

CONFIDENTIAL

Testimony to the Select Committee to Inquire into the Handling of the Severe Acute
Respiratory Syndrome Outbreak by the Government and the Hospital Authority

Submitted by Dr. Stephen Kam-cheung Ng, MB,BS, DrPH, DABPed

February 28th 2004

Background

2. At the end of March 2003 when SARS was spreading rapidly at Amoy Gardens, I discussed the outbreak with colleagues in community medicine and several of us, who are all epidemiologists from the University of Hong Kong and the Chinese University of Hong Kong, agreed to form an Epidemiologic Task Force to assist the Hong Kong Government investigate this outbreak on a pro bono basis.
3. At that time the Department of Health (DH) had already refused several offers of help from individual colleagues and was not sharing any Amoy Gardens data with either University. Since timely epidemiologic investigation was critical in solving the puzzle, I decided not to contact the DH or the Health, Welfare and Food Bureau (HWFB) again but instead to approach the Chief Executive Mr. C.H. Tung to get his help to obtain Amoy Gardens data.

4. Through the intervention of Dr. Victor Fung, I had a meeting with Mr. Tung in the afternoon of April 3rd 2003 at around 2.30 pm.
5. During the meeting I explained to Mr. Tung that the DH might be short-handed in their epidemiologic investigation as they needed to go through a lot of data in a short time. I explained that there were only a handful of qualified epidemiologists in Hong Kong and those of us who worked outside the government were willing to help for free. If we were allowed access to data we could speed up the investigation. Mr. Tung was receptive to the idea. He called Dr. E.K. Yeoh, Secretary for Health, Welfare and Food (SHWF) on the phone and arranged for me to see him immediately.
6. I met Dr. Yeoh in his office at around 3 pm on April 3rd 2003. I explained to him the composition of the Epidemiologic Task Force and our desire to help. I also told him the difficulties of getting Amoy Gardens data from the DH. He told me that he had asked Dr. Paul Saw, former deputy Director of Health, to come out of retirement to co-ordinate the DH's SARS investigations. I then suggested that the task force be assigned to work with Dr. Saw. Dr. Yeoh agreed but said he had to first discuss the arrangement with Dr. Margaret Chan, then Director of Health.

April 4th 2003

7. I received a phone call in the morning from Dr. Paul Saw asking me to go to his office the following week to look at some SARS data.
8. Shortly afterwards I received a call from Dr. Sarah Liao, Secretary for the Environment, Transport and Works (SETW) asking me if I could help her review some data from Amoy Gardens that evening. Mr. Tung had informed her earlier that I was available to help. Dr. Liao is a personal friend but I did not realize she was involved in the SARS investigations until she called me. I told her I was available and she said she would call me back after discussing with Dr. Yeoh.
9. I received a call from Dr. Liao's secretary later in the afternoon asking me to attend a meeting at around 6 pm in Dr. Liao's office. The meeting was scheduled to prepare an updated report to the Chief Executive on April 5th 2003. I arrived on time at Dr. Liao's office. Present at the meeting were Dr. Liao, her

personal assistant, two ladies from her bureau, Dr. Thomas Tsang, Dr. Paul Saw, and myself. During this meeting results from examination of the sewage system of Block E at Amoy Gardens were discussed. No leakages were detected other than a crack on a vent pipe on the 4th floor. I was also given epidemiologic data of the Amoy Gardens outbreak from March 21st to April 3rd 2003.

10. I first suspected the involvement of rats in the Amoy Gardens outbreak on April 2nd 2003 after going through all the newspaper reports I could gather. After looking at the Amoy Gardens outbreak distribution my suspicion grew stronger. The outbreak looked like a common source epidemic with very unusual speed and distribution that cannot be explained by human-to-human transmission alone. An infected animal vector was very likely. I shared this view with the other participants at the meeting.
11. At that time the environmental team also suspected the involvement of pests such as rats and cockroaches and had started trapping rats and cockroaches in Amoy Gardens. Their view however was that these pests, especially cockroaches, acted as passive carriers only. My belief was that unless these pests were actively infected they could not have caused such a massive outbreak as a tremendous amount of virus was needed and some mechanism of amplification was necessary.
12. I suggested that they perform autopsies on trapped rats and test their serum for antibodies to the SARS coronavirus to find out if they were infected.
13. The group decided to meet again the following morning at around 10 am in Dr. Yeoh's office to finalize the report to the Chief Executive.
14. I studied the epidemic curve and distribution of cases by individual blocks at Amoy Gardens that evening at home and became even more convinced that the epidemic was caused by infected rats.
15. Since I gathered from the meeting earlier that there were no confirmed SARS cases between April 2nd to 4th from Amoy Gardens, I was under the impression that the epidemic was over. I therefore thought that Amoy Gardens was safe since according to my hypothesis infected rats recover in about 7 days and the first rats were infected 20 days ago.

April 5th 2003

16. When I was getting ready to go to the morning meeting, I heard over the news that there were new confirmed SARS cases from Amoy Gardens on April 4th.
17. I realized then that the epidemic was not yet over and became very worried. If rats were still spreading SARS, Amoy Gardens residents would be living in a very dangerous environment.
18. I hurried over to Dr. Yeoh's office at around 9 am and told him my reasoning and concern. I asked that the rest of the Amoy Gardens residents be evacuated immediately. He told me that the evidence so far was not sufficient to warrant such a drastic move as there were over 17,000 residents living in Amoy Gardens. After this discussion I went to the conference room to wait for the meeting to start.
19. Shortly before 10 am Dr. Paul Saw arrived in an agitated state and announced that rat results were positive. Specifically 4 out of 8 rat droppings and one throat swab were PCR positive. He was quite convinced at that point that rats were responsible for the Amoy Gardens outbreak and had called in Dr. Ellis Trevor, the government veterinarian consultant and Mr. Yuen, head of the Pest Control Unit, to attend the morning meeting.
20. I verified with Dr. Saw that the PCR was correctly performed using SARS coronavirus primers and not rat coronavirus primers. Dr. Saw assured me that the tests were carried out properly.
21. Around 10 am Dr. Thomas Tsang, Dr. Trevor, Mr. Yuen and another colleague from the Pest Control Unit, Dr. SV Lo from HWFB, and a few others arrived for the meeting. They were all told about the rat findings earlier.
22. Everyone in the meeting was worried. We discussed what should be done immediately. My concern was to verify the rat hypothesis with more studies. 4 rats were trapped the previous night. I requested that these 4 rats be autopsied immediately to see if they showed signs of recent coronavirus infection. I described to Dr. Ellis what the possible pathologies were and he left immediately to do the autopsy.

23. Dr. Yeoh joined the meeting shortly after Dr. Ellis left. He was told earlier by Dr. Saw of the rat findings. He was also worried and said: 'I also guessed it was rats, but did not guess it could amplify' (我都估到係老鼠，不過估吾到會 amplify). A discussion followed on the broader ramifications of the spread of SARS by rats. We all agreed that it would deal a severe blow to Hong Kong's economy as travel and trade might be further restricted by foreign countries. Rats and disease reminded people of plague. Hong Kong's image would be tarnished and Hong Kong could lose its status as a world-class city. At one point Dr. Yeoh expressed the fear that there might be riots in Hong Kong.
24. We next discussed the methods of rat elimination. Mr. Yuen estimated that there were at least 400 rats around Amoy Gardens. Trapping was not very efficient as rats had become quite smart. Warfarin, an anticoagulant and the most commonly used rat poison, was not very lethal and rats had to ingest it more than once to bleed to death. The more toxic rat poisons were not environmentally safe. It was decided that the more potent rat poisons be used and that an all out effort be made to trap and kill as many rats as possible.
25. I then suggested various other studies that should be done on rats to further elucidate their mechanisms of disease transmission. I was especially anxious to find out if rats were chronic carriers of the SARS coronavirus. I suggested that rats that were virus positive be kept alive to observe how long the virus stayed active in them.
26. The discussion then moved on to what to say to the public. We all agreed that it would create a big alarm if the public were told that rats spread SARS at Amoy Gardens. After some discussion Dr. Yeoh suddenly suggested that an alternative was not to tell the public anything and just concentrate on killing rats. He thought that it would make no difference whether the public was informed as long as the government was doing all it could to eliminate rats. He further suggested stopping all rat investigations since positive findings would have to be disclosed to the public. On the other hand 'if you don't do anything, there is nothing to tell' (吾做就吾駛講) and he could not be accused of withholding information. The rat hypothesis could be downplayed as just one of the many possibilities as long as there was no confirmation.
27. Objections were raised by some members of the group. Dr. Thomas Tsang

remarked that it had never been possible to keep anything in the DH secret and that the press was already asking questions on results of tests on pests. Dr. Yeoh then said that all those present should keep the rat findings confidential. I said that even if it were possible to keep it secret in Hong Kong, scientists from other places would eventually find out the truth if the rat hypothesis was correct. These objections were ignored. Dr. Saw mentioned that Dr. Trevor was already on his way to perform autopsies on 4 rats. Dr. Yeoh then sent someone to call Dr. Trevor to stop the autopsies. Dr. Trevor however could not be reached on the phone at that time.

28. I raised the point that rats could never be completely eliminated and suggested that all other residents of Amoy Gardens be evacuated under the same pretext as the Block E residents. Dr. Yeoh said he did not have the facilities to house so many people. I asked the possibility of using empty public housing flats but was told that these were not furnished and not ready for occupation. Dr. Yeoh then said 'for the sake of the majority, some people have to be sacrificed' (為左顧全大局，有啲人係要犧牲嘅).
29. I mentioned that at least we should warn people to keep their household rat-safe by closing windows and covering their food. Dr. Yeoh said he would consider this suggestion.
30. Dr. Yeoh then added that I should now understand their reluctance to share data with researchers outside the government. 'Not everyone has a broad overview like you' (吾係個個睇嘢好似你咁全面) he told me.
31. I sensed the compliment was a subtle nudge to coax me into silence. I found myself faced with a dilemma as on one hand I did not want to breach my promise of confidentiality but on the other I felt duty-bound to warn the public of potential danger. I decided that the only honest thing to do was to extricate myself from further involvement in official investigations and to remain an independent observer. So I told Dr. Yeoh that since there was nothing further for me to do I would terminate my involvement with the investigation. Dr. Yeoh said that I could, if I wanted, stay to look at some other data. I thanked him but declined. I left the meeting at around noon while the rest stayed to discuss the report to the Chief Executive.

April 7th 2003

32. After mulling over the issues during the weekend I wrote a letter to Dr. Yeoh on April 7th 2003 urging him not to give up the rat investigations. This letter was also copied to Dr. Thomas Tsang and Dr. Sarah Liao. I sent the letter off by fax, email, and post (**Appendix III**).
33. I sent an email to Dr. Thomas Tsang asking him to take advantage of the evacuation of Block E and start trapping rats in individual units to re-enact the outbreak distribution. This email and his reply are in **Appendix IV**.
34. I sent another email to Dr. Liao explaining my hypothesis and asked her to follow up on my letter to Dr. Yeoh. This email and her reply are in **Appendix V**.

April 8th 2003

35. Dr. S.V. Lo called me in the morning to thank me on behalf of Dr. Yeoh for my letter of April 7th and told me that the decision not to continue the rat investigation was reversed shortly after I left the meeting. He assured me that the DH would do all it could to find out the truth.
36. I then requested that I be allowed to work on further rat investigations and told Dr. Lo that I had previously arranged with Prof. Yuen Kwok Yung of the University of Hong Kong to do serum antibody tests on rats. I requested samples of rat sera and Dr. Lo promised that these would be delivered to Prof. Yuen the following day.
37. I first discussed the rat hypothesis with Prof. Yuen around April 4th 2003 and asked him whether he could perform rat serum antibody tests for SARS. He said he would consult his colleagues and later told me that colleagues from the Department of Zoology, University of Hong Kong could help us out. I called Prof. Yuen after I spoke with Dr. Lo and informed him that rat specimens from Amoy Gardens would be sent to him the following day and asked him to get ready to perform the serum antibody tests.

April 9th 2003

38. I telephoned Prof. Yuen in the afternoon and found out that he had not received

any rat specimens.

39. I called Dr. Lo and he apologized that because of regulations of the DH no specimens could be given to Prof. Yuen until their own investigations were over.
40. I then called Prof. Yuen to tell him that the DH would not be sending him any specimens at this time.

Subsequent Development

41. I subsequently tried to find out results of rat studies carried out by the DH but was told that these were confidential information.
42. I followed further development through newspaper articles and wrote a scientific paper 'Possible role of an animal vector in the SARS outbreak at Amoy Gardens' that was published in the August 16th 2003 issue of the Lancet (**Appendix VI**).
43. I learned later from Dr. Trevor that he did not receive any phone call on April 5th 2003 asking him to stop the rat autopsies. He autopsied those 4 rats but have since not done any further rat autopsy. The DH also confirmed later that a total of 4 rats from Amoy Gardens were autopsied with negative findings.
44. From various other sources I learned that about 40 rats were trapped from Amoy Gardens. The DH examined throat swabs and droppings and performed about 20 serum tests. Of the 62 samples tested (which included serum, swabs, and droppings), 6 droppings and 2 throat swabs were PCR positive for the SARS coronavirus. The rest of the tests were negative.
45. To thoroughly investigate the rat hypothesis a large number of rats (preferably in the hundreds) should be examined. There are probably more than 400 rats in Amoy Gardens (the usual estimate is between 3 to 10 rats per inhabitant). Even if there were only 400 rats, a sample of 40 represents only 10% of the population. It is imperative that all 40 rats trapped be autopsied as soon as possible (except those from which live SARS coronavirus was isolated in which case they should be observed for a period of time) since rats recover very quickly from a coronavirus illness and pathologic changes may disappear after about a month. To autopsy only 4 rats out of the 40 trapped is inadequate and inexplicable. Furthermore, for each rat trapped the following tests should be done: i) PCR

and viral culture on throat and rectal swab, urine, and blood (8 tests per rat); ii) serum antibody tests (1-2 tests per rat depending on the method used). For the 40 rats trapped there should be at least 360 tests. In addition each sample of rat dropping picked up at Amoy Gardens should be examined by both PCR and viral culture for presence of the SARS coronavirus. The total number of tests that should have been done given a sample of 40 rats is therefore close to 400. The DH performed only a small fraction of the necessary tests and concluded that they have ruled out infection in rats. This is scientifically untenable. The limited investigation cannot be attributed to a lack of resources as both the University of Hong Kong and the Chinese University of Hong Kong are willing to take up some of the analyses at no cost to the DH.

The Issues

46. At issue here is not whether the rat hypothesis is correct. Very little supporting evidence was available on April 5th 2003 and it would have been perfectly legitimate for Dr. Yeoh to question the validity of the rat hypothesis on scientific grounds and not take any drastic action that would undermine public confidence. However, enough suspicion was raised on April 5th 2003 that rats were either actively infected or passive carriers of the SARS coronavirus to warrant telling the public to take simple precautions such as closing windows and covering up their food to protect their health. No such advice was given. Instead people were told to keep their windows open to let in fresh air. After April 5th there were 72 additional SARS cases from Amoy Gardens. Whether a different course of action would have prevented any of these cases is anybody's guess. It is a matter for this Committee to decide whether the wanton exposure of the public to potential health hazard constitutes a gross dereliction of duty of a public health official.
47. No government can hope to promote public health and control infectious disease without the cooperation of its citizens. The spread of diseases is determined to a large extent by personal behavior. Every member of the community has to cooperate to win the war. For individuals to take appropriate actions, they must understand the rationale behind them. Open and full disclosure of information is therefore mandatory. To sacrifice public health for economic and political reasons is foolhardy and unconscionable, as public health ultimately underpins economic development and political stability. Both China and Hong Kong have suffered huge losses from SARS because of official secrecy. As this Committee

will find out for itself, the absence of transparency was not limited to the Chinese authorities on the Mainland.

48. As a scientist I find it inexcusable that Dr. Yeoh, having seen and agreed that preliminary findings support a possibility that rats may be actively infected and transmitting SARS, chose to initially stop and later curtail further rat research for economic and political considerations. The outbreak of SARS at Amoy Gardens is a mystery that still intrigues the world. Dr. Yeoh has deprived Hong Kong a chance to contribute unique and important knowledge to humanity. It would have been a big contribution either to corroborate or refute the rat hypothesis. Recently scientists from both the United States (**Appendix VII**) and Canada (**Appendix VIII**) have successfully infected mice with the SARS coronavirus to produce a mild illness that lasts about 7 days. It is therefore biologically plausible that rodents are vectors of SARS. As recent events in Guangzhou demonstrate, the rat hypothesis is still an active possibility and Hong Kong could have prevented the new outbreak or at least helped in the search for a source of infection had more rat studies been carried out in the Amoy Gardens investigation.

Personal Note

49. My original intention to get involved in the SARS investigation was simply to help the Hong Kong Government solve a complicated puzzle to expedite the removal of the WHO Travel Advisory on Hong Kong. I promised to keep official epidemiologic data confidential and had no intention to publish any paper out of this research. After all other efforts failed I finally wrote the Lancet article to get the rat hypothesis out to the scientific community to stimulate further research. I have honored my commitment and did not use any confidential data in my article.
50. I choose to testify before this Committee because this is the right forum to discuss all the relevant issues. I did not disclose the incidents described here to the previous Expert Committee on SARS because I was waiting for an opportunity to give my testimony under oath. We can learn from experience only if we realize what went wrong. I hope by examining what actually took place painful lessons will be learned and unfortunate mistakes not be repeated. There are no possible personal gains for me testifying. On the contrary I am doing it at considerable personal sacrifice and risk. My personal concerns

however are immaterial in the face of a devastating illness that threatens the lives of millions of people. This, I recall, was the reason I became a public health physician.

April 7, 2003

Dr. E.K. Yeoh
Secretary for Health, Welfare and Food
The Hong Kong SAR Government
Hong Kong

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Dear Dr. Yeoh,

Thank you for allowing me to work on the outbreak investigation of SARS at Amoy Gardens. I believe I have presented to your team a viable hypothesis that has been initially corroborated by evidence so far collected. Further work needs to be done to elucidate epidemiologic risk factors and mode of transmission from host to human. In addition more studies on infection and transmission among rats are paramount. We are at the epicenter of the world epidemic and we owe it to humanity to elucidate every single aspect of this disease that we are capable of doing.

Whether rats are the cause or result of the initial outbreak at Amoy Gardens is important for control of future outbreaks. I therefore urge your team to start detailed autopsy studies of rats found at Amoy Gardens, since pathological changes within rats disappear 30 days after infection by other rat coronaviruses. We should still be able to determine approximate date of infection of rats caught at this time. Further delay of autopsy studies would lose forever a valuable chance to elucidate the mode of transmission of this very deadly virus and the origin of the Amoy Gardens outbreak. Serological tests of rats should also be done with other viral studies to determine length of infection, existence of immunity, and more importantly the existence or not of a carrier state. Needless to say, rats from other parts of Hong Kong should also be studied and a rat monitoring system be set up in Hong Kong.

Case-control studies of Amoy Gardens residents should also be done to elucidate other risk factors for infection. Since we are still unsure how viruses are transmitted from rat to man, we must look into all aspects of difference between cases and controls, especially those living in very similar environments such as household members. I believe the

answer lies in daily personal habits such as time of work, time of use of toilet or kitchen, hygiene, breakfast habit, etc. which allow patients to come into contact with rat saliva or excreta within 3-6 hours of deposit.

For prevention I think rat control is of utmost importance. This does not consist only of environmental removal of rats. Households should be made rat-proof and residents alerted to close their windows at night to prevent rat entrance (in contrast to present recommendation to leave windows open for better ventilation.) In addition sewage should be disinfected before being discharged from each household. For example bleach can be added to the toilet bowl before each flushing. Chlorination of the salt water flushing system should be strengthened. Garbage should be disposed quickly and safely out of reach of rats. These measures will, I believe, go a long way to cut down on the number of newly infected cases at Amoy Gardens and other areas where similar transmission may arise.

On a more positive note I think it is unlikely that rat contamination occurred through the sewage system. Our flush water is chlorinated and viral discharge from a single patient, no matter how big, would be diluted in the sewage system. The suspected index patient did not lead to any outbreak in his own apartment, nor did any other SARS patients in their own building. So my hypothesis is that the rat infection at Amoy Gardens was an unfortunate fluke and occurred in the apartment of the brother of the suspected index patient. He probably left some infected material such as tissue paper, left over food, etc. in the garbage where it was picked up by a rat. If this is true then the chance of another outbreak like Amoy Gardens will be greatly decreased with rat control and tightened garbage handling procedures.

Epidemiologic work on this outbreak must continue at full speed, since we have a responsibility to ourselves and the rest of the world community. WHO is eagerly watching and waiting for our results. Our neighbors in China and South-east Asia will benefit greatly from our experience. We have a lead-time in this fight and we must not waste it. While I know there are political and administrative difficulties that I may not comprehend, I think 'see no evil' is a greater moral lapse than 'say no evil.' Moreover, researchers in other countries may soon find out what we have found.

I want to congratulate the dedication and hard work of your team. They have accomplished a lot in the last few weeks. I will be happy, as always, to assist in any further work that needs to be done.

I remain,

Yours truly,

A handwritten signature in black ink, appearing to read 'Stephen K. Ng', with a stylized flourish at the end.

Stephen K. Ng, MB,BS, DrPH, DABPed

c.c. Dr. Thomas Tsang

Dr. Sarah Liao

[REDACTED]

寄件者: "stephen ng" <[REDACTED]>
收件者: <thomas_[REDACTED]>
副本: <[REDACTED]>
傳送日期: 2003年4月7日 PM 03:49
主旨: Going forward

Dear Thomas,

Sorry I did not have much time to talk to you during the last two meetings. I know you are a well-trained epidemiologist and can handle all the necessary work to further this investigation if you are given enough support. This investigation must go on, at full speed, without interference from political considerations. Whether the results will be announced is immaterial to collecting the data and documenting carefully what actually happened. We owe it to posterity and history to do the right things.

What is urgently needed now are careful studies of the rats. I suggest that rat cages be put within apartments on all floors of Block E to capture as many Block E rats as possible. They are hungry now and should be easier to catch. Preferably there should be a mix of patient apartments and control apartments in Block E. Since we know that rats are territorial and habitual animals, hopefully they will re-enact the crime. Needless to say you should leave some windows (those closest to outside pipes) open in the apartments to facilitate entry of rats. This is the most likely mode of entry and transmission. If you can install video cameras on the most affected floors and apartments it would also help to understand their behavioral pattern and what they have touched.

If you need help drop me an email or call me at [REDACTED]

[REDACTED] Happy Hunting!

Stephen

No masks required! Use MSN Messenger to chat with friends and family.
<http://go.msnserver.com/HK/25382.asp>

>
 >

> CC:

> |[]

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Printed: Monday, January 19, 2004 2:40 AM

From : <sliao [REDACTED]>
 Sent : Tuesday, April 8, 2003 8:26 AM
 To : "stephen ng" <[REDACTED]>
 Subject : Re: Fwd: Update April 4, 03

Dear Stephen,

Thanks for the memo.

The state of affair is panicky- we must have calm and cool headed scientists and doctors to conduct thorough investigations. It is most dangerous to draw conclusions before the hypothesis is put to the test. I am sure it will be very useful to bounce ideas with you. The problem right now is to find the time.

Please keep in touch by email.

Sarah

"stephen ng"

<[REDACTED]>

To: sliao [REDACTED]

cc:

07.04.2003 01:25 PM

Subject: Fwd: Update April

4, 03

☐ Urgent

☐ Return
Receipt

Dear Sarah,

I forwarded this email to you last Friday using my china server. Apparently you did not receive it. I am sending it to you again to clarify my arguments. I hope you will consider carefully what I put in my letter to EK today.

Regards,

Stephen

>From: "skcng" <[REDACTED]>
 >To: "ng stephen" <[REDACTED]>, [REDACTED]
 >[REDACTED], [REDACTED] <[REDACTED]>
 >Subject: Update April 4, 03
 >Date: Fri, 4 Apr 2003 10:38:22 +0800
 >
 >Dear All,
 >
 >Dr. Victor Fung, Prof. Lap-chee Tsui and I met with Mr. Tung for about 20
 >minutes yesterday. Obviously he was quite stressed to have some answers
 >to
 >the epidemic and welcomed our help. He called EK on the phone and we went
 >over to see EK immediately. He told us that he has requested Paul Saw to
 >come out of retirement to co-ordinate the epidemic investigation. He said
 >Paul was a seasoned epidemic investigator but may not be up-to-date with

>sophisticated data analysis. I took that up and said that it will then be

>appropriate that we work with Paul (who probably is a volunteer like us)
>to

>look over the investigation. I said specially that because they are busy
>with Amoy we would like to look at [REDACTED]. He was quite receptive to

>that idea and said that he would handle the situation with Margaret and
>let

>us know thru Thomas Tsang.

>
>I don't know how soon we can start working on the data collection at

M Hotel >[REDACTED] or look at data on Amoy. But I guess we better be prepared
>ourselves by listing the research questions that we want to be answered.

>There are a lot of questions on [REDACTED] that the Amoy case brings up.

M Hotel >[REDACTED] actually may be more educational since it is a small outbreak.

>Coming back to the Amoy case I guess there are several important points to

>consider for any hypothesis:

>
>1. Is it single source and from where.

>
>I guess we all agree that it is single source. From where or whom is not
>settled. Now there is this theory of urination at the construction site.

>EK said that the timing of contamination coincides with the renal
>patient's

>visit to his brother.

>
>2. How does this single patient pass his viruses to the environment?

>
>Urine, sputum, droplet? If it is aerosol then it must have occurred
>outside Block E.

>
>3. Is this single contamination of sufficient quantity to deliver
>sufficient dose to infect over 200 people?

>
>I guess if it is airborne, waterborne, or foodborne this is possible. Any

>other method, such as passive carriage by rodents or insects (as suggested

>by EK) would probably need amplification of dose, ie infection of the
>carrier. EK does not believe in infection of the carrier. He thinks the
>patient left enough virus for cockroaches to carry around to all the
>blocks. His theory is that roaches were the carriers and visited all the
>infected household to spread the disease by contact.

>
>
>3. Distribution system

>
>Airborne or waterborne are both effective distribution systems from a
>single source. Airborne is definitely possible here. We are not thinking

>about foodborne at this point. Waterborne is more difficult here since 4
>blocks are involved. Therefore anything other than airborne would need a
>sub-distribution system. In this case the most likely sub-distributors are

>rodents and insects.

>
>4. Infection of the patients

>
>Airborne is straightforward. But the challenge is for the single source
>to
>infect all the 200 people and then disappear, as it is likely here looking

>at the epidemic curve. Those infected people have to be at home during
>the

>time of the aerosol formation to be infected. This aerosol formation
>probably did not last very long. We will know about this by looking at
>the

>data. Infection by contact of contaminated surfaces would need a lot of
>contamination for 200 people to be infected. Even cockroaches do not
>wander around all parts of a household. Therefore the kitchen and
>bathroom

>are more likely areas of contamination and therefore housewives should be
>at higher risk. We can tell from the data. I still believe some

>contamination of common source within a block or household, e.g. flush
>water system, is a more likely and efficient distribution system to the
>patients directly. EK said there were a lots of leaks in the pipes at
Amoy
>Garden.
>
>Pass around your thinkings and hope we can start work next week. Anybody
>interested to visit Amoy Gardens?
>
>Stephen

No masks required! Use MSN Messenger to chat with friends and family.
<http://go.msnsnserver.com/HK/25382.asp>

THE LANCET
32 Jamestown Road London NW1 7BY UK

Possible role of an animal
vector in the SARS
outbreak at Amoy Gardens

Stephen K C Ng

Reprinted from THE LANCET
16 August 2003 Vol. 362
No. 9383 Pages 570-572

Hypothesis

Possible role of an animal vector in the SARS outbreak at Amoy Gardens

Stephen K C Ng

A mass outbreak of severe acute respiratory syndrome (SARS) in the Amoy Gardens housing complex in Hong Kong at the end of March, 2003, affected more than 300 residents in less than a month, and has epidemiologists all over the world puzzled about the mode of transmission of this new disease, which until then was thought to be transmitted solely by respiratory droplets. The source of the outbreak was later traced to an individual with SARS who spent two nights at Amoy Gardens. Official explanations failed to account for the large number of residents infected over a wide area within a short time. A powerful environmental mechanism that efficiently amplified and distributed the causal agent must have been at work to cause this outbreak. One such mechanism could be an animal vector, most probably roof rats, that was infected by the index patient and subsequently spread the disease to more than 150 households.

An outbreak of severe acute respiratory syndrome (SARS) caused by a novel coronavirus^{1,2} arose on 21 March, 2003, among residents of Amoy Gardens, a private housing estate in East Kowloon, Hong Kong. When the outbreak ended in mid-April, a total of 321 residents from 15 blocks had been affected.³

The epidemic had all the features of a common source outbreak, and has been classified by Riley and colleagues as a single "super-spread event".⁴ They also postulated that initial exposure happened on March 19.⁴ Since the mean incubation period of SARS is estimated to be 6.4 days,⁵ and the mean serial interval 8.4 days,⁶ most of the 267 people who fell ill in the first 12 days (March 21 to April 1) must have been primary cases from the same exposure.

This initial exposure was traced to a 33-year-old patient of the Prince of Wales Hospital who had chronic renal disease.³ He lived in Shenzhen and visited his brother in unit 7 on a mid-level floor in Block E of Amoy Gardens on March 14 and 19, and stayed overnight. The index patient developed SARS symptoms on March 14, and had two episodes of mild diarrhoea. SARS virus was subsequently isolated from his blood, urine, and stool. The timing and nature of the epidemic suggest that the outbreak was caused by one but not both of his visits.

There are no communal facilities in Amoy Gardens where a large number of residents can congregate. A common source of food or water contamination has not been identified. Airborne transmission is thought to have been unlikely by the WHO team sent to investigate the outbreak.⁷ How could one person have infected more than 200 others during a single visit?

Prevailing hypotheses

Several hypotheses have been proposed to explain the initial outbreak: (1) contaminated sewage droplets were sucked back into bathrooms by powerful bathroom fans through dried-up floor drains, then escaped through windows and

rose as a plume in a narrow light well (chimney effect); (2) passive carriage by pests; and (3) faecal-oral contact through contaminated surfaces.³

None of these hypotheses can satisfactorily account for the three main puzzles of this outbreak: dose, timing, and spatial distribution. Although we do not know the exact amount of virus needed for clinical disease, to infect more than 200 people with a sole contamination (after dilution of the virus upon leaving the host), the index patient would have needed to excrete a tremendous amount of virus into the environment. A single viral discharge from the index patient has a finite window of infectiousness. Although some research has shown that the SARS virus can live for up to 4 days in diarrhoeal fluid,⁸ on dry surfaces the survival time is estimated to be 24–48 h.⁹ The Amoy Gardens epidemic, therefore, would have required delivery of the virus to more than 200 people within 1–2 days.

Moreover, within block E of the building, floors above the one visited by the index patient were affected more than those below. Households in unit 8 (which had its own separate sewage pipe) were more severely affected than unit 7. Neither observation can be fully accounted for by contaminated sewage. Units hundreds of metres away from the index light well, both upwind and downwind, were affected. The initial cases arose in over 150 apartments in 15 blocks covering thousands of square metres and rising over 100 m into the air.

Static versus dynamic common source

The index patient did not have the mobility nor sufficient dose to serve as a static common source of the epidemic. However, the introduction of an intermediate infected vector as a dynamic common source of infection would provide simultaneously an amplifier and distributor of infectious material. Infected vectors can produce live virus for days, providing the large dose required for the outbreak as well as removing the constraint of survival time of the virus. The most likely vector at Amoy Gardens is the roof rat (black rat, *Rattus rattus*).

The rat vector hypothesis

I suggest that the epidemic could have been started on March 14 by a rat from block E going into the apartment visited by the index patient and being infected by contaminated material, such as used tissue paper, leftover food, or excreta. The incubation period in rats infected by

Lancet 2003; **362**: 570–72

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naturally occurring coronavirus such as the sialodacryoadenitis virus is short (2–5 days), thus the first infected rat would have become contagious around March 19. Naturally occurring coronavirus disease is benign, lasting about 7 days, and there is no carrier state.⁸ Secretions from infected rats, such as urine, droppings, or saliva, contain large amounts of virus and are highly contagious.⁹ Roof rats prefer to forage for food above ground in elevated areas.¹⁰ They are also territorial and habitual, and tend to follow the same pathways between their nest and food sources and make return visits time after time.¹¹ Their range of activity when looking for food is about 30–45 m.¹¹ The lightwell between units 7 and 8 of block E is very narrow (1.5 m) with two separate sewage pipes running vertically along the walls close to the bathroom windows. Clothes-lines are installed outside the bathrooms of each unit, and these almost touch one another, providing convenient bridges for rats to travel up and down the building. The first infected rats would probably have been used to visiting the middle and upper floors of units 7 and 8 in block E, and subsequently made many returns to these units, accounting for the unusual concentration of cases on these floors. Roof rats seldom go to the bottom of a building to look for food, thus the lower floors were spared.

The infection could have been passed from rat to man either by rats entering households and leaving infectious material in bathrooms and kitchens, or by contamination of clothing on clothes-lines. The first infected rats could also have spread the virus to other rats in block E and in other blocks, starting an epidemic among rats, and providing the common source for the epidemic in people. That rats further away from block E were less likely to be infected would account for the fact that the epidemic was earliest and most intense in the blocks closest to block E.³ The epidemic started to decline on April 1, 2003, when residents in block E were evacuated, when rats would have recovered from their infection, and when extensive rat trapping and baiting started at Amoy Gardens. However, the epidemic did not end for another 2 weeks, with 54 more cases.

Circumstantial evidence for the existence of a rat vector

Several pieces of circumstantial evidence lend support to the theory of a rat vector. First, virologists strongly suspect that the SARS coronavirus originated from animals and jumped species to infect man. A virus virtually identical to the SARS coronavirus was isolated in Shenzhen, China, from six masked palm civets and a raccoon dog.¹² Antibodies to this virus were also found in the blood of a badger.¹² Thus, the SARS virus can probably survive and infect animals as well as humans.

Second, viral remnants have been detected in four of eight samples of rat droppings found around Amoy Gardens and in the throat or rectal swabs of five housecats, one dog, and at least one rat from the estate.¹³ One of the cats also tested positive for antibodies to the SARS virus.¹³

Third, Amoy Gardens is located in one of the most densely populated areas in Hong Kong, known for poor hygiene and rat infestation.¹⁴ If rat infestation is common, an epidemic in rats can easily cause an epidemic in humans.

Fourth, rats are territorial, mobile, and can reach high floors through external pipes. The sewage and water pipes at Amoy Gardens are located very close to bathroom windows and allow rats easy access into households.

Fifth, viral footprints were found around toilet bowls,

kitchen sinks, and on kitchen floors in several households in block E, but not in bedrooms¹⁴—an unlikely pattern if contamination was caused by man. In other smaller outbreaks elsewhere in Hong Kong, remnants of SARS virus were detected on the surface of a pipe on the roof of an affected building¹⁵ and on the window sill of an unaffected neighbour of a household affected by SARS;¹⁶ both places are unlikely to have been contaminated by people.

Sixth, presenting symptoms and clinical course of patients from Amoy Gardens differed substantially from those of other SARS patients, with more diarrhoea, more admissions to intensive care units, and higher mortality,¹⁷ suggesting a different route of infection, substantial mutation of the virus, or both.

Lastly, coronaviruses are RNA viruses with a great ability to reshuffle genes. The SARS virus has already shown genome sequence differences in different reports.^{18,19} Haijema and co-workers²⁰ successfully incorporated the coat protein gene from a mouse coronavirus into a feline coronavirus (feline infectious peritonitis virus, FIPV) by injecting cat cells with FIPV and adding a gene fragment from a mouse coronavirus. The exchange of the feline coat gene and the mouse coat gene took only several hours and made the new FIPV infectious to mouse cells. If rats at Amoy Gardens had naturally occurring rat coronavirus and were exposed simultaneously to the SARS virus, gene reshuffling might have produced a new SARS virus that was transmissible to both rats and humans.

Weaknesses of the rat vector hypothesis

This theory also has some weaknesses. So far no rodent model for SARS has been established. Autopsies done on four rats caught around Amoy found no signs of active disease.⁷ However, as suggested by Haijema and colleagues, the simultaneous presence of another rat coronavirus might be necessary to successfully infect rats with SARS. Rats might also be able to transmit SARS without overt disease.

Although virus was found in rat droppings, this contamination could have been caused passively. Furthermore, the mode of transmission of the virus from man to rat and back to man is not clear. Finally, to start an epidemic affecting so many residents, many rats would have to be infected within a short period of time, and infectiousness among rats would have to be short-lived for the epidemic to die out eventually.

Future work

The rat vector hypothesis is a strong possibility that needs to be further explored. Epidemiological case-control studies could be undertaken to identify behavioural risk factors and possible mechanisms for rat-to-man infections. For example, if rat contamination occurs at night, people using kitchen and bathroom facilities early in the morning, when cooking breakfast, taking showers, and so on, will be at increased risk. Housewives will be affected more than husbands working away from home. Small children who crawl on the floor will also be at higher risk.

Detailed comparisons of incubation period, presenting symptoms, clinical course, and outcome can be done between patients from Amoy Gardens and other patients with SARS. The existence of several distinct types of SARS should be explored. Viral studies of Amoy isolates should be done to ascertain whether they have undergone substantial mutation when compared with isolates from other patients. Viral genomes from different series of patients should be compared.

To seek evidence of viral infection in the proposed vector, rats and droppings should be sampled from all the blocks in Amoy Gardens. Investigations of rat populations (if any) in the many blocks that were completely unaffected by SARS might provide clues. Rats in neighbourhoods around Amoy Gardens and elsewhere, where clusters of cases have occurred, should also be studied. Droppings should be assayed for viral presence by culture and PCR. Rats should be thoroughly autopsied to study for pathological changes and to determine the distribution of virus and viral gene products in tissues, urine, saliva, and faeces. Serological studies should be done to detect antibodies.

Infection of rats could be investigated experimentally by exposure to SARS virus by inhalation, ingestion, and injection, in rats of different ages, and in pregnant rats to assess intrauterine infection. After exposure, disease occurrence, antibody formation, ability to pass virus to the environment, and development of tolerance and carrier state could be investigated.

Conflict of interest statement

None declared.

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INFECTIOUS DISEASES

SARS Researchers Report New Animal Models

WASHINGTON, D.C.—Scientists have reported three new animal models that could provide relatively cheap and practical ways to test drugs and vaccines against severe acute respiratory syndrome (SARS), the disease

the Netherlands says it has infected two bigger animals with the virus.

During the peak of the SARS crisis last April, virologist Ab Osterhaus and colleagues at Erasmus University in Rotterdam reported that cynomolgus macaques infected with a newly discovered coronavirus developed a pulmonary infection resembling SARS in humans. That study provided proof that the new virus was indeed the culprit, as well as the first animal model. In Rotterdam and elsewhere, researchers are now studying SARS pathogenesis and testing candidate drugs in infected monkeys.

But using monkeys poses ethical questions; besides, they're cumbersome and expensive animals to experiment with, especially under strict biocontainment standards. At a meeting last week, organized by the Institute of Medicine's Board on Global Health, NIAID's Kanta Subbarao said she had sprayed the SARS virus into the noses of mice and found that, although the animals didn't get sick, the virus started replicat-

ing inside their bodies—sufficient for an animal model. "Everybody is calling us to test their pet vaccine," says Subbarao, who has submitted the results for publication.

In a paper that has been accepted by *Nature*, meanwhile, Osterhaus reports that his group has infected two other species with SARS and found that the virus readily replicates in both. Osterhaus declined to reveal the two species pending publication, but he says they are more closely related to masked palm civets and ferret badgers—two species in which the SARS virus has been found in China (*Science*, 18 July, p. 297)—than they are to mice. The findings suggest that the virus may have a remarkably broad range of hosts, Osterhaus says.

Subbarao's announcement was one of the few tangible steps forward reported during last week's meeting. With drug and vaccine studies in their infancy and the flu and cold season about to hit the Northern Hemisphere, many questioned whether overstretched public health systems will be able to cope if SARS reemerges. Summarizing his feelings after the meeting, National Center for Infectious Diseases director James Hughes said, "What I've heard doesn't make me sleep any better."

—MARTIN ENSERINK

Image not
available for
online use.

Guinea pigs. The SARS virus replicates in the lungs of macaques. Now researchers have infected several other species.

that erupted from southern China last spring but was stamped out by summer. Researchers at the U.S. National Institute of Allergy and Infectious Diseases (NIAID) said at a meeting here last week that they have managed to get the SARS virus to replicate in mice; separately, a team from

DEEP-SEA DRILLING

Same Crew to Run New Program

Thanks to a budget squeeze on its U.S. sponsor, the future of scientific ocean drilling will look a lot like the past—at least for a few years.

Last week the National Science Foundation (NSF) awarded the same team that has managed the 19-year-old Ocean Drilling Program a 10-year, \$626 million contract to run its successor, the International Ocean Drilling Program (IODP). Initially, the new program—a joint U.S.-Japan project that also hopes to have European participation—will rely on the current drill ship, the *JOIDES Resolution*. The contract went to Joint Oceanographic Institutions Inc., which has teamed up with the Lamont-Doherty Earth Observatory of Columbia University and with Texas A&M University to run IODP.

NSF's original plan was to either upgrade the *Resolution* or acquire another ship, says Bruce Malfait, head of the NSF marine geosciences section. Japan would finish outfitting and testing its behemoth drill ship *Chikyu* by late 2006 and join the

United States in funding IODP, matching NSF's contribution over the decade.

But that plan went by the boards earlier this year, when NSF couldn't get approval from the White House to ask Congress for the \$100 million or so needed for the acquisition and upgrade. Waiting another year to begin the project would have meant "a long drilling hiatus" until the middle of 2006, says Malfait, "which is probably unacceptable to the community."

Instead, an unmodified *Resolution* will return to scientific drilling next June in the northeast Pacific

Ocean—its last ODP voyage ended last month—and continue 2-month drilling cruises possibly through fall 2005. If legislators grant it the money next year, NSF hopes to upgrade the *Resolution* or convert another ship by fall 2006, says Malfait.

The only prospect for enhanced scientific drilling before then comes from Europe. The European Consortium for Ocean Research Drilling met earlier this month with Japanese representatives to discuss taking another drilling platform to the ice-covered Arctic Ocean as early as next summer as part of IODP.

—RICHARD A. KERR



Plugging away. The *JOIDES Resolution* will resume scientific drilling next summer for a new international program.



Printed: Monday, February 16, 2004 1:42 AM

From : Heinz Feldmann <[REDACTED]>
Sent : Monday, October 27, 2003 11:48 PM
To : "stephen ng" <[REDACTED]>
Subject : Re: mice model for SARS

Dear Stephen:

Thanks for the note and the PDF file. We did similar work here in Winnipeg. Mice get infected but do not show any disease. The virus replicates in several organs starting at around day 3 post infection. The mice normally clear the infection by day 7 to 9 post infection. Titers are low but we could re-isolate the virus from the organs.

Osterhaus infected cats and ferrets. According to him, the virus replicates in cats but does not cause any disease. In ferrets the virus replicates and causes diseases (respiratory symptoms). As far as I know 1/4 animals died. This is accepted for publication in Nature, I believe.

Best wishes,
 Heinz

<p>"stephen ng" <[REDACTED]> heinz_feldmann [REDACTED] m> [REDACTED] 2003-10-26 08:05 PM</p>	<p>To: [REDACTED], [REDACTED], [REDACTED] cc: Subject: mice model for SARS</p>
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Dear All,

Looks like finally someone successfully inoculated mice. My sources told me that Osterhaus infected a domestic cat and a ferret. SARS CoV is capable of multiple species infections.

Regards,

Stephen

No masks required! Use MSN Messenger to chat with friends and family.
<http://go.msnsnserver.com/HK/25382.asp>