCs**
- **Infection rates in LRC hospitals ~ 3-5 times higher than in industrialized countries**
- **HAIs in 5-10% of admissions to acute care hospitals in industrialized countries, but in >40% of hospitalizations in developing countries in Asia, Latin America and Africa.**
- **In ICUs of LRCs: 66% of admitted patients develop a HAI; ~ 25% of admitted patients in ICUs in industrialized countries develop HAI (w/25% mortality)**
- **VAP mortality rates ~ 16% to 94% in LRCs**

Special Challenges of HAIs in LRCs

L. Raca, J. Hospital Infec, 2009; V. Rosenthal et al., AJIC, 2008

-Neonate mortality rates in LRCs 3-20 times higher than in developed countries

-Estimated rates of re-used needles/syringes~ 2% - 70%

-Hepatitis B, C and HIV transmission rates increase significantly

-Lack of supplies, overcrowding, understaffing all challenge LRCs

-Patients in LRCs sometimes share beds and supplies

- Antibacterial resistance even bigger problem in LRCs than in industrialized countries

"Poverty and infection in the developing world: Healthcare-related infections and infection control in the tropics"

P. Shears, J. Hospital Infec, 2007

- **Poor building infrastructure**

- **Inadequate water supply**

- **Electricity for a few hours/day**

- **Patients lying on floors**

- **No resources for cleaning environment, beds or equipment**

- **Absence of soap**

Special Challenges of HAIs in LRCs

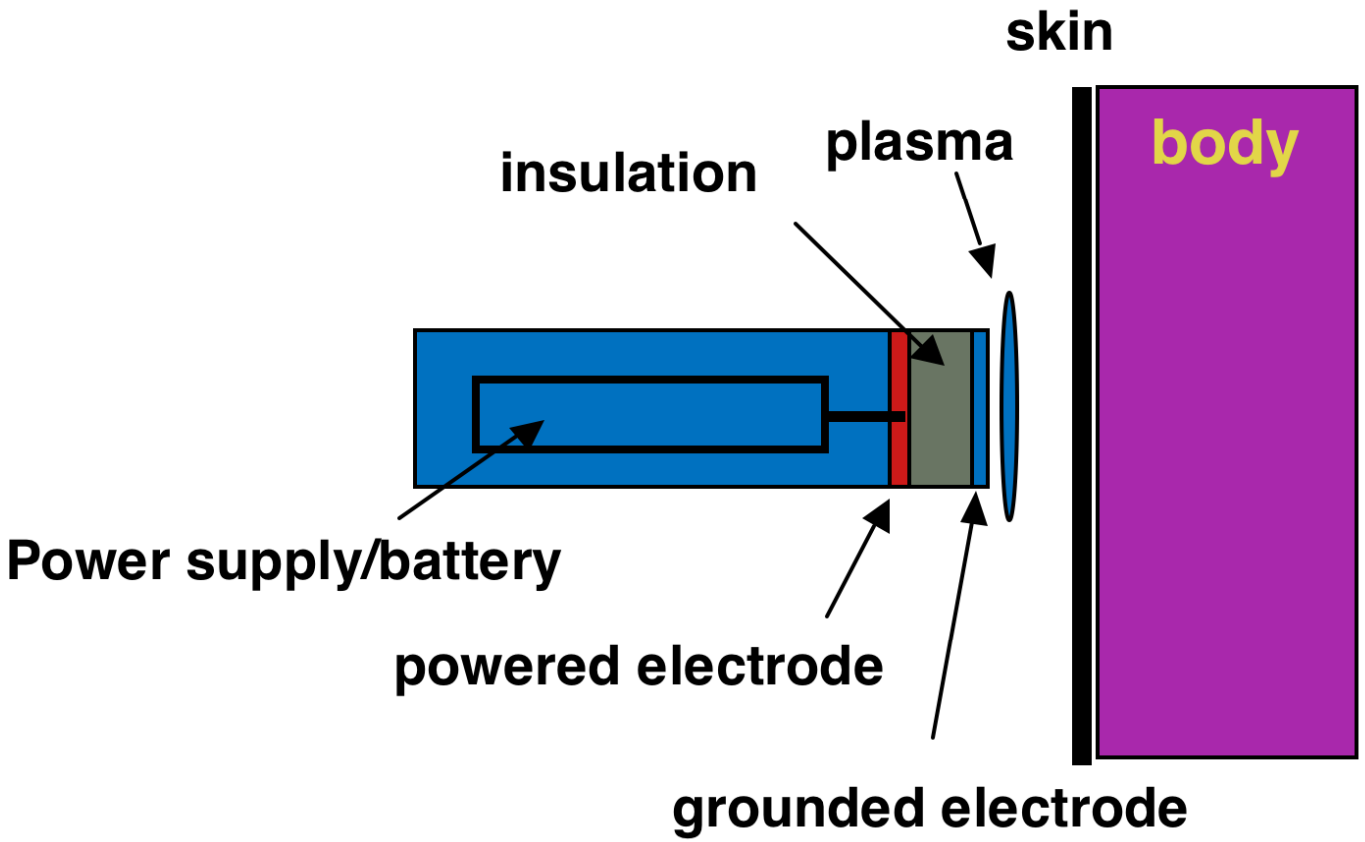
L. Raca, J. Hospital Infec, 2009

Table I Overall healthcare-acquired infection (HCAI) rates in facilities from developing countries[5]

Country	Type of study/ unit	HCAI rate (%)	Year	Author
Argentina	Multicentre adult ICU	27.0	2003	Rosenthal
Brazil	Multicentre adult ICU	29.6	2006	Salomao
India	Multicentre adult ICU	12.3	2005	Mehta
Mexico	Multicentre adult ICU	24.4	2006	Ramirez
Saudi Arabia	Newborn ICU	35.8	2002	Al-Ghamdi
Tanzania	Adult medical ICU	40.0	2003	Gosling
Kosova	Adult ICU	68.7	2006	Spahija
Turkey	Neurology ICU	88.9	2005	Cevik

ICU, intensive care unit.

Plasma Device Proposed: Handheld Air DBD



Advantages of Plasma-Based Devices for LRCs?

Devices are inexpensive, simple to employ, and use little electricity.

Obvious applications include catheter/surgical site incision wound disinfection/sterilization/antisepsis, including dental care;

- wound *healing* and other uses a bonus

Device manufacture/repair in LRCs appear feasible.

Also, advantages in emergencies or natural disasters where secondary infection control is difficult due to lack of supplies

Air Plasma for Catheter/SS Wound Antisepsis in LRCs

Antisepsis (cleaning skin) needed for catheter insertion and surgical site preparation, among others.

Conventional supplies: alcohol, povidone-iodine, chlorhexidine.

Likely advantages of plasma?

- **speed of antisepsis**
- **cost**
- **no need for stored supplies; need 'only' electricity**

Air Plasma for Antisepsis: Speed

Morfill et al (2009) report 2-5 sec exposure leads to 10^5 bacterial reduction *in vitro*; indirect plasma ('HandPlaster').

Fridman et al (2009) report similar high rates with direct plasma FE-DBD.

(with minimal or no short-term skin damage.)

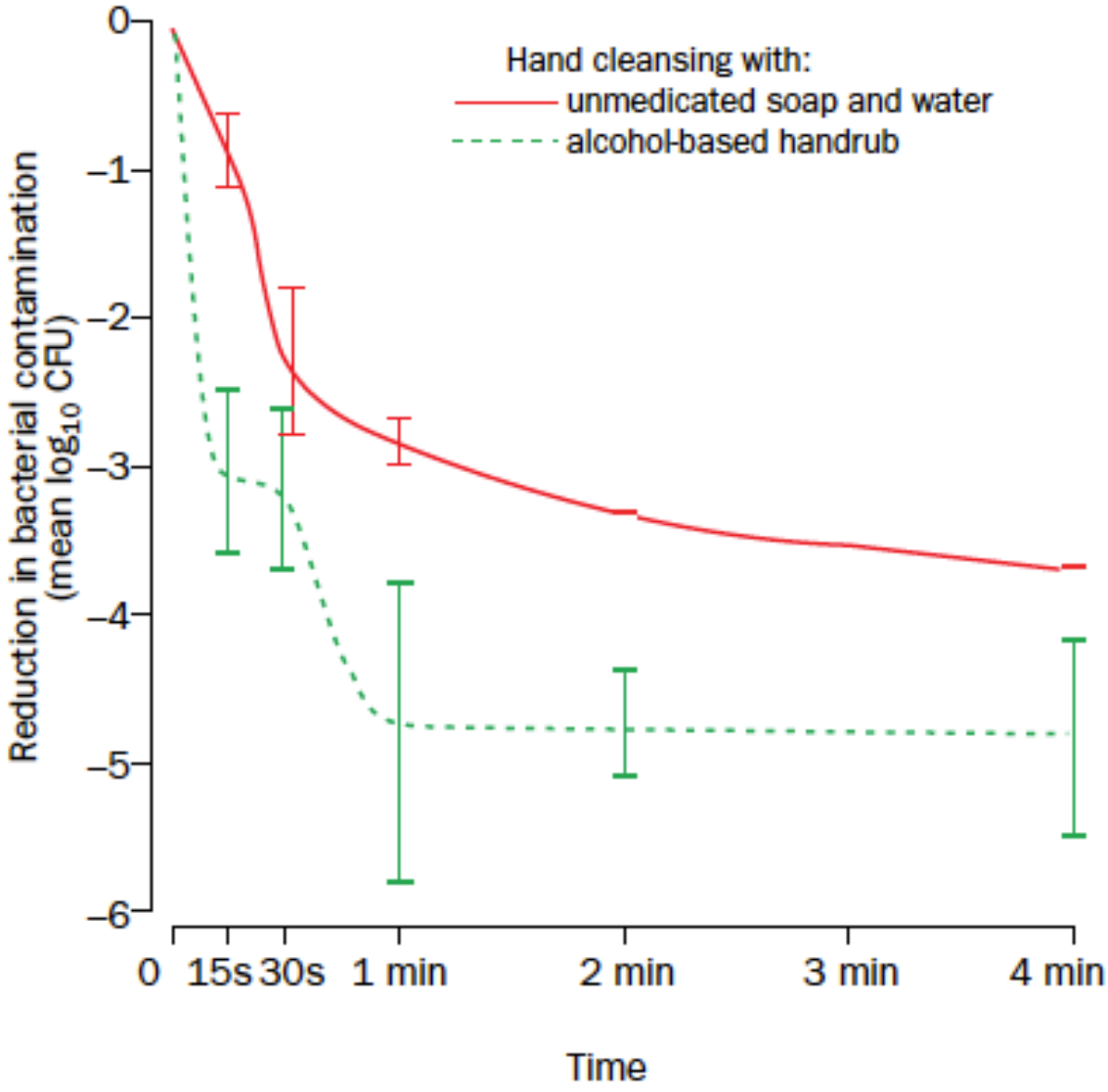
But…

a. **How do these results translate into *skin antisepsis*?**
a. **How does this compare to *conventional skin antisepsis*?**

Maybe the proper question is:
How well does the plasma protect against catheter and surgical site infections?

Conventional Antisepsis: Hand Cleaning

Pittet and Boyse, The Lancet,: Infectious Disease, 2001



Conventional Skin Antisepsis, II

M. Reichel et al, Antimicrobial Agents and Chemotherapy (2009)

- Wiping skin with swab (3 times), 89.5% alcohol/ water.

- Reductions on forehead: best results from n-propanol.

- Swab-tested reductions:

~ $10^{1.8}$ (2 min); ~ $10^{2.1}$ (3 min); ~ $10^{2.4}$ (4 min)

Conventional Skin Antisepsis: Cost

In developed world, chlorhexidine for skin antisepsis:

~ $1 per catheter site preparation
~ $10 per surgical site preparation

In developing world, costs appear much lower:

~ $0.03/application for pre-delivery vaginal antisepsis/baby cleaning (Egypt, 2005)

Advantages of Plasma-Based Devices for LRCs?

1. **Speed of operation may be advantage for plasma**
   - ***must be proven to reduce infections under realistic conditions***

2. **Cost will depend on device manufacture/operating cost**

But real advantage may come thanks to freedom from need for supplies (except electricity and air)….

…as suggested by Rick Satava yesterday!

Challenges for Plasma-Based Device Economics?

1. **Battery-powered (re-chargeable) device economics improves with more efficient power supply (replace batteries less often)**

2. **How to deal with regulatory issues? FDA or …?**

3. **How to promote technology and train medical personnel to use it?**

4. **How to establish *LOCAL* manufacturing and repair capability?**

Concluding Remarks

-Infectious disease remains a major worldwide threat and various factors suggest it will grow with time

- Hospital-acquired infections are particularly dangerous with rise in antimicrobial resistance with few new antimicrobials being developed

- Suggest need *for new field of infection control science and engineering* – including plasma-assisted technologies, perhaps analogous to other plasma-related fields such as semiconductor processing that have used plasma–assisted technologies

Plasma Healthcare Developing Countries, **Concluding Remarks**

1. **Obvious and pressing needs for infection control and other healthcare applications of plasmas in dev. world (LRC);**

2. **It appears that plasma biomedical devices and procedures are suited to the challenges, constraints and opportunities in LRCs. *Power supply design a current pressing need!***

3. ***Int. Society for Plasma Medicine*** **may want to consider initiating special efforts to involve technical and medical organizations and individuals from LRCs.**