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GLOBAL HEALTH SECURITY

EPIDEMIC ALERT & RESPONSE

# Consensus document on the epidemiology of severe acute respiratory syndrome (SARS)

World Health Organization

DEPARTMENT OF COMMUNICABLE DISEASE SURVEILLANCE AND RESPONSE

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SURVEILLANCE AND RESPONSE

***Acknowledgement***

*This document has been produced by the Severe Acute Respiratory Syndrome (SARS) Epidemiology Working Group and the participants at the Global Meeting on the Epidemiology of SARS, 16-17 May 2003.*

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# Table of Contents

# I. Introduction

On 16-17 May 2003, the World Health Organization held the first global meeting on the epidemiology of SARS in Geneva, Switzerland. The objectives of the meeting were to:

- Produce a WHO consensus document on our current understanding of the epidemiology of SARS as it informs public health practice.
- Identify gaps in our knowledge for the planning of additional epidemiological studies if required.

There are still considerable gaps in our knowledge of the global epidemiology of SARS, which is the first severe and readily transmissible new disease to emerge in the twenty-first century. WHO is coordinating the synthesis and interpretation of the body of work that is being produced around the world and is promoting the sharing of data and experience in containing and controlling this epidemic.

Participants were asked to present data and analysis relevant to answering the epidemiological questions in the agenda (Annex 1) either from their experience of SARS outbreaks in their countries and territories or based on the analysis of data from countries reporting cases of SARS. The final list of participants is attached as Annex 2.

Participants were representatives of the Centres (institutions, national and regional public health authorities and other health protection agencies) that have experienced outbreaks of SARS and also included leading international experts in the fields of public health and communicable disease epidemiology, mathematical modelling and clinical virology. Seven topics for discussion (see below) were selected on the basis of their importance as epidemiological indicators of the potential impact of the SARS epidemic and the potential for prevention, containment, elimination or eradication. Participants presented their findings to a broad audience on Friday 16 May and a smaller group met on Saturday 17 May to review the data and formulate draft recommendations for wider dissemination.

Professor Angus Nicoll (Health Protection Agency, Colindale, London England), the invited chair, opened the meeting, welcomed the participants and outlined the meeting's objectives. Dr David Heymann (Executive Director, Communicable Diseases Cluster, WHO) also welcomed the participants and thanked them on behalf of Dr Brundtland (Director-General, WHO) for their participation. Dr Guénäel Rodier (Director, Communicable Disease Surveillance and Response Department, WHO) highlighted the importance of sharing data and experience and the need to reach a consensus on the epidemiology of SARS to enable evidence-based public health action.

Discussions at this meeting focused on seven main topics:

- Incubation period
- Infectious period
- Case-fatality ratios
- Routes of transmission, exposure dose and risk factors for transmission
- The presence and significance of subclinical infection
- Reproduction number in different transmission settings and under different control strategies
- Animal and environmental reservoirs

The main findings and recommendations arising from the meeting are summarized by topic followed by the studies under way. However, given the rapid evolution of our knowledge about SARS, the document also incorporates published data and data presented at the SARS Clinical Management Workshop, 13-14 June 2003, Hong Kong, Special Administrative Region of China, the WHO Global Conference on Severe Acute Respiratory Syndrome, Kuala Lumpur, Malaysia, 17-18 June 2003 and during teleconferences of the WHO Ad Hoc Working

Group on the Epidemiology of SARS. It therefore provides a synthesis of our current understanding of the epidemiology of SARS and the priorities for public health research.

# II. Recommendations from the global meeting on the epidemiology of SARS

The participants recognized that striking progress had been made in global understanding of the science of SARS, and the coronavirus[1] that is its cause (SARS-CoV), since the first information began to be gathered in March. The experience in affected areas has already shown that the transmission of the SARS-CoV can be prevented by adherence to basic public health measures, including rapid case detection, case isolation, contact tracing and good infection control, including hand washing and the use of personal protective equipment (PPE). However they also recognized that much more needs to be known so as to protect the public and achieve WHO's goal of containing and pushing back SARS out of its human host. To help achieve this, the participants made the following **recommendations** that have been updated in light of new data:

## 1. Incubation period

1.1. Refined estimates of the incubation period can rapidly be achieved by combining data internationally on the approximately 200 cases with clearly defined exposure histories. WHO to coordinate a global analysis of the incubation period by defining a minimum data set, with a data dictionary and coding sheet.

1.2. Centres to prioritize laboratory testing of the approximately 200 SARS cases with clearly defined exposure histories. These cases should be tested for SARS coronavirus by one or more assays[2] to identify cases with laboratory evidence of infection, and ideally with evidence of seroconversion as the laboratory gold standard.[3]

1.3. WHO to establish and achieve agreement on a protocol to investigate "outliers" in both tails of the incubation period distribution.

1.4. WHO to review its public health recommendations informed by the incubation period immediately after the analysis of the combined data set is completed.

1.5. WHO to facilitate the development of an applied research plan to evaluate the public health policies for SARS containment and control that are based on a 10-day incubation period.

## 2. Infectious period

2.1. Centres to relate clinical data on the onset and/or change in the symptoms and signs of SARS (fever, cough, dyspnoea, and diarrhoea and chest X-ray changes) to viral shedding studies both retrospectively and prospectively.

2.2. WHO to encourage Centres to analyse linked clinical and laboratory data sets in order to better describe the infectious period and other clinical epidemiology.

2.3. WHO to facilitate modelling and data analytic studies to estimate infectiousness by time since onset from detailed epidemiological data sets.

2.4. WHO to encourage Centres to carry out detailed case-studies on "superspreading events"[i] (this terminology was considered more accurate than "super spreaders") and to coordinate collection and synthesis of these data. A review of "superspreading

[i] A "superspreading event " is a transmission event that generates many more than the average number of secondary cases.

events" should explore the connectedness of social networks that may facilitate transmission and the current infection control and other public health measures that need to be improved to prevent future "superspreading events".

2.5. Based on current evidence and experience, WHO to re-affirm that hospital discharge and follow-up recommendations published on 28 March 2003 are acceptable public health practice.

2.6. WHO to revise the *Management of Contacts of Probable SARS Cases* (11 April 2003)[4] to indicate that where SARS, is present or there is a reasonable suspicion that an individual is infected (for example on the basis of travel history), the need for prompt isolation of the individual and investigation of relevant contacts after onset of any symptoms suggestive of SARS.

2.7. WHO to publish a statement on what is currently known about the infectious period of SARS.

2.8. Centres to undertake quantitative studies of SARS-CoV shedding, wherever possible before and after the onset of symptoms suggestive of SARS, and continuing beyond resolution of these symptoms to determine the time period of potential infectiousness in relation to onset and resolution of symptoms, as a basis for appropriate isolation procedures.

# 3. Case-fatality ratios

3.1. Simple methods for calculating case-fatality ratios (CFRs) from aggregate data will not give reliable estimates during the course of an epidemic. Centres to review CFRs using statistical methods that provide valid and robust estimates such as non-parametric and/or parametric survival analyses. These methods require case-based data, preferably with laboratory confirmation.

3.2. The effects of factors such as age, sex, the presence of co-morbidities and the effectiveness of clinical management on the CFR for SARS need to be determined at the global level. WHO to facilitate the systematic collection of data on co-morbidities, including underlying immunosuppression, cardiorespiratory disease and other chronic diseases, clinical management and clinical outcome.

3.3. WHO to analyse data on the CFR for health care workers as a specific population at risk of SARS.

3.4. WHO to establish criteria for cause of death in relation to SARS through collaboration with the WHO Update Reference Committee for the International Classification of Diseases and Vital Statistics unit. There is a need to distinguish between SARS as the cause of death and dying of other causes with SARS as co-morbidity.

# 4. Routes of transmission, exposure dose and risk factors for transmission

4.1. WHO to review *Definition of a SARS Contact* in *Management of Contacts of Probable SARS Cases* in Web document [4] to include:

- analysis of SARS cases by probable route of transmission, including the proportion of cases currently unexplained by established chains of transmission
- explicit reference to exposure during the symptomatic period of a SARS case while investigating the role, if any, of infectivity in the pre-clinical period
- that special consideration should be given to confined spaces (such as within aircraft, taxis, other vehicles, some work environments) and hospital settings

- that there is a need for flexibility and judgement in the assessment of the risk of SARS transmission to contacts
- that current evidence indicates casual contacts are not at risk for SARS except when there has been sustained, close contact with a case of SARS or in high-risk transmission settings, such as health care settings and households
- that Centres report unusual transmission events to WHO to help build the evidence for as yet unrecognized routes of transmission and better define risky environments and behaviours such as clinical procedures that result in aerosols, including the use of nebulizers and difficult intubations.

4.2. Centres to undertake or continue detailed epidemiological, laboratory and environmental investigations on unusual transmission events, including transmission that cannot be explained by close, sustained contact (defined as having cared for, lived with or having had direct contact (<1 metre) with respiratory secretions or other body fluids of a suspect or probable case of SARS).

4.3. WHO to recommend that persons who have an acute febrile respiratory illness should not travel until their symptoms have resolved.

4.4. Centres in collaboration with WHO to undertake careful evaluation of all aspects of exit and entry screening.

4.5. WHO to review overall guidelines for cleaning and disinfection of hospitals and other settings after the presence of people with SARS.

4.6. WHO to facilitate a collaborative international study on SARS in pregnancy to understand the role of vertical transmission if any, the impact of SARS on pregnancy outcomes for both the mother and the fetus and the impact of pregnancy on the clinical course and outcome of SARS.

4.7. Centres to design and carry out immunological studies and surveys among children for evidence of infection and transmission in this age group where virus has been circulating. The use of methodologies for rapid serological assessment should be considered while awaiting the design and approval of formal epidemiological studies.

# 5. The presence and significance of subclinical infection

5.1. Centres to complete serological testing of cohorts of contacts of probable and suspect SARS cases to determine the proportion of contacts who developed symptomatic and asymptomatic infection.

5.2. WHO to synthesize the results of serologic testing of SARS contacts at a global level.

5.3. WHO to facilitate Centres pooling data and experience on unusual laboratory findings (for example isolated SARS-CoV positive serology or positive polymerase chain reaction (PCR) in individuals with no or minimal symptoms) so as to determine the public health significance of these events and the action they should trigger.

# 6. Reproduction number in different transmission settings and under different control strategies

6.1. WHO to introduce additional data variables in the global line listing of SARS cases to facilitate the ongoing determination of the reproduction number and impact of control measures as the epidemic evolves (see also recommendation 8.3).

6.2. WHO to facilitate modelling and other studies to estimate the impact of different control measures on the effective reproduction number in different countries.

6.3. WHO to access the International Connectance Database (air travel statistics) in order to more accurately assess the risk of international spread of SARS.

6.4. WHO to support or assist in the analysis of detailed epidemiological data from mainland China and Taiwan province to evaluate the effectiveness of public health measures by assessing the effective reproduction number.

6.5. The WHO Western Pacific Regional Office to negotiate China's participation in data sharing including the synthesis of global data via the global minimum data set.

# 7. Animal and environmental reservoirs

7.1. Centres to undertake urgent studies to determine whether animal reservoirs exist based on epidemiological evidence of exposure risk and laboratory evidence of infection and transmission potential.

7.2. WHO to collaborate with Centres on studies of viral inactivation to develop additional guidance on environmental decontamination in the context of SARS, particularly for the cleaning of hospitals and residential buildings (see also recommendation 4.5).

# 8. Cross-cutting issues

8.1. Those responsible for the health of the public need to ensure that clinical, laboratory, and epidemiological resources are efficiently coordinated to best respond and manage an outbreak and to evaluate these activities. This includes the undertaking of well-coordinated, priority studies to generate the information needed for public health action, and the timely access by public health decision-makers to this information.

8.2. WHO to facilitate closer collaboration between clinical, laboratory and epidemiology networks to address public health priorities in the diagnosis, containment and control of SARS.

8.3. WHO to achieve consensus from Centres on their participation in developing a global minimum data set for international analysis in order to better describe the epidemiology of SARS, especially for uncommon events to increase sample size and the power of any study.

8.4. WHO to leverage a data sharing agreement between Centres which addresses issues of confidentiality, use of data and publication rights.

8.5. WHO to work with Centres to analyse the global data set and to present these findings as a consensus statement by the partnership at the WHO Global Conference on Severe Acute Respiratory Syndrome, Kuala Lumpur, Malaysia, 17-18 June 2003.

8.6. WHO to review published clinical data collection tools and define a minimum clinical data set.

8.7. WHO to facilitate the development of an applied research plan to evaluate the public health policies for SARS containment and control that are based on findings such as the 10-day incubation period, conclusions on when people are infectious and other key epidemiological questions.

8.8. All participating Centres to support WHO in achieving the above goals by sharing relevant data and experiences.

# III. Key epidemiological distributions

The following key distributions of SARS are discussed in this section – incubation period, infectious period and case-fatality ratios.

## 1. Incubation period

The estimates for the incubation period for SARS are starting to converge as tabled below. Estimates are derived from an analysis of SARS cases with single point exposures or exposure over a well-defined interval (Table 1). They will later be refined by the addition of laboratory data.

Most countries reported a median incubation period of 4-5 days, and a mean of 4-6 days. The minimum reported incubation period of 1 day was reported from China (4 cases) and Singapore (3 cases) and the maximum of 14 days was reported by China.

Donnelly et al analysed 1425 cases notified to 28 April in the Hong Kong Special Administrative Region of China (Hong Kong SAR) for whom epidemiological, demographic and clinical data were linked. The data were fitted to γ distributions by maximum likelihood estimation methods with allowance for censoring. The maximum likelihood estimate of the mean and variance of the time from infection to onset was 6.37 days (95% CI 5.29-7.75) and 16.69 days respectively; therefore 95% of the patients would experience the onset of symptoms within 14.22 days of infection.[5] Four Centres stated that the maximum observed incubation period was 10 days.

There was considerable discussion about the range of the incubation period and the effect of "outliers" at the upper end of the incubation period on existing recommendations on the isolation of cases and their contacts. "Outliers" beyond a 10-day maximum incubation period are few in number and have not necessarily been subjected to rigorous and standardized investigation. However, it was noted that other mammalian coronavirus infections have long right-hand tails for incubation periods, so a long tail is also biologically plausible for the SARS-CoV. Statistical methods can be used to enable the inclusion of cases with defined periods of exposure rather than point exposures alone in order to increase sample size. There was also some concern that SARS cases arising from a single exposure may not be representative of all SARS cases.

Centres agreed that a detailed investigation of "outliers" is needed before public health policy is changed to extend the incubation period beyond 10 days, as any extension of the incubation period will have considerable impact on health service practice and resources. Participants also agreed on the need to combine data sets into a standardized international data set (N≅200 cases) to refine current estimates of incubation period. Although the focus of the investigation should be on the right-hand tail of the distribution (maximum incubation period) because of its public health importance, the shortest incubation periods seen in SARS influence the mean incubation period more than the upper tail and should also be reviewed.

It remains unclear whether the route of transmission influences the incubation period.

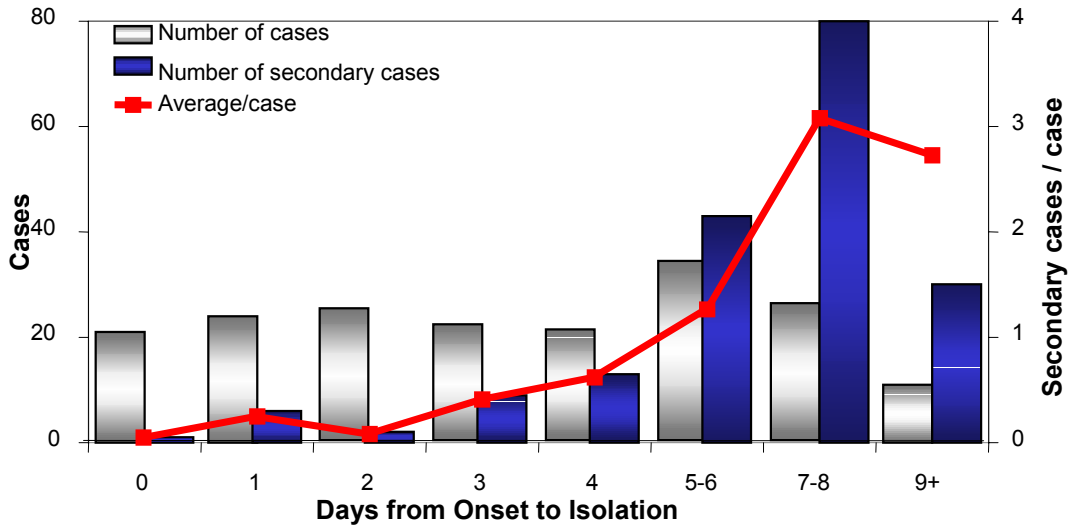
**Table 1. Summary of SARS incubation period estimates**

| Area | Minimum | Mean | Median | Maximum | Comments |
|---|---|---|---|---|---|
| Canada | 2 | 4.8 | 4.2 | 10 | Based on 42 cases with a single exposure to a source case. The median and mean were calculated using a parametric fit, while the minimum and maximum are from the data. |
| People's Republic of China | 1 (4 cases) | 4 | 4 | 12 | Based on 70 cases from Guangdong. 5 cases with an incubation period of >10 days. |
| | | | | 14 | Beijing and Guangdong. |
| China, Hong Kong SAR | – | 6.37 (95% CI 5.29–7.75) | – | – | Based on 57 cases with one exposure to SARS over a limited time scale. Incubation period of ≤14.22 days in 95% of cases (parametric fit). |
| China, Taiwan | – | – | – | 10–14 | Based on household transmission studies. |
| Singapore | 1 (3 cases) | 5.3 | 5 | 10 | Based on 46 cases with a single exposure. |
| Viet Nam | 5 | 6–7 | – | 10 | Based on health care associated exposure to a source case. |
| WHO European Region | 5 | 7.2 | 7 | 10 | Based on two episodes (5 cases) with a single exposure to a source case. |

## 2. Infectious period

Transmission efficiency appears to be greatest from severely ill patients or those experiencing rapid clinical deterioration, usually during the second week of illness. Data from Singapore (Figure 1) show that few secondary cases occur when symptomatic cases are isolated within 5 days of illness onset.[6]

**Figure 1. Secondary cases of SARS by days to isolation of the source case. Singapore, reported to 15 April, 2003**



This inference of infectivity by time since onset derived from epidemiological observations correlates very closely with laboratory data on cases. Maximum virus excretion from the respiratory tract occurs on about day 10 of illness and then declines. Peiris et al[3] from Hong Kong SAR presented the results of quantitative reverse transcriptase (RT)-PCR on sequential nasopharyngeal aspirates/throat and nose swabs (NPA/TNS) from 392 patients (adapted in Table 2). Virus shedding in stool begins later than in respiratory secretions but also followed an inverted "V" distribution; 100% of stool samples from 50 patients were PCR positive by days 12-14 and then the detection rate declined.

Similarly, RT-PCR data from the Government Virus Unit, Hong Kong SAR, indicate that 36% of NPA/TNS test positive on days 0-2, peaking at 61% positive on days 9-11 and then the percent positive declines to 0% by day 23.[7] This source also reports that 22% of stools tested by RT-PCR are positive on days 0-2 of illness, peak at 100% on 12-14 and falls to 50% on days 21-23. Detection of viral RNA has a much lower yield from serum with only 19% of samples positive on days 0-2, peaking at 39% on days 6-8 of illness and being undetectable by day 12.[7] Lim also quantified viral excretion in stool; the highest number of viral copies per millilitre occurred on days 10-15 of illness and fell quickly thereafter. Viral excretion in NPA specimens peaked on days 12-14 of illness but at two orders of magnitude lower than viral excretion in stools.

Data linkage is required to determine whether there is a direct relationship between clinical severity and viral load and excretion.

## Table 2. RT-PCR positivity in respiratory specimens, stool and urine*

| Sample (% positive) | Days from illness onset | | | | |
|---|---|---|---|---|---|
| | 0-2 | 3-5 | 6-14 | 15-17 | 21-23 |
| NPA/TNS (n=392) | 31 | 43 | 57-60 | 35 | 13 |
| Stool (n=50) | 0 | 57 | 86-100 | 33 | 43 |
| Urine (n=20, **n=19) | | | 50 (day 10) | 35 (day 16) | 21** (day 21) |

*Adapted from Peiris et al[3] and the Hong Kong SAR presentation delivered by Dr Margaret Chan, Director of Health, 16 May 2003.

There are a number of counter examples to the inference that infectivity is greatest in the second week of illness. There is anecdotal evidence of transmission in the early prodromal period from a small number of source cases (Canada). Two index cases reported by European countries were infectious at days 1-2 and day 6 after the onset of symptoms. Further elucidation of the risk of transmission from cases with mild illness, and transmission during the prodromal period is urgently needed.

The existing WHO guidelines on the clinical management[4] and medical follow-up of patients with SARS[8] were reviewed in light of the epidemiological findings on the period of infectivity. There are no reports of transmission beyond 10 days of fever resolution consistent with the total period of isolation following fever defervescence recommended by WHO. Based on the evidence now available, the WHO discharge policy remains valid.

There are differences in the discharge policies of Centres at this time. Most Centres' discharge policy is consistent with that of WHO, while the period of medical follow-up is longer in Hong Kong SAR where patients are monitored for 19 days after defervescence and a normal chest X-ray. The duration of medical follow-up after discharge from hospital varies across China although defervescence and resolution of chest X-ray changes is a universal requirement before hospital discharge.

Few serial clinical specimens have been collected and some Centres have experienced difficulty in linking clinical, laboratory and epidemiological data to build up a complete

picture of the interaction between the SARS-CoV, its human host and transmission environments. There is an urgent need for well-defined virus shedding studies linked to the clinical progression of disease.

Virus shedding studies are under way in Singapore, Hong Kong SAR, Canada and China. Singapore is specifically investigating virus excretion in a convalescent cohort of patients.

Participants agreed on the following priorities for the elucidation of the period of infectivity:

- Review of published and anecdotal data on the period of infectivity. Additional epidemiological and laboratory studies are needed to fully describe the period of communicability, including quantitative virology.
- Determination of the shedding pattern of SARS cases throughout the duration of illness and convalescence. The analysis should stratify patients by clinical status (symptomatic or convalescent) and severity of illness.
- Virus shedding and serological studies among quarantined contacts of SARS cases to determine the onset and duration of infectivity (Hong Kong SAR). Overall in Hong Kong, 223 of 19 386 family and social contacts under surveillance developed SARS (1.2%) and 28 of 1158 contacts on home confinement (the subset of household contacts from the broader contact cohort above) subsequently developed probable SARS (2.4%).
- Compilation of a case series on "superspreading events" in order to better define the contribution of behaviour (time from illness onset to isolation), other host characteristics, virus characteristics and the environment in which "superspreading events" have occurred.
- Review of existing health worker training and broader community education on SARS and other relevant infections in all countries to ensure adherence to recommendations for health care settings, domestic infection control and other hygiene procedures.
- Modelling of data sets with known links between individual cases.

# 3. Case-fatality ratios

SARS is a condition associated with substantial morbidity and mortality. On 14 May 2003, WHO published a synthesis of revised CFR estimates using three statistical methods.[9] The revision was based on an analysis of the latest data from Canada, China, Hong Kong SAR, Singapore, and Viet Nam.

The case-fatality ratio of SARS is estimated to range from 0% to more than 50% depending on the age group affected, with an overall CFR estimate of approximately 15%.[ii] Using a non-parametric survival analysis estimated from interval-censored data, which provides an unbiased estimation of case-fatality, WHO estimated a crude CFR of 14% in Singapore and 15% in Hong Kong SAR. The method used to calculate CFR in China has not been reported; accordingly, it is unclear whether the lower age-specific CFR among older age groups in China reflects a healthier cohort of elderly and aged persons than elsewhere or the effect of the method of CFR calculation.

Table 3 synthesizes the estimates of CFR presented at the meeting.

Multivariate analysis of risk factors associated with SARS-related mortality from Hong Kong include increasing age, male sex, the presence of co-morbidity and health care seeking behaviour.

However, given that in some Centres, most SARS deaths occurred in the elderly, there is a need to distinguish between SARS as the direct cause of death and dying with an

[ii].A global case-fatality ratio of 11% was recorded at the end of the outbreak (see also IV.2.1).

intercurrent SARS infection. WHO participants were tasked with liaising with the WHO Update Reference Committee for the International Classification of Diseases regarding recommendations on the death certification in SARS and reporting back to the partnership.

Gender differences in case-fatality also need further investigation as the results above are based on small numbers.

Laboratory testing is important to determine whether the CFR in the United States of America and Europe may be the result of strain variation in the SARS-CoV or due to a high false-positive rate among clinically diagnosed cases.

The differences in CFR estimates support the need for a larger data set (see below – *The global minimum data set*). WHO was asked to provide an updated synthesis of CFR when data from the global minimum data set become available.

## Table 3. Case-fatality ratios

| Area | Crude CFR | Comments |
|---|---|---|
| Canada | 16.7% in probable cases<br>9.3% of probable and suspect cases combined | Median age of SARS deaths 75 years: 83% over 60 years.<br>Diabetes and co-morbidities independently associated with mortality. |
| People's Republic of China | The crude CFR in Beijing appears lower than published data. HCW have a low CFR of 1.4%.<br>Method for determining age-specific CFR not defined. | Age-specific CFR<br>20-29 0.9%<br>30-39 3.0%<br>40-49 5.0%<br>50-59 10%<br>60-69 17.6%<br>70-79 28%<br>80+ 26.3% |
| China, Hong Kong SAR | Non-parametric competing risk analysis: 15%<br>Males have a worse outcome than females in all age groups.<br>Age-specific CFR lower among HCWs. | Age-specific CFR<br>0-24 0% (n=0)<br>25-44 6% (n=29)<br>45-64 15% (n=35)<br>65+ 52% (n=87) |
| China, Taiwan | 13 % (34 deaths out of 264 probable cases). | |
| Singapore | Non-parametric competing risk analysis: 14% | |
| United States of America | 0% | Only 6 of 64 probable cases have laboratory evidence of SARS-CoV infection. |
| Viet Nam | 9.7% | |
| WHO European Region | 0% | Of 39 probable cases in 11 countries, only 8 are known to have laboratory confirmation of SARS-CoV infection. |

## The global minimum data set

Centres agreed in principle on a global minimum data set of SARS cases to answer a range of public health questions on SARS. This data set will be based on the existing WHO line listing and data dictionary[10] which will be enhanced with additional fields. Some of the key additional variables are listed below.

- Unique identifier of source case
- Demographic details, including occupation
- Global positioning system (GPS) code for case location
- Laboratory results, including results of convalescent phase serology (ideally collected ≥28 days after illness onset), polymerase chain reaction (PCR) results, virus isolation and evidence of co-infection
- Risk factor data, including co-morbidities, treatment received and pregnancy
- Options for additional dates of exposure for cases who had multiple exposures
- Clinical descriptors and outcomes
- Date of isolation of the case (in a health care facility)
- Date of home isolation of contacts who subsequently become cases (i.e. prior to illness onset in secondary cases)

A data dictionary will accompany the global minimum data set.

# IV. Routes of transmission exposure dose and risk factors for transmission

## 1. Routes of transmission

Available evidence suggests that SARS emerged in Guangdong Province, in southern China in November 2002. More than one third of early cases, with dates of onset before 1 February 2003, were in food handlers (persons who handle, kill, and sell food animals, or those who prepare and serve food).[11]

Throughout the outbreak, the primary mode of transmission appears to be direct mucous membrane (eyes, nose, and mouth) contact with infectious respiratory droplets and/or through exposure to fomites. Cases have occurred primarily in persons with close contact with those very ill with SARS in health care and household settings. Transmission to casual and social contacts has occasionally occurred when as a result of intense exposure to a case of SARS (in workplaces, airplanes or taxis) or in high-risk transmission settings, such as health care settings and households. Molecular analysis can help to describe transmission trees.

A basic reproduction number ($R_0$) of approximately 3 is consistent with a disease spread by direct contact or larger virus-laden droplets that travel only a few meters rather than by lighter airborne particles. By contrast, if a disease is transmitted by aerosols, a single person can infect an entire room by coughing, as can happen with measles and influenza. If so, then simple infection control techniques, such as frequent hand washing can go a long way toward slowing the spread of the disease.

Aerosolizing procedures in hospitals, and other events[12] that promote aerosolization of infectious respiratory droplets or other potentially infectious materials (such as faeces or urine) in hospitals or other settings, may amplify transmission. Survival of the SARS-CoV needs further investigation in a variety of settings and under a variety of conditions (e.g. in fomites or carpets) and the importance of cleaning surfaces without generating dangerous aerosols was emphasized. There need to be careful studies to determine the minimum practical methods of inactivating the virus, for example through cleaning, following the presence of a patient with SARS or suspected SARS.

Appropriate respiratory precautions should be sustainable in a fully functioning hospital and there is a need to establish the "new norm" in respiratory precautions. The public health sector should focus its efforts on general surveillance of respiratory illnesses, SARS case finding and investigation, isolation of close contacts of SARS cases, and public and

professional education. These activities are consistent with the recommendations of the World Health Organization.[4,13]

The role of faecal-oral transmission is unknown; however, there is no current evidence that this mode of transmission plays a key role in the transmission of SARS though caution was expressed on this point because of the lack of surveys and transmission studies among children where this is a common mode of transmission of other viral infection. Several animal coronaviruses are spread via the faecal-oral route.[14] Peiris et al reported watery diarrhoea in 55 (73%) of 75 cases from the Amoy Gardens outbreak.[3] The onset of diarrhoea occurred at a mean 7.5 days of illness with a maximum frequency of 6.3 stools per day. Diarrhoea was less frequent in other series; 38% of 138 SARS cases were associated with large volume diarrhoea at the Prince of Wales Hospital[15] and 16% of 1315 cases on the Hong Kong SAR Hospital Authority database.

In Viet Nam, approximately 50% of cases had diarrhoea during their illness (7% with diarrhoea at admission) with the most severe cases all having diarrhoea. In Guangzhou City, Guangdong province China 8.6% of 662 probable and suspect cases of SARS had diarrhoea at onset; diarrhoea at any time during the course of illness was not documented. In Taiwan, approximately 57% of cases had diarrhoea at any time. In Ontario, Canada, 28% of probable cases and 19% of suspect cases had diarrhoea throughout the course of illness; suspect cases developed diarrhoea earlier than probable cases. It was noted that in some cases, late diarrhoea may be related to antibiotic treatment rather than part of the natural history of the disease: however, given that viral excretion was greatest in stool, diarrhoea could still remain important for infectivity, regardless of its cause.[iii]

Under certain circumstances, such as in health care settings or other closed environments, contamination of inanimate materials or objects by infectious respiratory secretions or other body fluids (saliva, tears, urine and faeces have been found to contain virus) seems to occasionally play a role in disease transmission. Despite considerable opportunity there have been no reports of food or waterborne transmission; however studies are needed to further define the potential role of these routes.

# 2. Risk factors for transmission

## 2.1 The global epidemiology of SARS

The first cases of SARS are now known to have emerged in mid-November 2002 in Guangdong Province, China. The first official report of an outbreak of atypical pneumonia in the province, said to have affected 305 persons and caused 5 deaths, was received by WHO on 11 February. Around 30% of cases were reported to occur in health care workers. Confirmation that cases were consistent with the definition of SARS was made after permission was granted, on 2 April, for a WHO team to visit the province.

A cumulative total of 8422 probable cases, with 916 deaths, were reported from 29 countries during the outbreak (data current at 7 August 2003)[16]; WHO announced that the last chain of human transmission was broken on 5 July 2003. Of this total, 5327 cases and 349 deaths are reported from mainland China. A global case-fatality ratio of 11% was recorded at the end of the outbreak (see also III.3). These figures may be revised again following a process WHO has begun with all centres that reported cases to close off the historical data set of the outbreak. The epidemic curve of the outbreak by date of onset is presented in Fig 2. Total cases and attack rates per 100 000 inhabitants based on probable SARS cases reported to WHO by 7 August 2003, are presented in Figures 3 and 4 respectively.

[iii] Minutes of the 7 May World Health Organization Ad Hoc Working Group on the Epidemiology of SARS.

## 2.2 Risk factors for SARS

Risk factors for SARS were described in a number of studies. Health care workers, especially those involved in procedures generating aerosols, account for 21% of all cases, ranging from 3% of reported probable cases in the United States of America (1/33 cases) to 43% in Canada (108/251 cases).[16] Other risk factors include household contact with a probable case of SARS, increasing age, male sex and the presence of co-morbidities.[IV] The care and slaughter of wildlife for human consumption in the wet markets of southern China is associated with serological evidence of infection (see VII.1.2).[17]

The transmission of SARS in the Metropole Hotel[18] and the Amoy Gardens[12] has been attributed in part to environmental contamination, with a possible animal vector[19] contributing to the spread of the virus in the Amoy Gardens outbreak.

There has also been limited transmission associated with air travel (see IV.2.4).

The evidence presented at the Global Meeting on the Epidemiology of SARS and published data have confirmed the efficacy of traditional public health measures, which include early case identification and isolation, vigorous contact tracing, voluntary home quarantine of close contacts for the duration of the incubation period, and public information and education to encourage prompt reporting of symptoms.[20]

## 2.3 Special populations requiring investigation

### *SARS in children*

To date, there have been two reported cases of transmission from children to adults and no reports of transmission from children to other children. The epidemiological investigation of 8 of 10 children with SARS in Hong Kong SAR who had been attending school at the time of presentation found no evidence that they had spread the infection to their classmates.[21] Epidemiological investigations in Guangzhou City, Guangdong, China, also found no evidence of SARS transmission in schools.[22] These findings are in contrast to the secondary attack rates among adults.[23]

Serological studies using non-invasive diagnostics among children for evidence of transmission in settings where virus has been circulating are recommended.

### *SARS in pregnancy*

Additionally, there have been no reported cases of vertical transmission. Data from the Princess Margaret Hospital, Hong Kong SAR, from March-May 2003 show that of 10 women previously well, aged 27-44 years who developed SARS during pregnancy, 6 required admission to the hospital's intensive care unit, 4 were ventilated and 3 died. There was one maternal death among the 5 first trimester pregnancies and 4 spontaneous abortions; no virus was found in cord blood or liquor. Two maternal deaths occurred among the 5 late pregnancies; all 5 infants survived and no perinatal transmission was detected.[24]

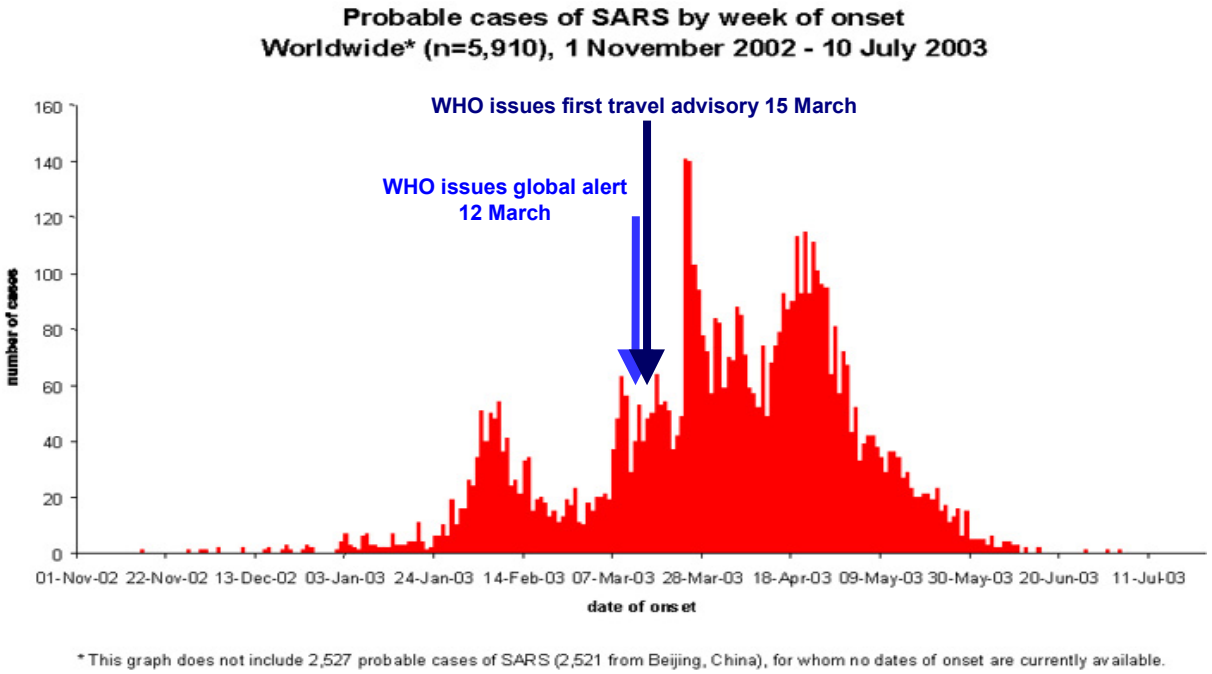
A global collaborative study on SARS in pregnancy is needed to increase the sample size of case series. Anker has estimated that there are 100 pregnant women among the more than 8000 probable SARS cases reported worldwide.[v] It is unlikely that any one country would have a large enough sample of pregnant women among their probable SARS cases to definitively answer questions about the course and outcome of SARS in pregnant and

[IV] Dr Margaret Chan. Hong Kong SAR presentation, Global meeting on the Epidemiology of SARS. World Health Organization, Geneva, Switzerland, 16-17 May 2003.

[v] Anker M. Calculations based on the age-sex distribution of SARS cases and national age-specific

lactating women, including whether pregnancy outcomes are affected by the gestational age at infection.

## Figure 2.




* This graph does not include 2,527 probable cases of SARS (2,521 from Beijing, China), for whom no dates of onset are currently available.

Adapted from World Health Organization. Epidemic curves – Severe Acute Respiratory Disease (SARS) http://www.who.int/csr/sars/epicurve/epiindex/en/index1.html

**Figure 3. Probable SARS cases in selected sites**[16]

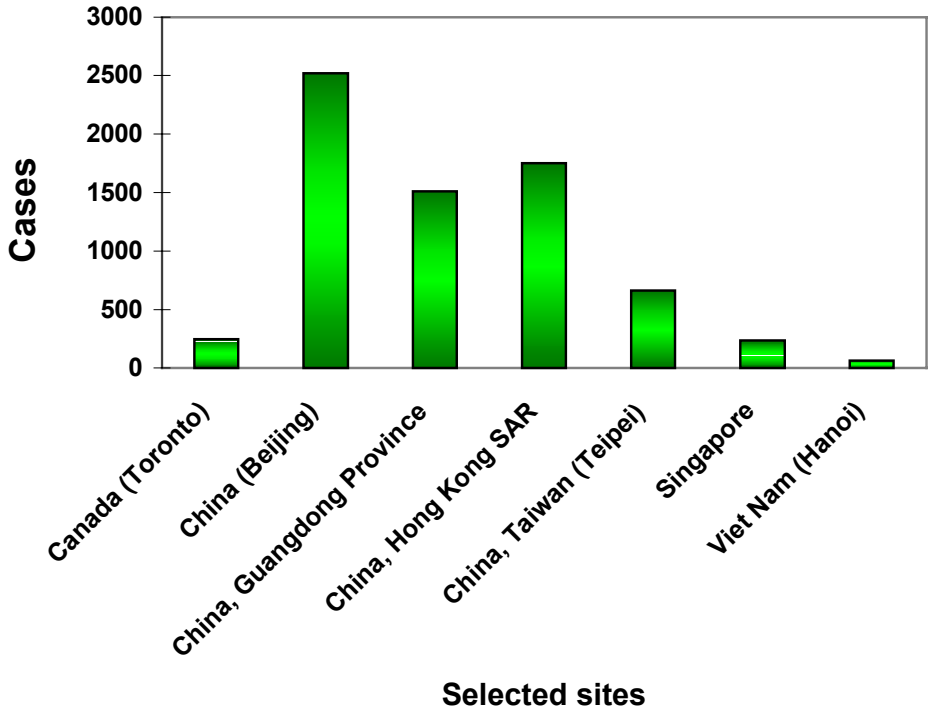
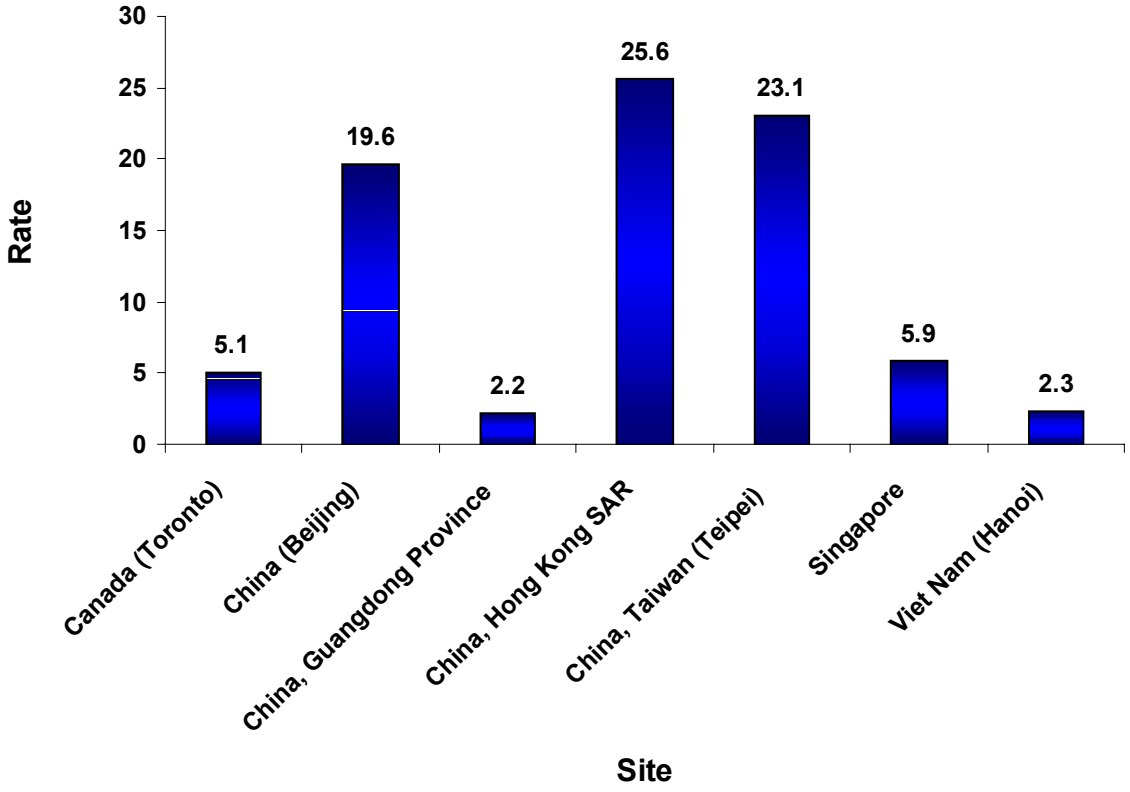



**Figure 4. Probable SARS cases in selected sites. Attack rates per 100 000 inhabitants**[16]



## 2.4 Airline transmission

WHO issued the first emergency travel advisory on 15 March[25] to airlines and travellers, providing case definitions for probable and suspect cases of SARS and advising airline crew of the need to report all such cases to airport and public health authorities. Additional guidance was issued on 27 March[26] that recommended measures to reduce the risk of the global spread of SARS, including the exit screening of air passengers departing from areas reporting local transmission. The following analysis only includes travellers fulfilling the WHO case definition of probable SARS issued on 27 March 2003.

The following data are current to 14 July 2003.[vi] WHO has received verified reports of 40 flights on which one or more probable SARS cases travelled while symptomatic (a total of 37 potential source cases, see Table 4). In addition, there are 40 flights involving 21 probable cases on which WHO is awaiting further details. These data are not yet complete; WHO continues to receive new data, and review and reclassification of cases are ongoing.

Five international flights have been associated with the transmission of SARS from symptomatic probable cases to passengers and/or crew; one of these flights (Flight C) constitutes a "superspreading event". Details of the flights are still under investigation.

The French public health authorities investigated a small cluster of cases associated with two international flights (Flights A/B: a two-leg journey on 22–23 March 2003). The source case, a physician, was estimated to be on day 3–4 of his illness when flying. Three persons who travelled on the flight later developed SARS – a flight attendant and two passengers, one sitting 1 row ahead of the source case and another 5 rows behind the source case. Exit screening was already in place at the port of departure but the explanation given by the physician for his symptoms did not preclude him from travelling.

The source case for Flight C was a 72-year-old man who had visited the Prince of Wales Hospital in Hong Kong SAR before flying on 15 March. This case was associated with a cluster of 24 probable cases of SARS representing 22 passengers and 2 flight attendants. Of these 22 infected passengers, 14 subsequently travelled on later flights (a total of 5 flights) while symptomatic. Of these subsequent flights, only one was associated with possible in-flight transmission (Flight E, see below). Seating information for the passengers on Flight C is incomplete; our current understanding is that passengers up to 7 rows in front and 5 rows behind the source case on both sides of the central aisle were infected. The number of secondary cases from transmission on this flight is still under investigation as at least one group of passengers travelling together may have been exposed while in an area with recent local transmission. The route(s) of transmission on flight C also remains undetermined – droplet, contact, faecal-oral and limited airborne transmission, or a combination of modalities, are all plausible.

### Table 4. Flights with symptomatic probable cases, 23 February–23 May 2003

| Travel period (2003) | Number of flights | Number of symptomatic probable cases on board |
|---|---|---|
| 23 February–14 March | 9 | 6 |
| 15 March–26 March | 10 | 18 |
| 27 March–23 May | 21 | 13 |
| 23 February–23 May | 40 | 37 |

[vi] Data extracted from the WHO Airline Transmission of SARS database

The source case on Flight D was a 33-year-old male physician who was on day 6-7 of illness when flying on 14-15 March. One secondary case (a flight attendant) was associated with possible transmission on the flight. Two family members travelling with the source case were also infected (one probable and one suspect case); they have not been included as air travel-associated secondary cases as the opportunities for domestic transmission exceed the likelihood of transmission exclusively on this flight.

Two passengers from flight C (15 March) were symptomatic when they travelled on flight E on 23 March. A passenger who sat next to one of the source cases (who was on day 6 of his illness) later developed SARS.

The International Air Transport Association (IATA) provided denominator data on commercial international flights and passengers, including transit passengers, for March 2003 to and from Beijing, Hong Kong SAR, Singapore, Taipei and Toronto. From the verified flights of March there are 6.5 passengers per million who travelled from these locations while symptomatic cases of probable SARS. However, we do not know how many of these persons were actually real cases of SARS-CoV infection.

There are a number of important findings from the preliminary data:

- A total of 29 secondary cases have been linked to probable cases of SARS who travelled while symptomatic. Only one flight (Flight C) resulted in a "super spreading event", on which limited airborne transmission cannot be excluded on current evidence. However, other modes of transmission also need to be considered. A detailed analysis of Flights A-E, which are associated with secondary cases, is under way.
- To date, no transmission has been confirmed on flights after the 27 March travel advisory in spite of at least 21 flights with probable SARS cases on board since that date. Given the highly effective internal public health measures implemented in jurisdictions with outbreaks (case identification, isolation and contact tracing), probable SARS cases detected after 27 March may be less likely to be “real” cases of SARS-CoV infection than earlier cases. Serological studies are needed to evaluate the predictive value of the surveillance case definition over time in this cohort.
- A crude estimate from the verified flights of March is that 6.5 passengers per million travelled as symptomatic probable SARS cases in March 2003 having departed from locations specified above with local transmission of SARS. On the current data, we are unable to calculate the reduction in risk associated with the travel advisory and other pre-departure surveillance implemented in affected areas. In addition, some of these “cases” may not have been real cases of SARS-CoV infection. IATA documented a 10.6% reduction in the number of passengers travelling to and from the cities listed above compared to March 2002.

Centres in collaboration with WHO are encouraged to carry out careful evaluations of all measures aimed at reducing the international spread of SARS. Convalescent phase serology should be collected on these cases to exclude persons who did not have SARS-CoV infection to refine the estimate of risk.

# 3. The SARS experience by geographical area

## *Canada*

Canada experienced a SARS epidemic with two clusters that were epidemiologically linked to two hospital outbreaks. Transmission of SARS in the Greater Toronto Area (GTA) began with an index case who had spent time in the Metropole Hotel, Hong Kong, in February 2003.[27] A family contact after becoming ill with symptoms compatible with SARS was treated at a hospital in the GTA and subsequently transmitted the illness to staff and patients in the hospital. Nearly 100 hospital workers at three GTA hospitals subsequently became ill. Initial descriptive epidemiology suggests that transmission occurred in contacts of patients and

visitors who were not identified as having SARS and were not in isolation precautions and contacts of ill family members. At the beginning of the outbreak, transmission occurred in health care workers prior to the implementation of hospital-wide infection control precautions.[28]

The first case linked to the second phase of the Ontario outbreak was a 96-year-old man admitted to an orthopaedic ward in the index hospital on 22 March 2003 with a fractured pelvis.[29] During the course of his SARS-related illness with onset date 2 April, he developed respiratory symptoms, fever, diarrhoea and radiological evidence of atypical pneumonia. Aspiration pneumonia and *Clostridium difficile*-associated diarrhoea were thought to explain his illness. On 20 May, 5 patients in a rehabilitation hospital in Toronto were reported with febrile illness; one patient had been referred from the orthopaedic ward of the index hospital and had been an inpatient at the same time as the first case. A second case was found to have SARS-CoV by nucleic acid amplification. After their identification, an epidemiological investigation of pneumonia cases at the index hospital identified 8 cases of previously unrecognized SARS among patients, and concluded that exposure to inpatients with unrecognized SARS after relaxation of strict SARS control measures probably resulted in transmission to health care workers, patients and visitors. Of the 74 cases reported to the Ontario public health service from 15 April-9 June, 67 (90%) resulted directly from exposure in the index hospital.

Transmission has been largely confined to health care settings, primarily acute care hospitals, in which there have been unrecognized SARS patients, and appropriate infection control measures have not yet been implemented. Attack rates among nursing staff in one Toronto hospital prior to the recognition of SARS, were: emergency room 22% (8/36), intensive care unit 10% (4/39) and cardiac care unit 60% (6/10).[28,29]

Canadian health authorities documented at least 2 transmission events involving health care workers wearing full PPE (N95 masks or higher, eye protection, gowns and gloves) infected during a difficult intubation. High-risk procedures (intubation, suction, nebulized aerosol therapy and positive pressure non-invasive ventilation) have resulted in transmission to health care workers.[30] In two events, undiagnosed SARS cases were identified as the source of transmission for 7 hospital staff. Although infection control precautions were in place, compliance may not have been complete. In the third, staff were reportedly compliant with infection control precautions except for one break in technique where a face shield was accidentally dislodged.[31]

Transmission of SARS to 10-11 hospital staff was also reported in lower risk settings. Affected staff included physicians, nurses, and service assistants (e.g. porter/housekeeper) working in 4 different low-risk SARS units and one community hospital. Investigation of these cases suggested that transmission occurred while staff were wearing recommended PPE and following all recommended infection control precautions.[31]

Transmission has usually involved severely ill source cases. Anecdotally some cases have had very little exposure involving either transmission occurring after short but intense exposure to very ill persons or transmission after exposure to suspect cases or persons with mild symptoms in their prodromal period.

Examples include:

- a paramedic, who may not have been under optimal infection control precautions, infected while spending a very short time with a severely ill patient
- an infected nurse aid whose only exposure was a very brief visit to a case household[32]
- health care workers in SARS units but without exposure to high-risk procedures infected while wearing full PPE (see above).

In most situations, implementation of aggressive airborne, contact, and droplet precautions provides effective protection for caregivers. Community acquired infection has been reported from close community contact, religious events (5 cases, plus an exported case)[33]

and in one workplace (1 case). There has been no known transmission in public access buildings (other than hospitals), schools and public transport.

As a result of their experience, Canadian public health authorities identified the following lessons learnt:

- The importance of early case identification, immediate reporting to public health authorities and rapid isolation cannot be overstated. Where transmission of virus in or between hospitals is suspected, active nosocomial surveillance of staff and patients for fever and other symptoms consistent with influenza-like illness, appropriate case management, including isolation and rapid investigation, is essential. Although the analysis of cases is ongoing, persons in the initial phase of illness may have SARS compatible X-ray changes in the absence of cough or dyspnoea. Had active fever surveillance been in place in all GTA hospitals since the end of the first epidemic wave, new cases of SARS may have been detected earlier.
- In homes, stringent application of contact and droplet precautions appears to provide effective protection.
- In hospitals, strict adherence to airborne precautions, including the use of N95 masks, in addition to contact and droplet precautions (including hand hygiene, gloves, gowns, and eye protection) is recommended for those caring for SARS patients. The available experience on SARS transmission during intubation has been reviewed. At the present time, it was felt that the evidence does not support a recommendation for use of enhanced respiratory personal protective equipment (e.g. Powered Air Purifying Respirators [PAPRs], Personal Protective Systems) when intubating SARS patients. Furthermore, enhanced PPE, and the increased complexity involved in the removal and disposal/cleaning/decontamination of this equipment, may increase the potential risk of self-contamination. Patient care protocols should be developed and in place prior to the need for high-risk procedures, including intubation of SARS patients, in order that the procedures are performed in a controlled setting. Specific recommendations include: ongoing assessment of patients to determine when intubation is likely to be necessary; limiting the number of persons in the room during intubation; ensuring that intubation is performed by the most experienced personnel available; reducing the risk of traumatic and prolonged intubation by procedures such as sedating the patient.
- As SARS is primarily acquired in hospital settings, it is critical that patient and staff movements within and between institutions can be accurately and quickly tracked, using readily available administrative records. When disease transmission is occurring, restriction of movement of patients within and between institutions should be seriously considered, as the disease may be difficult to diagnose in persons hospitalized with other illnesses. Similarly, where feasible, restriction of staff movement within and between facilities should be considered. In addition, education of contacts should include information on the upper range of the incubation period, to ensure that prompt self-isolation and notification of public health authorities is implemented.

Finally, unlike China, Hong Kong SAR and Singapore, Canada did not designate specific hospitals as SARS hospitals during the outbreak, although hospitals had designated SARS wards. The efficacy of consolidating SARS case management in specialized units compared to developing SARS capacity in every hospital requires further evaluation.

## *People's Republic of China*

On 2 January 2003, a concentrated outbreak of a previously unknown atypical pneumonia was reported to the Health Bureau of the Guangdong Province, China. [34] The outbreak was initially thought to be associated with influenza A (H5N1) after two cases of infection were confirmed and one suspected in a single family of Hong Kong residents who had travelled to Fujian Province in China before illness onset.[35] Both patients with confirmed influenza were

hospitalized and one died. The third family member died while in China, but testing was not done to confirm the cause of death.

A retrospective study of atypical pneumonia cases identified what were later regarded as the first identified cases of SARS occurring in November 2002. Between 16 November 2002 and January 2003, 7 cities in Guangdong province identified index cases of SARS, all but one were regarded as locally acquired with one imported from Guangzhou City.[36] No epidemiological link between these cases could be identified. Six of the 7 were associated with 2–3 generations of secondary transmission.

After mid-January 2003, SARS cases were concentrated in hospitals and household contacts of SARS cases.[36] Transmission settings included workplaces and aircraft, initially in Zhongshan and Guangzhou cities. By 12 June 26 of 31 provinces of mainland China, including autonomous regions and municipal cities, reported cases; 18.2% of the total 5327 reported cases occurred in health staff.

The WHO epidemiological mission to Guangdong province reported that throughout the epidemic there was a high proportion of community cases for whom no contact history was reported. A disproportionately large number of the early SARS cases worked in kitchens or wildlife markets in several of the affected cities in Guangdong province. From 16 November 2002–16 April 2003, 42.8% of SARS cases without a credible history of exposure worked in kitchens although there was no significant history of direct contact with domestic animals or birds (see VII.1.1).

Early in the course of the epidemic an epidemiological link could be established for 100% of cases; at the time of writing that was only true for 20% of recently reported cases. However a variety of reasons were suggested for this including the circulation of another respiratory virus.

There are at least two “superspreading events” identified in China.[37] The Guangzhou incident (patient 'ZH') resulted in transmission in two hospitals with 3 generations of infection and resulted in 82 cases epidemiologically linked to the source case, including an ambulance driver. Transmission in the first hospital occurred before the implementation of infection control measures and a number of health care workers were infected during a difficult intubation. An aerosolizing procedure was also reported in the second hospital to which the patient was transferred. No transmission occurred at the third (tertiary level) hospital with effective infection control.[37] A total 59 health care workers were infected in this incident. The attack rate was 61.7% (29/47) in the respiratory ward of the second hospital.

The second superspreading incident (patient 'Y') travelled to Guangdong province where she was infected with SARS-CoV. Eleven secondary cases (3 health care workers and 8 family contacts) occurred in Shanxi province and several health workers were also infected when she was transferred to a hospital in Beijing.

## *China, Hong Kong SAR*

A serological survey of 200 blood donors before the onset of SARS in Hong Kong showed that none tested positive for anti-SARS-CoV antibodies before the onset of the SARS epidemic. A follow-up serosurvey on blood donors involved a total 450 anonymized blood samples (50 tested each week). None tested positive (Dr Wilina Lim, Government Virus Unit, Hong Kong SAR, personal communication).

Over 90% cases have an identifiable link with a known case or cluster of SARS.

Two “superspreading events” have been identified in Hong Kong within a frequency distribution of over 1000 observations.[7]

Either respiratory droplets and/or fomites can explain most transmission events. A number of epidemiological studies are consistent with this view (the Metropole Hotel, Amoy Gardens

and Prince of Wales Hospital clusters) and infection control studies (Canada) and laboratory findings of virus viability in the environment (see VII.3).

The attack rate in medical students at the Prince of Wales Hospital was 100% for those who visited patients in beds adjacent to an index case, 50% for those who had entered the same cubicle as an index case and 0% for those who had only entered the same ward. These data support the need for proximity of contact for transmission to take place.[vii] Seto et al[38] used an unmatched case-control study on 458 staff (127 SARS cases and 331 controls; 884 observations) to evaluate the effectiveness of respiratory and standard precautions in a multi-centre study in Hong Kong SAR. Methods included a self-administered questionnaire and direct observation. The main findings were that the risk of infection was associated with the length of stay of patients with SARS and that infection control, including PPE use, must be rigorously applied to prevent transmission of SARS-CoV, especially given the correlation between risk of infection and length of inpatient stay of SARS cases, and the resultant risk of lapses in infection control due to staff fatigue.

## Table 5. Risk reduction in the transmission of SARS-CoV by adherence to PPE, Hong Kong SAR*

| Intervention | SARS-CoV Infected % (n=127) | Uninfected % (n=331) | p value |
|---|---|---|---|
| N95 mask | 85.8 | 99.4 | p<0.001 |
| Hand washing | 90.6 | 97.2 | p=0.004 |
| N95 mask + gloves + gown + hand washing | 40.0 | 81.0 | p«0.001 |

*Adapted from Seto[38]

Ho et al[39] examined risk factors for SARS in health care workers following intubation of patients with SARS using a retrospective case-control study in 4 hospitals in Hong Kong. Methods included data collection via a standardized questionnaire, personal interviews, chart audit, site visit and root analysis. Ninety-one intubations were included in the analysis of 8 case related procedures (3 probable and 5 suspect cases of SARS) and 83 control procedures.

## Table 6. Procedures comparison during intubation of patients with SARS, multi-centre study, Hong Kong SAR*

| Procedure | Cases (n, %) | Controls (n, %) | Odds Ratio | p value |
|---|---|---|---|---|
| Difficult intubation | 5/8 (62.5) | 13/83 (15.7) | 8.8 | p=0.002 |
| Extensive bagging | 5/8 (62.5) | 5/83 (6.0) | 25.9 | p<0.001 |
| Extensive droplet contamination | 3/8 (37.5) | 0/83 | Undefined | p<0.001 |
| Intubation in a general ward environment | 4/8 (50.0) | 9/83 (10.8) | 8.2 | p=0.008 |

*Adapted from Ho[39]

### *The Amoy Gardens outbreak*

The Amoy Gardens cluster is a "superspreading event".[40] The index patient in the Amoy Gardens outbreak was a 33-year-old man who lived in Shenzhen and visited his brother in Amoy Gardens regularly. He had chronic renal disease, which was being treated at the Prince of Wales Hospital. He developed SARS symptoms on 14 March 2003. On 14 March and 19 March he visited his brother who owned a flat in Block E of Amoy Gardens. He had diarrhoea

[vii] A cluster of Severe Acute Respiratory Syndrome among medical students in Hong Kong. Trip report compiled by Lee CK, WHO Short-term consultant, May 2003.

at that time and used the toilet there frequently. His brother, his sister-in-law and two nurses who attended to him at the Prince of Wales Hospital subsequently developed SARS.

Dry U-traps in bathroom floor drains provided a conduit for contaminated sewage droplets to enter households. A significant virus load had built up in the sewer system as an increasing number of SARS cases with diarrhoea excreted virus. Virus was aerosolized within the confines of very small bathrooms and may have been inhaled, ingested or transmitted indirectly by contact with fomites as the aerosol settled.

Person-to-person spread contributed to disease propagation in other blocks within the Amoy Gardens complex. Rodents and cockroaches may have acted as mechanical vectors of transmission.

### *The Metropole Hotel outbreak*

The Metropole Hotel, Kowloon, Hong Kong SAR cluster exemplified that potential international spread of infectious diseases.[41] The index cases in the Toronto, Hong Kong, Singapore and Hanoi outbreaks were associated with the hotel, as well as cases identified in Ireland and the United States that resulted in no secondary cases or one generation of local transmission respectively.[42] As of 12 June, 16 probable and suspect cases of SARS were associated with the cluster.[43]

The results of environmental sampling on the carpet outside room 911, the room in which the index case resided, and elevator area show a hot zone (possibly vomitus or respiratory secretions) which are PCR positive 3 months after the index case stayed at the Metropole Hotel. Although the signal only demonstrated the presence of SARS-CoV RNA and not viable virus, this finding may have implications for the persistence of the virus in the environment.

Although the Metropole Hotel outbreak is recognized as a "superspreading event", the index case in this outbreak did not have an unusually high viral load when tested on days 9 and 11 of illness.[7]

## *China, Taiwan*

The epidemic in Taiwan has had two phases occurring before and after 20 April 2003. From 7 March-19 April, 78% of probable cases were travel related, 6% were hospital-acquired and 16% occurred in households and among social contacts of SARS cases. From 20 April-16 May, 89% of cases were hospital-acquired, 9% travel related and only 2% community acquired.

There is an anecdotal report of transmission on a train although the passengers were not seated in the same carriage.

## *Singapore*

Close contact is usually required for transmission in most cases. Overall 84% of cases did not result in further transmission. A small number of "superspreading events" accounted for a very large number of cases. Five probable cases of SARS have been associated with "superspreading events"[44] and accounted for 103 of the total 206 cases reported.[45] Each of these patients appears to have infected over 10 health care facility staff or visitors and household and social contacts. The index case in Singapore was admitted in early March 2003 before WHO issued the first global alert.[46] For the first 6 days of admission, the patient was nursed in a general ward without barrier infection control measures. This case was directly linked to probable SARS infection in 21 persons. There was no further transmission within the hospital after the implementation of strict infection control measures (N95 masks, gown, gloves, and hand washing before and after patient contact). The authors commented that it was unclear which infection control measures were responsible for the decrease in transmission.

Over 120 cases were ultimately linked back to the index case largely as a result of 3 additional "superspreading events".[44] Case 2 and Case 3 were linked to two clusters of 23 persons each. Case 4 was ultimately linked to 62 cases; 40 cases had direct contact with this case and the remaining 22 cases had travelled the same corridor used by the patient. This case was originally admitted to Tan Tock Seng Hospital (TTSH) with an exacerbation of his chronic kidney disease and diabetes and later transferred to the Singapore General Hospital (SGH) for steroid-induced gastrointestinal bleeding. Case 5 was a 64-year-old vegetable hawker who visited Case 4 (his brother) at the SGH and subsequently was linked to infection in 15 secondary cases, including a number of community contacts (two taxi drivers who transported Case 5 to and from his vegetable stall and two hawkers at the wholesale market).

It is uncertain whether these "superspreading events" are due to special conditions conducive to virus transmission (superspreading environments), to some characteristic of the source case such as high viral load or the capacity to excrete large amount of virus or to a characteristic of the virus making it more transmissible. Detailed investigations of "superspreading events" are needed to further elucidate the relative importance of environment, host and vector, given that most SARS cases generate fewer than 3 secondary cases.

The number of secondary cases decreased with each generation but may in part be the result of earlier case detection and isolation.

There have been a small number of cases where transmission occurred after apparently transient exposure. On 8 April 2003, a 64-year-old man was admitted to the National University Hospital that was designated as a non-SARS hospital. He presented with a 2-day history of light-headedness, myalgia and a dry cough. He gave no credible history of exposure to a case of SARS nor to SARS hot spots within Singapore but an epidemiological link to his brother who was retrospectively identified as a case of SARS was subsequently made. When his condition deteriorated, he was transferred to the designated SARS hospital, TTSH, and died on 12 April. During the 12 hours of his stay at NUH, SARS-CoV was transmitted to 1 doctor, 2 nurses, 3 patients and 1 visitor and secondary transmission also occurred as part of this cluster.

## *United Kingdom*

The United Kingdom has reported three laboratory-confirmed cases of SARS who did not meet the WHO case definition either because they did not have a convincing history of exposure or did not have a documented fever above 38°C. Two of the 3 cases tested positive for SARS-CoV by at least two different assays and on serial testing using polyclonal antibodies. The third case was seropositive on a single specimen collected on day 9 of illness. No secondary transmission was associated with any of these cases. SARS-CoV is expected to have a spectrum of clinical presentations so milder cases are to be expected.

## *Viet Nam*

The index Viet Nam case, a business man who stayed at the Metropole Hotel, Hong Kong between 21 February and 23 February, arrived in Viet Nam from Hong Kong on 23 February 2003. Just nine weeks later, on 28 April, Viet Nam was removed from the WHO's list of SARS affected areas, making it the first country to have successfully controlled SARS. The total probable SARS case count for Viet Nam was 62 probable cases and five deaths: 36 hospital workers (58%), 8 patients (13%), 10 hospital visitors (16%) and 8 community contacts of cases (13%). This count includes only people who acquired their infection in Viet Nam and recovered or died in Viet Nam. It excludes the index case, a WHO staff member and 2 hospital workers who left Viet Nam.

In the week following the admission of the index case to the Hanoi French Hospital (HFH), an explosive outbreak of a serious respiratory illness occurred amongst hospital staff, visitors and other patients. Occupational risk (attack rate % by occupational risk group) has been calculated for the HFH. The attack rate for any doctor was16%, any nurse 35%, administrative staff 2%, other staff with patient contact 53% and others, 0%. The overall attack rate for the hospital was 18%. The attack rate for patients admitted for reasons other than SARS was 7%.

On 11 March the HFH discharged all non-SARS patients and closed to all new admissions, except for their own staff who became unwell with a SARS compatible illness. The Institute of Clinical Research in Tropical Medicine, Bach Mai Hospital was then designated as the SARS receiving hospital and admitted its first SARS case on 12 March. On 28 March the HFH transferred all but three SARS patients to the Institute of Clinical Research in Tropical Medicine. The last SARS patient in the HFH died on 12 April, after which time the hospital was closed for disinfection and refurbishment.

There was no transmission of SARS to staff of the Institute of Clinical Research in Tropical Medicine.

Two community clusters were identified. The first involved 3 family contacts of an expatriate doctor working at the HFH. The second involved 5 close contacts of a man who visited his daughter at the HFH during the SARS outbreak (although she was admitted for routine surgery and did not develop SARS). This second community cluster was located in and around a small town south of Hanoi. In one instance, transmission occurred during a car journey.

The total duration of the epidemic from the arrival of the index case to onset of symptoms in the last case was 43 days. Because of the concentrated nature of the contact between the cases within the HFH, it is not possible to track contacts between cases. However, in one chain of transmission four generations can be identified. The secondary attack rate among contacts of one well-tracked case was 6%.

The National Centre for Hygiene and Epidemiology maintained a SARS case list and shared this with the relevant Preventive Medical Service. The Preventive Medical Service was responsible for identifying close contacts and undertaking active surveillance for 10 days following the most recent exposure to the case.

### *WHO European Region*

The WHO European Region presented a report of secondary transmission associated with international airline travel (Flights A/B, see IV.2.4).

# V. The presence and significance of subclinical infection

The clinical spectrum of the SARS needs to be further characterized. There is a paucity of information on the presence and epidemiological significance of asymptomatic infection.

Canada reported SARS-CoV positivity and seroconversion in persons who do not meet the case definition for SARS.

Hong Kong SAR provided a preliminary report that 32 of 316 asymptomatic contacts of SARS cases from Amoy Gardens Block E who were placed under quarantine had laboratory evidence of SARS-CoV in their respiratory secretions and stool by reverse transcriptase (RT)-PCR. Some remained PCR positive for at least 10 days. However, the results of serological testing in these persons are pending. All but one of 161 asymptomatic Amoy Gardens residents tested while under isolation in the holiday camps were seronegative for evidence of infection with SARS-CoV; the one antibody positive contact was also PCR positive.

China reported that some health care workers who were exposed to SARS cases but remained asymptomatic had serological evidence of SARS-CoV infection. A consistent

observation is that children are rarely affected by SARS and further investigation is required to determine if children have asymptomatic or mild infections. Over 1000 paired serum samples have been tested in Hong Kong SAR, including approximately 200 from children. Only two have tested positive and those children were suspected SARS – there is serological evidence that children are not becoming infected.[7] However, a number of possibilities may account for these findings; children were less exposed to SARS cases than adults in Hong Kong, the SARS-CoV induces short-lived immunity or children are protected from infection in some way.

Ongoing studies in different countries to determine the presence and extent of asymptomatic infection include serologic testing of asymptomatic contacts (e.g. cohort studies in different transmission settings such as hospitals, households and aircraft). Some countries are also testing serum samples from special populations (e.g. blood donors and persons admitted to hospital for conditions unrelated to SARS).

There are currently no reports of the transmission of SARS from asymptomatic individuals.

The meeting participants recommended that WHO compile the results of serologic testing in contacts of SARS cases from all countries to determine the proportion of contacts who develop symptomatic and asymptomatic infection and to determine the public health significance of positive laboratory findings in asymptomatic individuals and people with symptoms that do not reach the criteria for a suspect or probable case of SARS.

# VI. Reproduction number in different transmission settings and under different control conditions

The basic reproduction number, $R_0$, is the average number of secondary infectious cases produced by an infectious case. $R_0$ determines the potential for epidemic spread in a totally susceptible population in the absence of specific control measures. This quantity determines the potential for an infectious agent to start an outbreak, the extent of transmission in the absence of control measures, and the ability of control measures to reduce spread.[47]

A number of researchers have estimated the basic reproduction number by fitting models to the initial growth of epidemics in a number of countries. Their observations indicate that the SARS-CoV is less transmissible than initially thought with estimates of $R_0$ in the range of 2-4. Importantly, SARS is less transmissible than most other respiratory infections and therefore potentially more susceptible to control measures.

The effective reproduction number, $R_t$, determines the potential for epidemic spread at time t under the control measures in place at that time, and must be $<1$ for an outbreak to be brought under control. There is a need to quantify $R_t$ in different settings to evaluate the effectiveness of public health interventions, ideally week by week.

Three modelling approaches were presented at the meeting and summarized below by presenter.[5,48,49]

### *Professor Roy Anderson*

Donnelly et al[5] used a stochastic patch model to analyse data on 1600 cases from Hong Kong, SAR. They estimate an $R_0$ (excluding "superspreading events") of 2.9 from the initial phase of the epidemic. Implementation of control measures reduced R to 0.4 by the beginning of April. However, more detailed transmission models are needed. This model factors out background transmission and “superspreading events”.

### *Assistant Professor Marc Lipsitch*

Based on data from Canada and Singapore the mean serial interval (defined as the time from the onset of symptoms in an source case to the onset of symptoms in a subsequent case infected by the source case) for SARS was approximately 10-11 days early in the epidemic,

reducing to 7–8 days following the introduction of control measures. Lipsitch et al[48] estimated $R_0$ from the initial rate of increase of cases (assuming exponential growth) to be 2.0–3.5 in Hong Kong SAR for mean serial intervals in this range.

Although the average number of secondary cases in the absence of specific control measures is approximately 3, there can be considerable heterogeneity in this number between individuals with some individuals being associated with very high numbers. This heterogeneity decreases the probability that a single importation will lead to an outbreak; however with multiple importations the probability of an outbreak is high.

Of the first 201 probable cases of SARS in Singapore, 103 were infected by five source cases; "superspreading events" can have a large influence on the early course of the epidemic but the frequency of "superspreading events" cannot be accurately estimated in the early phase of an epidemic.

### *Dr Jacco Wallinga*

Wallinga[49] estimated an $R_0$ of 3.3 in the early phase of the Canadian SARS epidemic, using the serial interval distribution and the number of cases by date of onset. R fell to less than 1 following the introduction of control measures.

In summary, all three models yield similar results i.e. $R_0$ is approximately 3 in the absence of specific public health measures such as case isolation. The results are encouraging; showing that R can be reduced to less than 1 by implementation of the recommended control strategies.

The importance of sharing data was stressed again in this session. Access to the International Connectance Database (air travel statistics) is needed to more accurately assess the risk of spread. WHO was asked to explore options for access to this restricted database. The use of GPS codes to record the location of cases was suggested as a method to enhance modelling of potential geographic spread. Mobile phone data can also be used to track people's movements.

The focus of modelling should be on improving understanding of the transmission dynamics of infection (e.g. contribution of hospitals to transmission, "superspreading events") and assessing the impact of public health interventions. An economic component could also be considered. For example, the costs of drastic measures early in the epidemic to limit population movements need to be considered and compared to the costs of the consequences of not carrying them out.

# VII. Animal and environmental reservoirs

## 1. Animal reservoirs

There has been considerable speculation about whether there is an animal reservoir for the SARS-CoV, and indeed if SARS is a zoonotic infection that has successfully crossed the species barrier.

A number of animal studies are under way to address these questions. The results of experimental inoculation are summarized below. Koch's postulates, as modified by Rivers, for viral diseases, were fulfilled by SARS-CoV as the cause of the clinical syndrome. Two cynomolgus macaques (*Macaca fascicularis*) infected orally became ill and excreted virus from the nose and throat demonstrated by virus isolation and RT-PCR by days 2-6 post inoculation; two other macaques seroconverted to SARS-CoV were shown to seroconvert by indirect immunofluorescence 16 days post inoculation.[50]

### 1.1 Domestic animals

- A number of animals living in the Amoy Gardens complex tested positive for SARS-CoV on one or more assays. These were all pets exposed to a high level of

contamination in block E or Block C. Oropharyngeal and rectal swabs were collected from cats from a multiple cat household and 2 dogs over a 14 day period after their owners were diagnosed with SARS; 8 cats and one of the dogs tested PCR positive. Spontaneous infection of cats from 3 multiple pet households was demonstrated by PCR on oropharyngeal and rectal swabs collected over a 14 day period (Dr Trevor Ellis, Agriculture, Fisheries and Conservation Department, Hong Kong, personal communication). SARS-CoV was also isolated from the cats and the sequenced virus was indistinguishable from the human isolates (Dr Wilina Lim, Government Virus Unit, Hong Kong SAR, personal communication). Serological confirmation of SARS-CoV infection by serum neutralization tests was obtained from one PCR positive cat from Block E and 4 of 5 cats (including the 3 PCR positive cats) from one household in Block C. The cats were penned in household groups in single cages and in separate rooms while in isolation. There was limited evidence of spread in the isolation cages (5 cats in close direct contact with these cats remained uninfected). The one susceptible dog remained uninfected despite close confinement for 14 days.

- Animal challenge studies on cats are being planned (Prof Albert Osterhaus, Department of Virology, Erasmus MC, the Netherlands, personal communication).[51]
- Rats, mice, poultry, pigs and rabbits are resistant to infection but antibody levels are yet to be determined.
- Rodent droppings collected during the Amoy Gardens investigation have tested PCR positive. However, there is no laboratory evidence that rodents can be infected; baby mice inoculated by intracerebral and intraperitoneal routes showed no evidence of infection.
- SARS-CoV was detected on the body surface and gut contents of cockroaches by PCR but their organs were negative. Cockroaches may act as mechanical vectors of virus transmission.
- Experimentally infected pigs have shown significant neutralizing antibody titres; however there is no evidence of excretion in faeces, tissues or blood.
- Poultry studies in the 5 most common domestic species (chickens, turkeys, ducks, geese and quail) have shown no evidence of illness or viral excretion.

## 1.2 Wildlife

There is evidence that natural infection with SARS-CoV may occur in a number of animal species indigenous to China and parts of south-east Asia. On 23 May 2003 research teams in Hong Kong SAR and Shenzhen, China announced the results of a joint study of wild animals taken from a market in southern China selling wild animals for human consumption. The study detected several coronaviruses closely related genetically to the SARS coronavirus in two of the animal species tested (masked palm civet and raccoon dog). The study also found that one additional species (the Chinese ferret badger) elicited antibodies against the SARS-CoV. These and other wild animals are traditionally considered delicacies and are sold for human consumption in markets throughout southern China.

All six of the civets included in the study were found to harbour SARS-CoV isolated in cell culture (2/6) or detected by a PCR technique (2/6) or were found to be positive by both methods (2/6).[17] The animals also seroconverted and their sera inhibited the growth of SARS coronavirus isolated from humans. In addition, human serum from SARS patients inhibited the growth of SARS isolates from these animals. Sequencing of viruses isolated from these animals demonstrated that the most striking difference between the two fully sequenced palm civet coronaviruses and those of human SARS-CoV was an additional 29 base-pair sequence in the animal viruses.[17] Of the human SARS-CoV sequences currently available in GenBank, only one has the additional 29 nucleotide sequence. Serological studies of animal and vegetable traders within the Guangdong market showed that 40% (8/20) of the wild animal traders, 20% (3/15) of the wild animal butchers and 5% (1/20) of the vegetable

traders were seropositive for SARS-CoV. None of those tested reported SARS-like symptoms in the preceding six months. [17]

A number of studies are under way in China to determine the prevalence of SARS-CoV infection in animals and the host range. Seven species have now tested positive to date either by PCR and/or serology – palm civets, the raccoon dog, the Chinese ferret badger (as above), cynomolgus macaques, fruit bats, snakes and wild pigs.[52,53] A Chinese government team has also released results showing that 66 out of 508 animal handlers tested at markets in Guangdong had antibodies against the SARS virus.[52]

Information on the potential role of animals in the transmission of SARS is important to the overall understanding of SARS. Much more research is needed before any firm conclusions can be reached as to the role of these and other animals in the transmission of SARS to human populations and as animal reservoirs of SARS-CoV. At present, no evidence exists to suggest that these wild animal species play a significant role in the epidemiology of SARS outbreaks. However, it cannot be ruled out that these animals might have been a source of human infection.

The studies indicate that the SARS virus exists outside a human host. However, many fundamental questions remain. The eradication of SARS-CoV is unlikely if infection is zoonotic. Priority areas for action include establishing the origins of SARS-CoV, the host range in domestic and wild species and viral ecology, factors leading to emergence of the virus (changes in the agent, host factors, farming practices and wildlife utilization) and models for the dynamics of infection. These studies need to be carried out as a matter of urgency using appropriate sampling frames and methods, and with validated tests utilizing panels of human and animal sera.

# 2. Food safety

Food has not been shown to be infective for SARS-CoV. However, symptomatic patients with febrile illnesses of any sort should not handle or prepare food for others. A question still remains whether people shedding the virus in convalescence should handle food, especially if she/he is a professional food handler.

WHO is developing recommendations for food safety, given the trade and marketing implications if food and food handling were to be associated with the transmission of SARS.

In addition, WHO has issued the following advice following the finding of coronavirus-infected animals in southern China; “As a precautionary measure, persons who might come into contact with these species or their products, including body fluids and excretions, should be aware of the possible health risks, particularly during close contact such as handling and slaughtering and possibly food processing and consumption.”

# 3. Stability and resistance of the SARS coronavirus

Data on the stability of the SARS-CoV on surfaces and in the environment were briefly discussed. Preliminary findings have been summarized by the WHO multi-centre collaborative network on SARS diagnosis.[54]

Virus is stable in faeces and urine at room temperature for at least 1-2 days. Virus is stable for up to 4 days in stool from patients with diarrhoea because of its higher pH compared to normal stool. Data from the Chinese University in Hong Kong indicated that SARS-CoV has been isolated from stool on paper, a Formica surface and a plastered wall after 36 hours, on a plastic surface and stainless steel after 72 hours, and after 96 hours on a glass slide. Hospital environmental samples from a number of sites, including walls and the ventilation system, tested PCR positive in Canada.

Virus loses infectivity after exposure to different commonly used disinfectants and fixatives. Heat at 56°C rapidly kills approximately 10 000 units of SARS-CoV per 15 minutes.

Participants agreed there is need for additional guidance on environmental decontamination in the context of SARS, particularly for the effective cleaning of hospitals and residential buildings that is good enough to prevent the transmission of SARS-CoV and other common infections while remaining practical.

As control of "close contact" spread is effective and we move towards eradication any environmental contribution becomes more important. Low exposure of large populations may be adequate for continued transmission.

Operational research priorities[55] needed to build the evidence for an environmental reservoir of SARS-CoV include:

- further investigation of cases with no credible history of exposure
- analysis of the role of the environment in "close contact" transmission to determine the attributable risk associated with person-to-person transmission versus contact (fomite) transmission
- determination of the efficiency of environmental transmission (some work has already been done on virus stability outside the human host, above).

# VIII. Cross-cutting issues

Participants identified a number of cross-cutting issues needing resolution so that effective collaboration can occur at the international level. Such collaboration is essential if SARS is to be defeated as individual countries will not have the data or expertise to determine the necessary information to design effective control measures. The degree of information exchange between clinicians, laboratory experts and epidemiologists has varied across the Centres that have experienced the largest number of SARS cases, leading to gaps in understanding of key determinants of the risk of SARS and its epidemiology. Participants agreed that there was a need to agree on a process for closer global collaboration between Centres. It was also agreed this would be facilitated by a set of principles governing confidentiality and the use of data, and publication rights. However, global collaboration can only proceed effectively if there is a coordinated approach to the investigation of SARS at national and local levels.

Public health decision-makers need timely access to information for action. Those responsible for the health of the public need to ensure clinical, laboratory, epidemiological and other resources are efficiently coordinated to best respond and manage an outbreak and to evaluate these activities. This includes the undertaking of well-coordinated, priority studies to generate the information needed for public health action.

Within WHO there is also a need to facilitate closer collaboration between the epidemiology, laboratory and clinical networks at policy, planning and operational levels to address public health priorities in the containment and control of SARS.

Participants agreed in principle to share data internationally and to undertake multi-country work so that all countries can make public health decisions about SARS based on evidence and international good practice.

WHO was specifically tasked with achieving consensus among Centres on their participation in developing a global minimum data set for international analysis in order to better describe the epidemiology of SARS (see III.3), to work with Centres to analyse the global data set and to present these findings as a consensus statement by the partnership at the WHO Global Conference on Severe Acute Respiratory Syndrome, Kuala Lumpur, Malaysia, 17-18 June 2003. A consensus presentation from this partnership would be a powerful demonstration of global collaboration and the power of epidemiological analysis for public health policy development.

The data set will be set up initially to refine estimates of the incubation period. In the next phase, it should also include demographic, clinical, epidemiological and laboratory data elements that accommodate all the key epidemiological questions relevant to SARS and be designed in accordance with a set of specific objectives and surveillance standards.

# References


1 Drosten C, Günther S, Preiser W, van der Werf S, Brodt H R, Becker S et al. Identification of a novel coronavirus in patients with severe acute respiratory syndrome. *New England Journal of Medicine,* 2003, 348:1967–1976. (Published online 10 April 2003 )

2 World Health Organization. Use of laboratory methods for SARS diagnosis. http://www.who.int/csr/sars/labmethods/en/

3 Peiris JSM, Chu CM, Cheng VC, Chan KS, Hung IFN, Poon LLM et al. Clinical progression and viral load in a community outbreak of coronavirus-associated SARS pneumonia: a prospective study. *Lancet,* 2003, 361:1761–1766. (Published online 9 May 2003 )

4 World Health Organization. Management of severe acute respiratory syndrome (SARS). Revised 11 April 2003. http://www.who.int/csr/sars/management/en/

5 Donnelly CA, Ghani AC, Leung GM, Hedley AJ, Fraser C, Riley S et al. Epidemiological determinants of spread of causal agent of severe acute respiratory syndrome in Hong Kong. *Lancet* , 2003, 361:1761–1766. (Published online 7 May 2003)

6 Gay N, Ma S. Presentation on the modelling of data from Singapore, Global Meeting on the Epidemiology of SARS World Health Organization, Geneva, Switzerland, 16–17 May 2003.

7 Lim W, Government Virus Unit, Department of Health Hong Kong SAR. Presentation at the epidemiology breakout session, WHO Global Conference on Severe Acute Respiratory Syndrome, Kuala Lumpur, Malaysia, 17–18 June 2003.

8 World Health Organization. WHO hospital discharge and follow-up policy for patients who have been diagnosed with severe acute respiratory syndrome (SARS). Revised 28 March 2003. http://www.who.int/csr/sars/discharge/en/

9 World Health Organization. Update 49 – SARS case-fatality ratio, incubation period. http://www.who.int/csr/sars/archive/2003_05_07a/en/

10 World Health Organization. Global surveillance for severe acute respiratory syndrome (SARS). *Weekly Epidemiological Record,* 2003, 78:100–110.

11 Breiman RF, Evans MR, Preiser W, Maguire J, Schnur A, Li A et al. Role of China in the quest to define and control severe acute respiratory syndrome. *Emerging Infectious Diseases,* 2003, 9:1037–1041.

12 Ministry of Health, Welfare and Food, Hong Kong SAR. Transcript of SHWF on the findings of an investigation of severe acute respiratory syndrome outbreak at Amoy Gardens (Parts 1 and 2), 17 April 2003. http://www.info.gov.hk/gia/general/200304/17/0417290.htm and http://www.info.gov.hk/gia/general/200304/17/0417308.htm

13 Schabas R. SARS: prudence, not panic. *Canadian Medical Association Journal,* 2003, 168:1432–1434. (Published online 23 April 2003)

14 McIntosh K. Coronaviruses: a comparative review. *Current Topics in Microbiology and Immunology*,1974, 63:85–129.

15 Sung J. Atypical presentations and extra-pulmonary manifestations of SARS. Presented at the SARS Clinical management Workshop, 13–14 June 2003, China, Hong Kong SAR.

16 World Health Organization. Summary table of SARS cases by country, 1 November 2002–7 August 2003. http://www.who.int/csr/sars/country/en/country2003_08_15.pdf

17 Guan Y, Zheng BJ, He YQ, Liu XL, Zhuang ZX, Cheung CL et al. Isolation and haracterization of viruses related to the SARS coronavirus from asnimals in southern China. *Science*, 2003, 302:276–278. (Published online 4 September 2003 )

[18] Tsang T. Environmental issues. WHO Global Conference on Severe Acute Respiratory Syndrome (SARS), Kuala Lumpur, Malaysia, 17 - 18 June 2003. http://www.who.int/csr/sars/conference/june_2003/materials/presentations/en/environmental.pdf

[19] Ng SKC. Possible role of an animal vector in the SARS outbreak at Amoy Gardens. *Lancet,* 2003, 362:570–572.

[20] World Health Organization, Communicable Disease Surveillance and Response. *Severe acute respiratory syndrome (SARS): Status of the outbreak and lessons for the immediate future.Geneva, 20 May 2003*. http://www.who.int/csr/media/sars_wha.pdf

[21] Hon KLE, Leung CW, Cheng WTF, Chan PKS, Chu WCW, Kwan YW et al. Clinical presentations and outcome of severe acute respiratory syndrome in children. *Lancet,* 2003, 361:1701–1703. (Published online 29 April 2003).

[22] Wang M, Du L, Zhou D–H, Di B, Liu Y–F, Qin P–Z et al. Study on the epidemiology and measures for control of severe acute respiratory syndrome in Guangzhou City (English Abstract). In *Collection of papers on SARS published in CMA Journals*. Beijing: Chinese Medical Association, 27 May 2003, p50.

[23] Peiris JSM, Lai ST, Poon LLM, Guan Y, Yam LYC, W Lim W et al and SARS study group. Coronavirus as a possible cause of severe acute respiratory syndrome. *Lancet,* 2003, 361:1319–1325.

[24] Ho LC. SARS and pregnancy. Experience in Hong Kong March – May 2003. SARS Clinical Management Workshop, 13–14 June 2003, China, Hong Kong SAR.

[25] World Health Organization. World Health Organization issues emergency travel advisory, 15 March 2003. http://www.who.int/csr/sars/archive/2003_03_15/en/

[26] World Health Organizaiton. Update 11 - WHO recommends new measures to prevent travel-related spread of SARS, 27 March 2003. http://www.who.int/csr/sars/archive/2003_03_27/en/

[27] Poutanen SM, Low DE, Henry B, Finkelstein S, Rose D, Green K et al. Identification of acute severe respiratory syndrome in Canada. *N ew England Journal of Medicine,* 2003, 358:1995–2005. (Published online 30 April)

[28] Varia M, Wilson S, Sarwal S, McGeer A, Gournis E, Galanis E, Henry B, for the Hospital Outbreak Investigation Team. Investigation of a nosocomial outbreak of severe acute respiratory syndrome (SARS) in Toronto, Canada. *Canadian Medical Association Journal*, 2003,169:285–292.

[29] SARS Investigation Team, CDC; Wallington T, Berger L, Henry B, Shahin R, Yaffe B, Toronto Public Health; Mederski B, Berall G, North York General Hospital; Christian M, McGeer A, Low D, University of Toronto; Wong T, Tam T, Ofner M, Hansen L, Gravel D, King A, Health Canada. Update: Severe Acute Respiratory Syndrome – Toronto, 2003. *Canada Communicable Disease Report,* 2003, 29:113–117.

[30] Ofner M, Lem M, Sarwal S, Vearncombe M, Simor A and SARS Investigative Team, CDC. Cluster of severe acute respiratory syndrome cases among protected health care workers – Toronto, Canada, April 2003. *Morbidity and Mortality Weekly Report,* 2003, 52:433–436.

[31] Health Canada. SARS Epidemiologic Summaries: April 26, 2003. SARS among Ontario health care workers. http://www.hc-sc.gc.ca/pphb-dgspsp/sars-sras/pef-dep/sars-es20030426_e.html

[32] World Health Organization. SARS outbreak in the Philippines. *Weekly Epidemiological Record,* 2003, 78:189–192.

[33] Health Canada Summary of Severe Acute Respiratory Syndrome (SARS) Cases: Canada and International, 16 April, 2003. http://www.hc-sc.gc.ca/pphb-dgspsp/sars-sras/eu-ae/sars20030416_e.html

[34] Chinese Center for Disease Control and Prevention. Overview of epidemics and responses to the Severe Acute Respiratory Syndrome (SARS) in the People's Republic of China. 16 June, 2003.

[35] World Health Organization. Influenza A(H5N1) in Hong Kong Special Administrative Region of China, 19 February 2003. Disease outbreak reported. http://www.who.int/csr/don/2003_2_19/en/

[36] He J-F, Peng G-W, Zheng H-Z, Juo H-M, Liang W-J, Li L-H et al. An epidemiological study on the index cases of severe acute respiratory syndrome which occurred in different cities in Guangdong province (English Abstract). In *Collection of papers on SARS published in CMA Journals*. Beijing: Chinese Medical Association, 27 May 2003, p44.

[37] Breiman R. Chain of Transmission Pt "ZF". Presentation at the *Epidemiology for Public Health* breakout session, WHO Global Conference on Severe Acute Respiratory Syndrome, Kuala Lumpur, Malaysia, 17-18 June 2003.

[38] Seto WH. SARS: Nosocomial infection and infection control. SARS Clinical management Workshop, 13-14 June 2003, China, Hong Kong SAR.

[39] Ho PL. Risk factors for SARS in HCWs following intubation of SARS patients – a retrospective multi-centre study. SARS Clinical management Workshop, 13-14 June 2003, China, Hong Kong SAR.

[40] Riley S, Fraser C, Donnelly CA, Ghani AC, Abu-Radda LJ, Hedley AJ et al. Transmission dynamics of the etiological agent of SARS in Hong Kong: Impact of public health interventions. *Science,* 2003, 300:1961-1966.

[41] Tsang KW, Ho PL, Ooi GC, Yee WK, Wang T, Chan-Yeung M et al. A cluster of cases of severe acute respiratory syndrome in Hong Kong. *New England Journal of Medicine,* 2003, 348:1977-1985. (Published online 30 April 2003)

[42] Tsang T, Lai-Yin T, Pak-Yin L, Lee M, Wu JS, Wu YC, Chiang IH, Chen KT, Hsu KH, Chen TJ, Lee LT, Twu SJ, Chunsuttiwat S, Sawanpanyalert P, Ungchusak K, Chaovavanich A, Ministry of Public Health, Thailand, Ministry of Health of Vietnam, WHO SARS Investigative Team,Vietnam. CDC SARS Investigative Team. Update: Outbreak of Severe Acute Respiratory Syndrome — Worldwide, 2003. *Morbidity and Mortality Weekly Report,* 2003, 52:241-248.

[43] Tsang T. Routes of transmission. SARS Clinical management Workshop, 13-14 June 2003, China, Hong Kong SAR.

[44] Leo YS, Chen M, Heng BH, Lee CC, Paton N, Ang B, Choo P, Lim SW, Ling AE, Ling ML, Tay BK, Tambyah PA, Lim YT, Gopalakrishna G, James L, Chew SK, Tan CC. Severe Acute Respiratory Syndrome – Singapore, 2003. *Morbidity and Mortality Weekly Report,* 2003, 52;405-411.

[45] World Health Organization. Update 83 – One hundred days into the outbreak, June 18. http://www.who.int/csr/don/2003_06_18/en/

[46] Hsu L-Y, Lee C-C, Green JA, Ang B, Paton NI, Lawrence L et al. Severe acute respiratory syndrome (SARS) in Singapore: clinical features of index patient and initial contacts. *Emerging Infectious Diseases,* 2003, 9:713-717.

[47] Anderson RM, May RM. *Infectious Diseases of Humans: Dynamics and Control*. Oxford: Oxford University Press, 1991.

[48] Lipsitch M, Cohen T, Cooper B, Robins JM, Ma S, James L et al. Transmission Dynamics and Control of Severe Acute Respiratory Syndrome. *Science,* 2003, 300:1966-1970. (Published online 23 May 2003)

[49] Wallinga J. Presentation at the Global Meeting on the Epidemiology of SARS World Health Organization, Geneva, Switzerland 16-17 May 2003.

[50] Fouchier RAM, Kuiken T, Schutten M, van Amerongen G, van Doornum GJJ, van den Hoogen BG et al. Aetiology: Koch's postulates fulfilled for SARS virus. *Nature,* 2003, 423:240.

[51] The Possible Role of Animals breakout session, WHO Global Conference on Severe Acute Respiratory Syndrome, Kuala Lumpur, Malaysia, 17–18 June 2003. http://www.who.int/csr/sars/conference/june_2003/materials/presentations/en/roleofAnimals180603.pdf

[52] Cyranoski D, Abbott A. Virus detectives seek source of SARS in China's wild animals. *Nature,* 2003, 423:467.

[53] News24. SARS found in pigs and snakes. 4 June 2003. http://www.news24.com/News24/World/News/0,,2-10-1488_1368983,00.html

[54] World Health Organization. First data on stability and resistance of SARS coronavirus compiled by members of WHO laboratory network. http://www.who.int/csr/sars/survival_2003_05_04/en/index.html

[55] Synthesis of the Environmental Issues breakout session, WHO Global Conference on Severe Acute Respiratory Syndrome, Kuala Lumpur, Malaysia, 17–18 June 2003 http://www.who.int/csr/sars/conference/june_2003/materials/presentations/en/environmental180603.pdf

# AGENDA

# Global Meeting on the Epidemiology of SARS
# World Health Organization, Room E230, Geneva
# 16 to 17 May 2003

## OBJECTIVES OF THE MEETING

1. Produce a WHO consensus document on our current understanding of the epidemiology of SARS.
2. Identify gaps in our knowledge for the planning of additional epidemiological studies if required.
3. Identify what this partnership can do towards filling those gaps.

Full day meeting (face to face and video linkage) on Friday 16 May to address the key epidemiological questions that will inform future SARS containment and control policy. Participants will be expected to present data and analysis relevant to answering these questions from SARS outbreaks in their countries/regions.

This will be followed on Saturday 17 May by a half day workshop of the secretariat and selected external epidemiologists to synthesize the proceedings of the meeting and key recommendations.

## *Friday 16 May 2003*

### PLENARY SESSION

**09:00-09:15** OPENING REMARKS AND INTRODUCTION

Professor Angus Nicoll (Chair)

Dr David L. Heymann

Dr Guénaël Rodier

**09:15-10:30** DETERMINATION OF KEY DISTRIBUTIONS

- Incubation period
- Infectious period
- Case fatality ratios

FIVE MINUTE PRESENTATIONS BY RELEVANT COUNTRIES

**10:30-11:00** **BREAK**

**11:00-12:15** GENERAL DISCUSSION AND SYNTHESIS BY TOPIC

**12:15-13:00** **LUNCH**

## PLENARY SESSION

**13:00-14:15** INFECTION DYNAMICS

- Routes of transmission
- Subclinical infection and contribution to SARS transmission
- Reproduction number in different transmission settings and under different control strategies
- Animal and/or environmental reservoirs

FIVE MINUTE PRESENTATIONS BY RELEVANT COUNTRIES

**14:15-15:30** GENERAL DISCUSSION AND SYNTHESIS BY TOPIC

**15:30-16:00** **BREAK**

**16:00-16:30** CONTINUATION OF GENERAL DISCUSSION AND SYNTHESIS BY TOPIC

**16:30-17:30** OVERALL SYNTHESIS AND RECOMMENDATIONS

**18:00** **COCKTAIL AT THE MAIN CAFETERIA**

## *Saturday 17 May 2003*

**INFORMAL WORKSHOP**

**09:00-13:00** INFORMAL SESSION AMONG SELECTED PEOPLE TO SYNTHESISE THE MAIN FINDINGS AND PREPARE A DRAFT PAPER FOR CIRCULATION TO ALL PARTICIPANTS FOR COMMENT.

**REFRESHMENTS PROVIDED**

# WORLD HEALTH ORGANIZATION

**Global Meeting on the epidemiology of SARS, WHO/HQ, Room E230, 16 May 2003 Room m505 17 May 2003** **/5**

**23 May 2003**

**Geneva, SWITZERLAND, 16 - 17 May 2003**

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