GLOBAL HEALTH SECURITY

EPIDEMIC ALERT & RESPONSE

WHO Scientific Research Advisory Committee on Severe Acute Respiratory Syndrome (SARS)

Report of the first meeting

Geneva, Switzerland
20-21 October 2003

World Health Organization

Department of Communicable Disease Surveillance and Response

WHO/CDS/CSR/GAR/2004.16

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Ackowledgement

The World Health Organization (WHO) wishes to ackowledge the important support given by Dr Douglas Lush in to the organization of this meeting and the preparation of this report

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Summary

The WHO Scientific Research Advisory Committee (SRAC) on Severe Acute Respiratory Syndrome (SARS) reviewed the existing state of knowledge on SARS as a disease and its etiological agent, the SARS coronavirus (SARS-CoV). Many gaps in the knowledge of the disease and its etiological agent were discussed and agreed over a day and a half of discussions, and a priority list of research topics and recommendations were developed to address key global research questions of public health importance. These have been listed, and will now be widely disseminated to international and national funding bodies to assist them in making decisions with respect to calls for research proposals and prioritizing research grant applications.

Background

The emergence of SARS is a major global public health threat that requires a coordinated global response in terms of continued and improved surveillance and of research into a number of important public health issues. While much has been learnt about SARS since it was brought to international attention in March 2003, there remain many unanswered questions about where it came from, how it spreads, and the effectiveness of public health and other measures employed to control the disease. Thus a major research effort to address these issues and other gaps in our knowledge could provide information to reduce the likelihood of recurrence and spread, lessen the vulnerability of health care systems to SARS, and mitigate the impact on individuals and communities. It could also improve the efficiency and effectiveness of control measures, and in the longer term, potentially impact on our response to future emerging diseases and nosocomial infections. There are also important cross cutting issues that underpin strategic research on SARS.

The importance of a concerted approach to public health research, and the need to determine a priority list of the most important immediate issues which should be addressed, was one of the major outcomes of the WHO Global Conference on SARS held in Kuala Lumpur, Malaysia, in June 2003. The conference participants recommended that a scientific task force be convened to discuss the various public health research needs, and that a priority list of research issues or questions be determined. This list should be made available to the international funding agencies to help guide their selection of possible future research projects.

Thus WHO established a SARS Research Advisory Committee with the following terms of reference:

1. To review the current knowledge of clinical, epidemiological and virological aspects of SARS with respect to public health imperatives.

2. To determine the information required for effective public health management of SARS, including the preparedness and response to further outbreaks.

3. To determine the gaps between 1 and 2.

4. To develop a list of the major research issues which are required to reduce the likelihood of recurrence and spread of SARS, to increase our public health capacity and capability to respond to SARS, and to mitigate the impact on individuals and communities of future outbreaks of SARS.

Participants were individuals with experience and knowledge of the science, impact and control of SARS. Committee members included a number of leading international experts in the fields of public health, communicable disease epidemiology, mathematical modelling, clinical and animal virology, risk communication, psychology, economics, infection control, and international health.

Introduction

Dr Anarfi Asamoa-Baah, Assistant Director General, Communicable Diseases, WHO, Geneva, welcomed participants to the meeting. He noted that SARS had brought to the world's attention some of the frightening aspects of globalization as well as some of the more positive aspects. SARS has shown that it is possible to contain a new disease with traditional public health methods and this provides support and hope. While WHO had received increased visibility through its work in the area, he credited much of the success to experts in different fields, many of whom were on the committee.

Professor John Mackenzie welcomed participants and called for nominations for the Chair. Professor Aileen Plant nominated Professor Angus Nicoll as the chairman and this was accepted.

Professor Nicoll outlined the tasks for the two-day meeting. He noted the huge strides in knowledge that had been made since SARS had emerged less than one year ago. He then called on members of the committee and the WHO secretariat to update the committee on research and development needs within differing fields of SARS.

Presentations on the current state of knowledge

Nineteen topics were selected for presentation and discussion according to their significance in the public health management of SARS. The presentations were given on the first day of the meeting, Monday 20 October 2003. Participants provided concise reports on the current state of knowledge in their particular areas of expertise, and gave an assessment of the research priorities which needed to be addressed in the future. The presentations provided an excellent evidence-based introduction to the subsequent discussions within the specific focus groups which were held on Tuesday 21 October.

Focus group discussions

The focus group discussions enabled breakout groups to discuss their topics in detail, and allowed the questions raised by the previous day's speakers to be further defined, and new questions to be developed and prioritized. The topics of the focus groups were:

1. SARS epidemiology, reducing vulnerability and interrupting transmission.
2. Laboratory methods including test standardization.
3. Animal studies on the origins of SARS-CoV and the risk of ongoing interspecies transmission.
4. Clinical issues including preventing transmission in health care settings, protecting staff and ensuring optimum outcomes in patients with SARS.
5. The social and economic impact of SARS and risk communication.
6. The public health management of SARS.

Discussion within the focus groups ranged widely, and a large number of research areas and issues that needed to be addressed were generated. The meeting had planned to prioritize these issues, but time restriction eventually made this impossible. Thus further work in developing the list of research priorities was carried out by several rounds of email correspondence. The list was also gradually coalesced as certain similar issues were combined and redeveloped.

The final list agreed to by participants has much greater breadth than the original list of individual research topics generated by the focus groups, and demonstrates the need to undertake broad-based, interdisciplinary approaches as well as the more specific research topics. The final list of research areas and their priority is shown in Annex 2.

The list will be circulated widely to international and national funding agencies to assist them in their deliberations and decision-making when prioritizing SARS research grant applications for funding, and to engender possible calls for directed research funding by these agencies.

Annex 1 - Presentations on the current state of knowledge

A. Biology, epidemiology and surveillance

? Coronavirus biology: lessons from animal coronaviruses	Dr Linda Saif
? Epidemiology	Dr Angela Merianos
? Disease modelling	Professor Roy Anderson
? Surveillance	Dr Thomas Grein

B. Animal reservoirs and environmental sources

? Wildlife reservoirs	Dr Pierre Formenty
? Environmental sources	Dr Jamie Bartram
? Animal models	Professor Albert Osterhaus

C. Laboratory diagnosis

? Progression of disease	Professor Malik Peiris
? Genomic diagnostics	Dr Christian Drosten
? Serology	Dr Wilina Lim

D. Clinical issues

? Clinical issues, including blood safety and treatment	Dr Simon Mardel
? Infection control	Dr Julia Garner
? Differential diagnosis	Professor Joseph Sung

E. Social and economic impact

? Risk communication	Dr Peter Sandman
? Economic consequences	Dr Emma Xiaoqin Fan
? The social response to SARS	Dr Fanny Cheung

F. Interrupting transmission

? Practical and public health management of outbreaks	Professor Aileen Plant
? Travel and quarantine related measures	Dr David Bell

G. Evidence and research priorities

? Assessment and comments on evidence base for SARS research	Dr Vittorio Demichelo

Annex 2

Priority issues for research (not in any specific order)

Epidemiology, reducing vulnerability and interrupting transmission

- What are the risk factors for SARS-CoV transmission?
- What are the most effective interventions in controlling SARS in health care/other facilities and in the community locally and internationally, in terms of cases detected, cases prevented, costs, and addressing public concerns?
- What is the attributable reduction in the risk of SARS transmission of the various interventions (see below) and how does their efficacy change during the course of an outbreak?
- What is the relative importance of super-spreading events, atypical SARS cases, mild disease in adults, paediatric cases and asymptomatic infections in spreading SARS and does their importance change as an outbreak evolves?
- What are the determinants of infection control behaviour, how can infection control practice be best monitored and how can infection control training be improved for sustainable behaviour change in health care workers?
- What are the safest, cost-effective respiratory protection strategies in different settings?
- What is the minimum level of preparedness required by all countries to reduce their vulnerability to SARS and other emerging infectious diseases and reduce the impact of outbreaks?

Interventions

- Heightening infection control in hospitals and other high-risk situations
- Case finding and early isolation of symptomatic individuals
- Restricting patient and staff movement
- Hospital staff screening
- Education of health care workers
- Quarantine of persons exposed to SARS-CoV
- Education of the public
- Entry and exit screening
- Education of travellers
- Restricting social gatherings
- Closing schools

Laboratory research

- How should we evaluate and standardize current and future diagnostic tests for SARS?
- How can serological tests be improved with respect to specificity and sensitivity?
- What is the nature of cross-reactions between the different coronaviruses?
- What is the importance of virus strain variation in developing diagnostic tests?
- What new technologies can be applied to develop inexpensive, sensitive and specific laboratory tests that are reliable in the first few days of illness?

Animal reservoirs research

- What is the natural animal reservoir(s) for SARS-CoV and related viruses, and what is the nature of exposure that leads to transmission from animals to humans?
- Which wild, farmed or domestic animal species are susceptible to SARS-CoV infection, and what is the prevalence of infection with SARS-CoV and related coronaviruses?
- Is there any evidence for viral persistence in any animal species?
- What is the prevalence and incidence of infection with SARS-CoV and related coronaviruses in human populations exposed to wildlife?
- Is there any evidence of different genetic strains of SARS-CoV circulating in animal populations?
- What are the risks for transmission from animal to humans and how can these be reduced where infection is endemic?

Social and economic impact research

- What brought about behavioural change during the SARS outbreak?
    - Among health care workers?
    - In the media?
    - Among decision-makers and the public?
    - Among patients and contacts?
    - Among families and children?
    - Among travellers?
    - Among consumers?
- Can the social impacts (e.g. health care worker stress, social stigma of patients with SARS, their families and communities) of effective containment and control measures (e.g. quarantine, isolation, traveler screening) be reduced?

Clinical research

- How do we improve the clinical management of SARS cases?
- How do we improve early clinical diagnosis of SARS?
- What clinical algorithms should be applied to allow the best management of persons under investigation for SARS at different stages of an outbreak?
- How do we identify the most effective treatment measures?
- What are the most sustainable and effective infection control measures to reduce nosocomial transmission?

Second order of priority issues for research (not in any order)

Epidemiology

- What is the molecular epidemiology of SARS-CoV and how should it best be studied to determine how this relates to pathogenicity and transmissibility?
- Which countries and settings are at higher risk of the introduction or re-introduction of SARS?
- What criteria/indicators should countries use to assess the most cost-effective suite of preparedness activities?

Laboratory research

- What is the role of other respiratory infections in the development of SARS? Is there any evidence for an enhancement of disease from co-infections with metapneumovirus, Chlamydia, etc?
- Does SARS-CoV persist in humans?
- What is the infectivity of SARS-CoV from stools, how long does virus excretion extend, and does infectivity vary over the period of excretion?

Social impact and risk communication

- What are the common misconception and institutional hurdles that hinder abilities to respond and how can we overcome these barriers?
- What should be the public health approach to vulnerable groups in unaffected countries such as the Chinese and South East Asian diaspora?
- What roles did the media and risk communication strategies play in the social responses to SARS, and how did they affect the responses of health care policy makers?

Animal reservoirs research

- What protocols and assays need to be developed to sample and test different animal species, and can these tests be standardized?
- What type of community level enhanced surveillance of animal handlers and other high-risk groups should be implemented in zones of potential re-emergence?
- What mechanisms need to be developed to promote better collaboration between public health, clinical groups and veterinary scientists in the face of emerging zoonotic diseases?
- What regulations should be in place in China and internationally to protect the public from SARS-CoV and other infectious diseases transmitted through trade and the consumption of wildlife?
- What is the geographic distribution of SARS-CoV-like viruses in wildlife species in southern and eastern Asia?

Clinical studies

- The development of a formal risk to determine which countries and which facilities are most at risk from SARS, and the magnitude of that risk? Could we systematically fail to diagnose SARS in certain areas?

The SARS Research Advisory Committee (SRAC) wishes to support the following recommendation from the WHO Informal Clinical Trials meeting, held immediately after the SRAC meeting:

> *"There is an urgent need for the development of an international SARS trials study group to assess risk benefit of potential therapies including those used so far, and assist in preparation of clinical trials in advance of re-emergence of SARS or other emerging disease."*

Annex 3 – Agenda
WHO Scientific Research Advisory Committee on Severe Acute Respiratory Syndrome (SARS)

20 October 2003

Convenor: Professor John Mackenzie

9:00 – 10:00	Welcome and setting the scene	
	• Introduction and welcome • Opening of the meeting • Agree on chairman and rapporteur(s)	Dr Guénaël Rodier Dr Anarfi Asamoa-Baah Professor John Mackenzie
10:00 - 10:20	BREAK	
10:20 – 11:30	Biology, Epidemiology and Surveillance	
	• Coronavirus biology: 20 minutes • Epidemiology: 15 minutes • Disease modelling: 10 minutes • Surveillance: 15 minutes • Discussion: 15 minutes	Dr Linda Saif Dr Angela Merianos Dr Roy Anderson Dr Thomas Grein
11:30 – 12:25	Animal reservoirs and environmental sources	
	• Wildlife reservoirs: 20 minutes • Environmental sources: 10 minutes • Animal models for SARS: 10 minutes • Discussion: 15 minutes	Dr Pierre Formenty Dr Jamie Bartram Professor Albert Osterhaus
12:25 – 13:30	LUNCH	
13:30 – 14:15	Laboratory Diagnosis	
	• Progression of disease: 10 minutes • Genomic diagnostics: 10 minutes • Serology: 10 minutes • Discussion: 15 minutes	Dr Malik Peiris Dr Christian Drosten Dr Wilina Lim
14:15 – 15:00	Clinical issues	
	• Clinical issues, including blood safety and treatment: 10 minutes	Dr Simon Mardel

	• Infection control: 10 minutes • Differential diagnosis in the post SARS era: 10 minutes • Discussion: 15 minutes	Dr Julia Garner Dr Joseph Sung
15:00 – 15:15	BREAK	
15:15 – 16:00	Social and economic impact	
	• Risk communication: 10 minutes • Economic consequences: 10 minutes • The social response to SARS: 10 minutes • Discussion: 15 minutes	Dr Peter Sandman Dr Emma Xiaoqin Fan Dr Fanny Cheung
16:15 – 16:45	Interrupting transmission	
	• Practical and public health management of SARS outbreaks: 15 minutes • Travel and quarantine related measures: 15 minutes • Discussion: 15 minutes	Professor Aileen Plant Dr David Bell
16:45 – 17:30	Evidence and research priorities	
	• Assessment and comments on evidence base for SARS research: 10 minutes • Review of the day's proceedings, summary of the tasks for the following day including principles for determining research priorities.	Dr Vittoria Demichelo

21 October 2003

9:00 – 11:00	Break-out groups for determining research needs	
	1. Epidemiology: information to inform public health control	Dr Angela Merianos
	2. Laboratory: standardization of laboratories	Dr Malik Peiris
	3. Animal reservoirs/environmental services: understanding the origins and preventing recurrence	Dr Pierre Formenty and Dr Andrea Ellis
	4. Clinical: preventing transmission and ensuring optimum outcomes	Dr Joseph Sung
	5. Social and Economic impact	Dr Max Hardiman
	6. Interrupting transmission	Professor Aileen Plant
11:00 – 12:00	Report back from break out-groups	
	1. Epidemiology: 10 minutes	
	2. Laboratory: 10 minutes	
	3. Animal reservoirs and environmental sources: 10 minutes	
	4. Clinical: 10 minutes	
	5. Social and economic impact: 10 minutes	
	6. Interrupting transmission: 10 minutes	
12:00 – 13:00	LUNCH	
13:00 – 15:00	**Cross cutting themes: break out-groups**	
	For optimal public health control of SARS:	
	1. What do we need to know about the origin of the SARS virus, its emergence and potential to re-emerge?	

	2. What do we need to know about viral transmission and pathogenesis?	
	3. What do we need to know about the effectiveness of control measures including patient management and treatment?	
15:00 – 15:30	BREAK	
15:30 – 16:00	Reporting back from the three breakout groups:	
	1. What do we need to know about the origin of the SARS virus, its emergence and potential to re-emerge?: 10 minutes	
	2. What do we need to know about viral transmission and pathogenesis?: 10 minutes	
	3. What do we need to know about the effectiveness of control measures including patient management and treatment?: 10 minutes	
	Recap of the terms of reference	
16:00 – 17:00	Confirming and prioritizing of the research SARS research needs for the public health management of SARS	Chair
17:30 – 18:00	Press briefing	Secretariat and Chair

****CLOSE OF MEETING****

Meeting of the WHO SARS Scientific Research Advisory Committee

20-21 October 2003

Salle A, WHO Headquarters, Geneva

LIST OF PARTICIPANTS

Advisory Committee

Professor Roy Anderson, Department of Infectious Diseases Epidemiology, Imperial College, London, UK
Dr Robert Breiman**,** Programme on Infectious Diseases and Vaccine Sciences, International Centre for Diarrhoeal Diseases Research, Dhaka, Bangladesh.
Dr Fanny Cheung, Department of Psychology, The Chinese University of Hong Kong, Hong Kong SAR, China
Dr Suok Kai Chew, Epidemiology & Disease Control Division, Ministry of Health, Singapore
Dr Christian Drosten, Bernhard-Nocht Institute for Tropical Diseases, Department of Virology, Hamburg, Germany
Dr Emma Xiaoqin Fan, Macroeconomics and Finance Research Division, Economics and Research Department, Asian Development Bank, Manila, Philippines
Dr Julia S. Garner, Centers for Disease Control and Prevention, Atlanta, USA
Dr Xu Jianguo, National Centre of Communicable Diseases, China
Dr Arlene King, Immunization and Respiratory Infections Division, Health Canada, Ontario, Canada
Professor Lam Sai Kit, Department of Medical Microbiology, Faculty of Medicine, Kuala Lumpur, Malaysia
Dr Linda Lambert, SARS Research Division of Microbiology and Infectious Diseases, National Institute of Allergy and Infectious Diseases, Bethesda, USA
Dr Ting Hung Leung, Department of Health, Wanchai, Hong Kong SAR, China
Dr Wilina Lim, Virology Department, Government Virology Unit, Hong Kong SAR, China
Professor Peter Ndumbe, Department of Microbiology and Infectious Diseases, Faculty of Medicine, University of Yaoundé, Yaoundé, Cameroon
Professor Angus Nicholl, Health Protection Agency, Communicable Disease Surveillance Centre, London, UK
Professor Albert D. M. E. Osterhaus, Erasmus University, Department of Virology, Netherlands
Dr Umesh Parashar, Respiratory and Enteric Viruses Branch, Centers for Disease Control and Prevention, Atlanta, USA
Professor Malik Peiris, Department of Microbiology, Queen Mary Hospital, Hong Kong SAR, China
Professor Aileen Plant, Division of Health Science, Curtin University of Technology, Perth, Western Australia, Australia
Dr Linda Saif, Food Animal Health Research Program, Ohio Agricultural Research & Development Center, Wooster, USA
Dr Peter Sandman, The Peter Sandman Risk Communication consultancy, Princeton, USA
Professor Joseph Sung, Gastroenterology and Hepatology Division, Department of Medicine and Therapeutics, The Chinese University of Hong Kong Prince of Wales Hospital, Hong Kong SAR, China
Professor Bob Swanepoel, Special Pathogens Unit, National Institute of Virology, Johannesburg, South Africa
Professor John Tam, Department of Microbiology, Faculty of Medicine, Prince of Wales Hospital, Hong Kong SAR, China
Dr Kiyosu Taniguchi, Division of Intelligence and Policies, Infectious Disease Surveillance Centre, National Institute of Infectious Diseases, Toyama, Tokyo, Japan

Dr Lin-Fa Wang, Commonwealth Scientific & Industrial Research Organisation, Livestock Industries, Australian Animal Health Laboratory, Geelong, Australia
Dr Dong Xiaoping, National Institute of Virology, Beijing, China
Dr Maria Zambon, Enteric and Respiratory Virus Laboratory, Central Public Health Laboratory, London, UK

Observers

Dr Ray Arthur, Global Health, Centers for Disease Control and Prevention, Atlanta, USA
Dr Mike Catton, Victorian Infectious Disease Laboratory, Carlton, Australia
Dr Ian Lipkin, Mailman School of Public Health, Columbia University, New York, USA
Dr John Watson, Health Protection Agency, Communicable Disease Surveillance Centre, London, UK
Dr Vivian Wong, Professional and Medical Development, Hong Kong Hospital Authority, Hong Kong SAR, China

Advisors to the committee

Dr David M. Bell, National Center for Infectious Diseases, Centers for Disease Control and Prevention , Atlanta, USA
Dr Vittorio Demicheli, Servizo Sovazonale di Epidemiologia, Alessandria, Italy
Dr Nigel Gay, Health Protection Agency, Communicable Disease Surveillance Centre, London, UK

WHO regional offices

AFRO - Dr Paul Lusamba, Regional Adviser, Communicable Disease Surveillance and Response (CSR)
AMRO - Dr Oliva Otavio, Regional Adviser, Communicable Diseases, Division of Disease Prevention and Control (AD/THS)
EMRO - Dr Hassan El Mahdi Elbushra, Regional Adviser, emerging Diseases, RA/CSR
EURO - Dr Bernardus Ganter, Regional Adviser, Communicable Disease Surveillance & Response (CSR)
SEARO - Dr M.V.H. Gunaratne, Regional Adviser, Communicable Disease Surveillance & Response (CSR)
WPRO - Dr Hitoshi Oshitani, Regional Adviser, Communicable Disease Surveillance & Response (CSR)

WHO secretariat

Department of Communicable Disease Surveillance and Response (CDS/CSR/GAR):
Dr Guénaël Rodier, Director, Department of Communicable Disease Surveillance and Response (CSR)
Dr Mike Ryan, Coordinator, GAR
Dr Martha Anker
Ms Peggy Creese
Mr Pat Drury
Dr Pierre Formenty
Dr Tom Grein
Dr Max Hardiman
Dr Kandebure O Bai Kamara
Dr Katrin Leitmeyer
Dr Douglas Lush
Dr John Mackenzie
Dr Simon Mardel
Dr Angela Merianos
Dr Cathy Roth
Dr Nikki Shindo
Dr Gail Thomson
Dr Denise Werker

FCH/VAB/IVR/VIR
Dr Marie-Paule Kieny, Director
Dr Jose Esparza, Coordinator

FCH/VAB/EPI
Dr David Heymann, Representative of the Director-General for Polio Eradication

CDS/CME
Mr Dick Thompson

CDS/CSR/LYO
Dr Diego Buriot, Director
Dr Bradford Kay
Dr Denis Coulombier
Dr Philippe Dubois
Dr Julia Fitzner
Dr Christian Mathiot
Dr Nicoletta Previsani
Dr Kaat Vandemaele
Dr Mohammad Toma Youssef
Dr Stella Chungong

CDS/CSR/RMD
Dr Stefano Lazzari, Coordinator
Dr Klaus Stöhr

CDS/CPE/ZFK
Dr Francois X. Meslin, Coordinator
Dr Andrea Ellis
Dr Peter Ben Embarek

HTP/EHT/BTS
Dr Neelam Dhindra-Kumar

SDE/PHE/WSH
Dr James Bartram, Coordinator