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care equipments or iSTAT for Glucose, BUN, Bilirubin, lactate and Blood gas analysis. Disposable Digital oxymeters can be used for early detection of hypoxia at affordable price.

Another milestone is the recent evidence of Artesunate as superior to quinine for better survival rate (AQUAMAT and SEAQUAMAT study)

Use of blood transfusion has not yet been studied conclusively, but recent reports indicate that Erythropoiesis has a promising possibility. Use of albumin has not been established. Bolus fluid therapy was shown to be deleterious.

We conducted a study on use of anti-oedema measure (mannitol in cerebral malaria) and the results strongly contraindicated its use.

Similarly caution should be taken in using Enteral therapy in comatose patients and frequent use of Central venous catheters.

The mortality can be influenced by early Renal replacement therapy. Use of recent biomarkers to detect Acute Kidney Injury early for intervention may hold the key in coming years. (viz. NGAL etc)

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#### **Type: Invited Presentation**

Final Abstract Number: 26.001

Session: *Initiatives for the Control of Infectious Diseases*

Date: Friday, June 15, 2012

Time: 15:45-17:45

Room: Lotus 1-4

#### **Novel resources to fund health enterprises and develop new drugs**

F. Waldvogel

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Development of novel drug entities and their adequate distribution to patients in diverse social and geographical settings are amongst the formidable challenges to science, industry, governmental agencies and health organizations. Both processes are extremely complex, characterized by many hurdles and poor efficiency, due to lack of human motivation of administrative collaboration and of financial resources. This presentation will focus primarily on a better distribution and usage of the presently available financial resources.

Drug development is a process which flows from preclinical research (target identification, toxicity, pharmacokinetics) to phase 1-3 clinical testing (dose finding, proof of concept and pivotal trials), and finally to acceptance by the regulatory authorities. From 10'000 initial compounds, only 10 will lead to clinical trials and about 2 will eventually reach the market. The costs of such a process are considerable, in the range of 800 M US\$ in out-of-pocket expenses and require new modes of risk mitigation. Between 2006 and 2010, 10 large corporate and 10 large traditional venture funds have led this enterprise, totalling more than 700 deals, within a multi billion US\$ European and US market. The investment strategy, results and perspectives of one of the top funds, the Novartis Venture Funds, will be presented and discussed.

At the other end of the pipeline, novel or standard products have to reach the communities whether affluent or in financial need. Their distribution and the organization of adequate health policies for the poor in developing countries represent another, still largely unmet world challenge. It entails helping those with no or low income to have access to loans and to appropriate financial services and from there to adequate health care systems The microfinance movement, created in 1970 by Yunus in Bangladesh and which has

expanded rapidly worldwide, is one of the promising financial and economic strategies to meet this goal. There are presently 25 billion US\$ at work in the microfinance movement, for an estimated 250 billion US\$ potential. Principles, boundaries criticisms and outlook of this new financial system will be presented, taking Symbiotics Inc. – one of the large institutions providing such services – as an example.

Adequate utilization of the presently available resources – whether by financing innovation or providing acceptable services to the poor – should allow with time a better access of everyone to human health needs.

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#### **Clinical research in the context of rapidly emerging public health threats**

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A key lesson from a series of recent outbreaks of emerging pathogens of global public health importance including SARS-CoV, highly pathogenic avian influenza A (H5N1) virus, Nipah virus and the 2009 H1N1 virus pandemic was that mounting clinical research in response to a rapidly emerging infectious disease is extremely challenging and often delayed. During these events, important pathogenesis and clinical management data came mostly from sites that were already undertaking related clinical studies including those on inter-pandemic influenza (e.g., SEAICRN, Institute Pasteur Networks, Chinese University of Hong Kong, and University of Hong Kong) or from established national or regional research networks such as the Canadian and Australia/New Zealand Critical Care Trials Group. However there was very little cross-border coordination, unlike that which now exists in epidemiology and to an extent in virology and genomics. The clinical research response was cumbersome and slow despite years of global preparations for a potentially devastating influenza pandemic of avian origin or the next SARS-like outbreak. Although observational registries were mobilized, initiatives to launch randomized controlled trials or more sophisticated biologic studies generally missed the initial waves of the 2009 H1N1 pandemic and in many cases failed to enrol sufficient numbers of patients across the entire clinical spectrum of disease into studies, even during subsequent waves. During the 2009 H1N1 virus pandemic the efforts to prepare for a respiratory disease outbreak allowed a reasonably rapid and coordinated response on epidemiologic and diagnostic aspects of disease but failed in the timely conduct of clinical research aimed at improving patient management or understanding pathogenesis. The failure to have coordinated, comparable data on clinical management and pathogenesis of 2009 H1N1 virus infection meant that we missed the opportunity to improve patient outcomes. Indeed this has been a problem in almost all epidemics over the last decade (Nipah, SARS, H5N1, and in outbreaks of VHF) with very little research aimed at improving clinical management or understanding pathogenesis. This has demonstrated that unless something is done now to change the barriers faced in 2009, the next influenza (or other) outbreak will result in a similar missed

opportunity to save lives. Furthermore, no integrated analyses exist of combined microbiological/virological, immunological, clinical, epidemiological, and genetic data for comprehensive assessment of host-emerging pathogen interactions that can inform prevention and control activities, and guide clinical management. There is an urgent need to establish a sustainable consortium of clinical research groups with broad geographic coverage (including low resource settings), cross-border coordination, commitment to open access, and capacity to conduct complementary high-quality, hospital-based pathogenesis and clinical management studies and the flexibility to respond immediately to rapidly emergent threats. We need a new paradigm for clinical research in the context of rapidly emerging public health threats and one appropriate to the sorts of challenges we will face in the 21st Century.

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#### Infectious diseases surveillance and alert systems

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Prompt detection of infectious disease outbreaks is required to ensure timely responses that reduce morbidity and mortality, and mitigate social and economic disruption. Traditional public health surveillance systems rely on hierarchical structures where providers, laboratories and healthcare institutions report defined diseases to local authorities. Local authorities in turn report to regional authorities that report to national officials, who then report to international bodies such as WHO. While this system has many strengths, it is expensive and has critical weaknesses as well e.g., slow reporting, inevitable breaks in the chain of communication, disincentives to report, and failure to report undefined or unrecognized illnesses. The past twenty years has seen enormous innovation in nontraditional public health reporting systems. ProMED was perhaps the first system to exploit the Internet to allow nontraditional sources of health information such as media, firsthand clinician and lay observer reports to be widely disseminated and serve as early warnings of outbreaks, thus encouraging transparency in detection and reporting of emerging disease and other biohazardous threats. It has enhanced reporting in underserved areas through the development of regional programs such as PRO/MBDS in Southeast Asia. The growing "firehose" of data that can be mined for public health purposes has led to a number of novel strategies for harnessing this information. GPHIN and HealthMap utilize web crawling, coupled with human data curation, to rapidly report disease events. Other biosurveillance systems include Medisys and BioCaster. Deidentified search engine queries from Google and Yahoo, the so-called "searchstream," have been used to monitor community levels of influenza and dengue. The contents of Twitter messages and other social media content can be geolocated, monitored, analyzed, and interpreted to show trends in outbreaks and public sentiment regarding vaccination and other public health interventions. Cell phone usage patterns can detect unusual events such as disease outbreaks and can track patterns of movements and migration. Cell phones themselves, now nearly ubiquitous, have become tools for rapid reporting of health events.

The revised International Health Regulations, enacted in 2005 and adopted in 2007 have codified the use of informal information sources and promote the rapid and transparent flow of public health data.

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#### Delivering HIV treatment & care in resource limited settings - Therapeutic mobile units

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A weak state health infrastructure and a disparate system of rural clinics render the delivering of treatment and care of HIV/AIDS patients in sub-Saharan Africa extremely difficult. Furthermore, because patients living in remote areas do not have access to lab facilities, we developed a decentralized strategy based on bringing the needed services closer to the people, through the use of Therapeutic Mobile Units (TMU) as potentially useful means to follow up adults and children undergoing antiretroviral treatment.

Using the TMU of the National Public Health Laboratory of the Cameroon Ministry of Health, we conducted several cross-sectional surveys on epidemiological, biological and clinical features of HIV/AIDS in young and elderly patients in Cameroon. The screening of HIV-specific antibodies was carried out using rapid tests. Indeterminate or positive samples were immediately retested. People diagnosed as HIV-infected were provided free biological monitoring and referred to health care centres. The TMU was also equipped with the Auto40 cytometer for CD4 determination. A FACSCalibur cytometer was used as reference method.

From April 2005 to July 2011, 120 campaigns were organised in Cameroon (average of 277 volunteers tested per day). Out of 32,970 volunteers who received a pre-test counselling, 32,869 (20,937 males; 11,932 females) tested for HIV (acceptance rate of 99.69%). Their average age was 31 years. Amongst those, 32,569 (99.08%) received post-test counselling. The overall HIV prevalence was 6.06% [with higher rates in women, data not shown]. CD4 testing was performed using the Auto40 cytometer and gave a perfect correlation with the reference method (FACSCalibur) [mean±SD CD4 T cell count was 1041±317 cells/ml by Auto40, and 1032±294 cells/ml by FACSCalibur; r2=0.982]. For patients receiving ART, our medical staff provided support in monitoring treatment, recording information about patient's medical status, resolving the barriers to drug adherence and others factors that may affect a patient ART therapy (data not shown).