

新型インフルエンザの現状と課題

笹川平和財団講演会
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HIGHLIGHTS

Concern over flu pandemic justified

18 May 2009 -- The world is rightly concerned about the prospect of an influenza pandemic. When an infectious agent causes a global public health emergency, health moves straight to centre stage, said Director-General Dr Margaret Chan in her address today to the 62nd session of the World Health Assembly.



WHO/Cédric Vincensini
Dr Margaret Chan
addressing the 62nd World
Health Assembly.

[Dr Chan's address to the Health Assembly](#)

[World Health Assembly opens](#)

Influenza A(H1N1) virus

19 May 2009 -- As of 06:00 GMT, 19 May 2009, 40 countries have officially reported 9830 cases of influenza A(H1N1) infection, including 79 deaths.

[Current situation - update 33](#)

[Recommendations of the Strategic Advisory Group of Experts on influenza A\(H1N1\) vaccines](#)

[Full coverage of influenza A\(H1N1\)](#)

KEY WHO INFORMATION

[Director-General](#)

Director-General and senior management

[Governance of WHO](#)

WHO Constitution, Executive Board and World Health Assembly

[Media centre](#)

News, events, fact sheets, multimedia and contacts

[International travel and health](#)

Publication on travel risks, precautions and vaccination requirements

[World Health Report](#)

Annual report on global public health and key statistics



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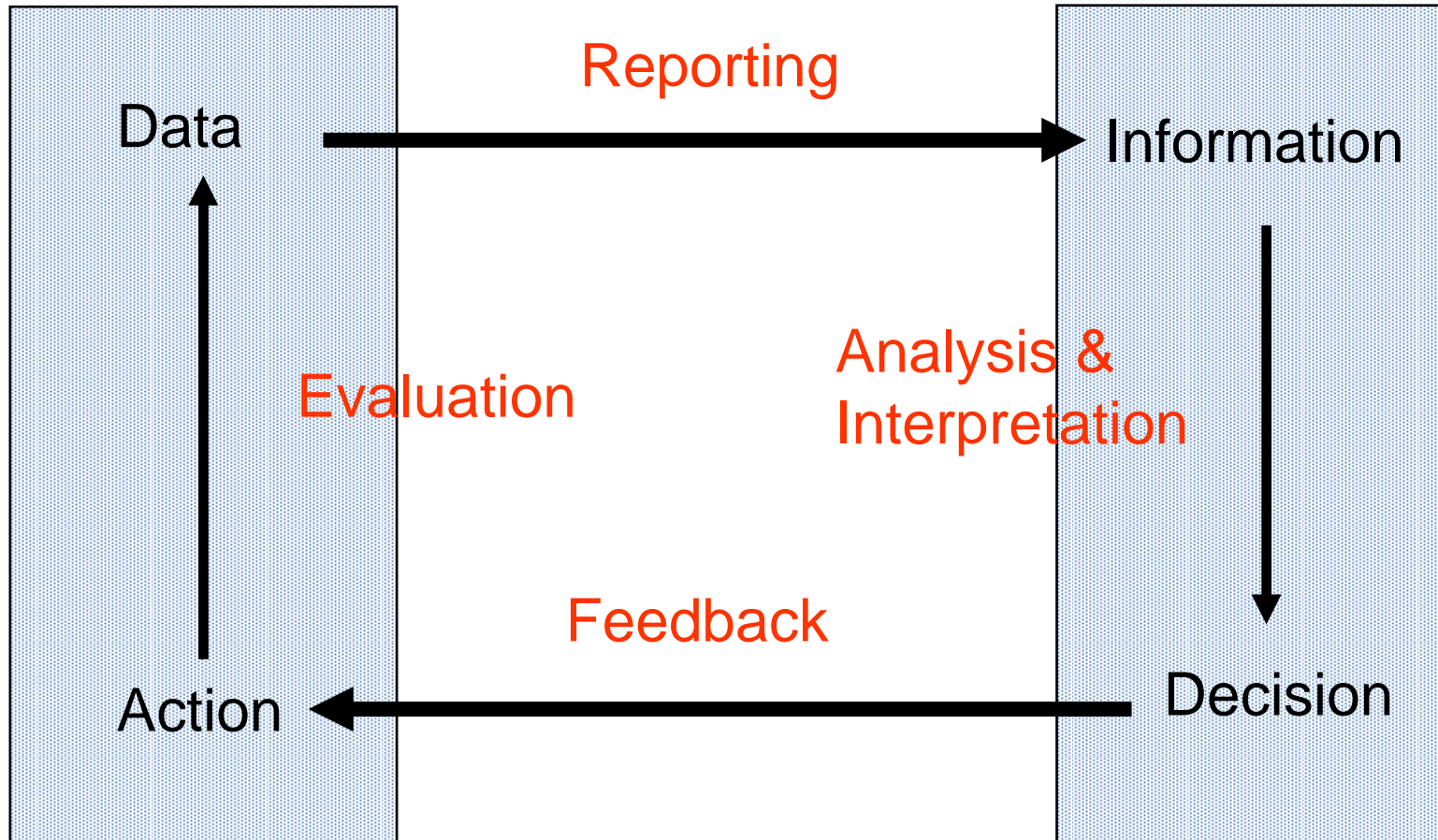
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As of today, there are 22 states around the country that are reporting widespread or regional influenza activity. **And unfortunately, based on the trends we're seeing, we do expect more illness, more hospitalizations and more deaths.** You may have heard that New York City and a few other places have had a number of outbreaks in schools, and some of them have issued recommendations for school closures at individual schools that have been affected. Those measures are consistent with the school guidance that we have updated, which suggests that there is a need for a localized response. The illness severity that we're seeing continues to be pretty similar to what is caused by seasonal influenza, and we feel this means we need to remain vigilant. We are now experiencing higher levels of influenza-like illness than is normal for this time of year. We're also seeing numerous outbreaks in schools, which is also very unusual for this time of year. Influenza is always serious, and influenza viruses are very unpredictable. **So unfortunately, it's uncertain right now how severe this outbreak will be in terms of the ultimate illness and mortality toll that it takes, or whether this virus will turn out to be worse than others that we've handled through the seasonal flu experience.** Things could change

Surveillance: General Principle

Health Care System

Public Health Authority





26 April 2009: 2 countries, reporting 38 cases





28 April 2009, 19:15 GMT: 7 countries, reporting 105 cases

◀ Previous Next ▶



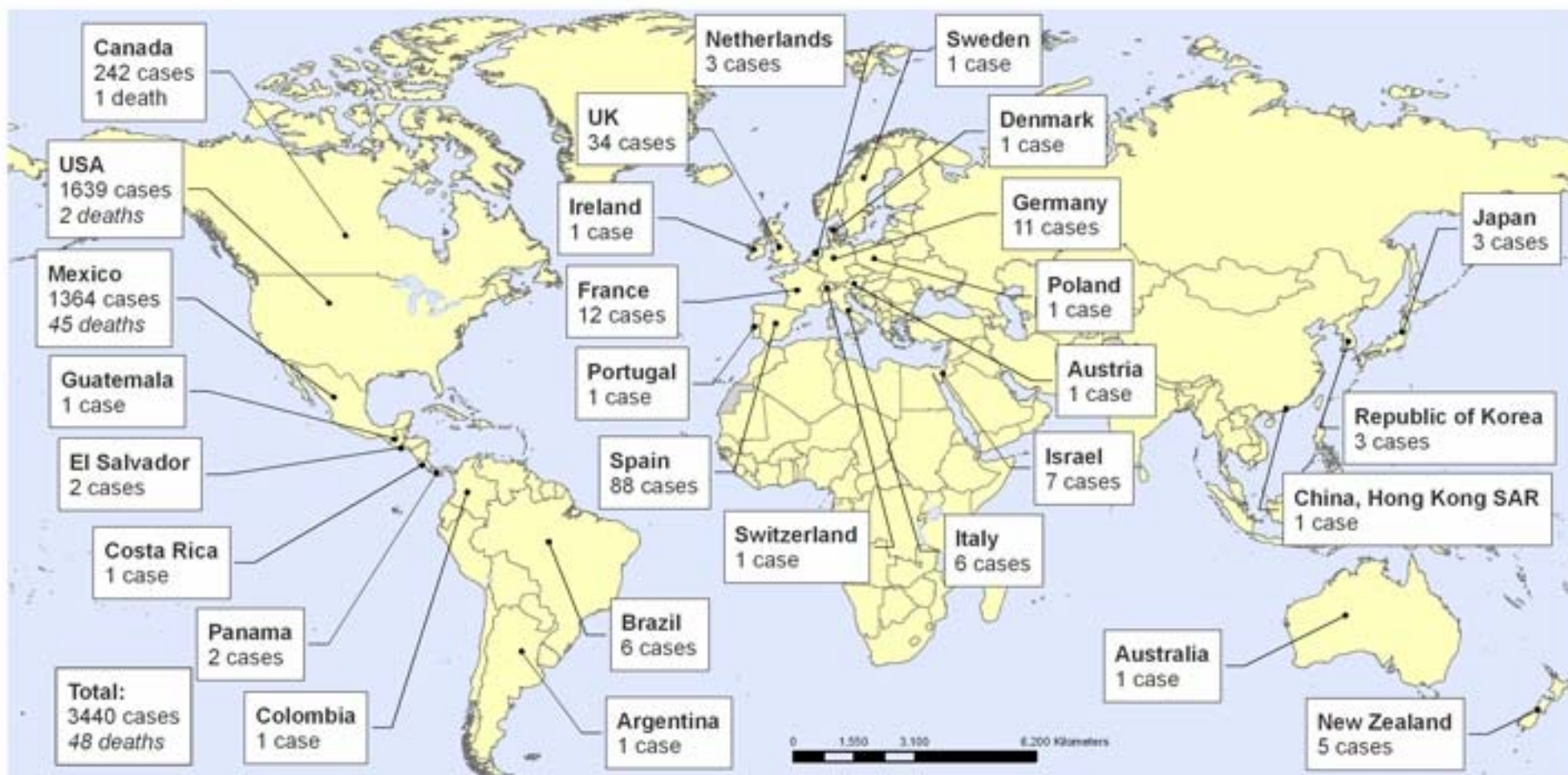


02 May 2009, 18:00 GMT: 16 countries, reporting 658 cases



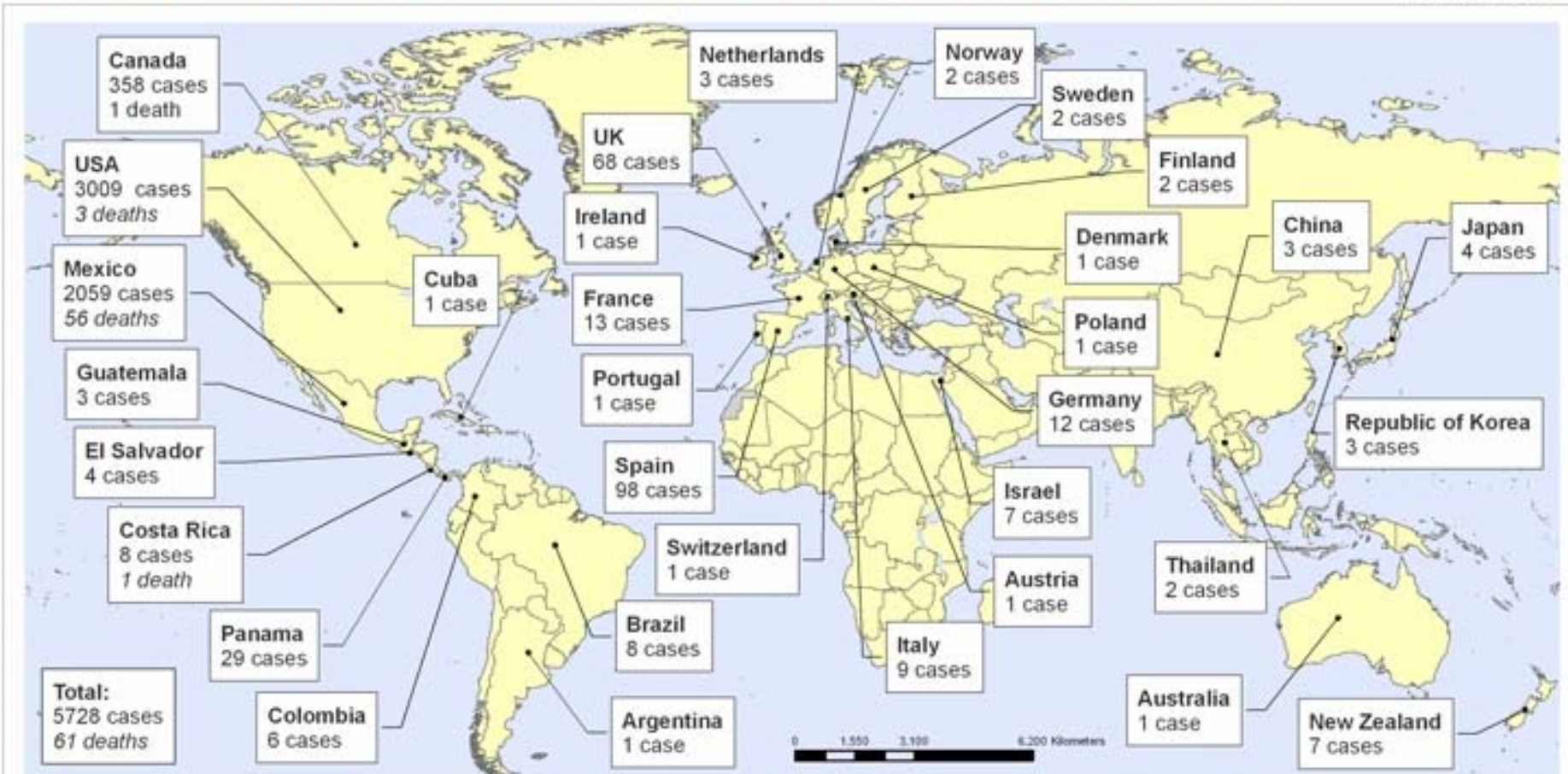


09 May 2009, 06:00 GMT: 29 countries, reporting 3440 cases





13 May 2009, 06:00 GMT: 33 countries, reporting 5728 cases





18 May 2009, 06:00 GMT: 40 countries, reporting 8829 cases

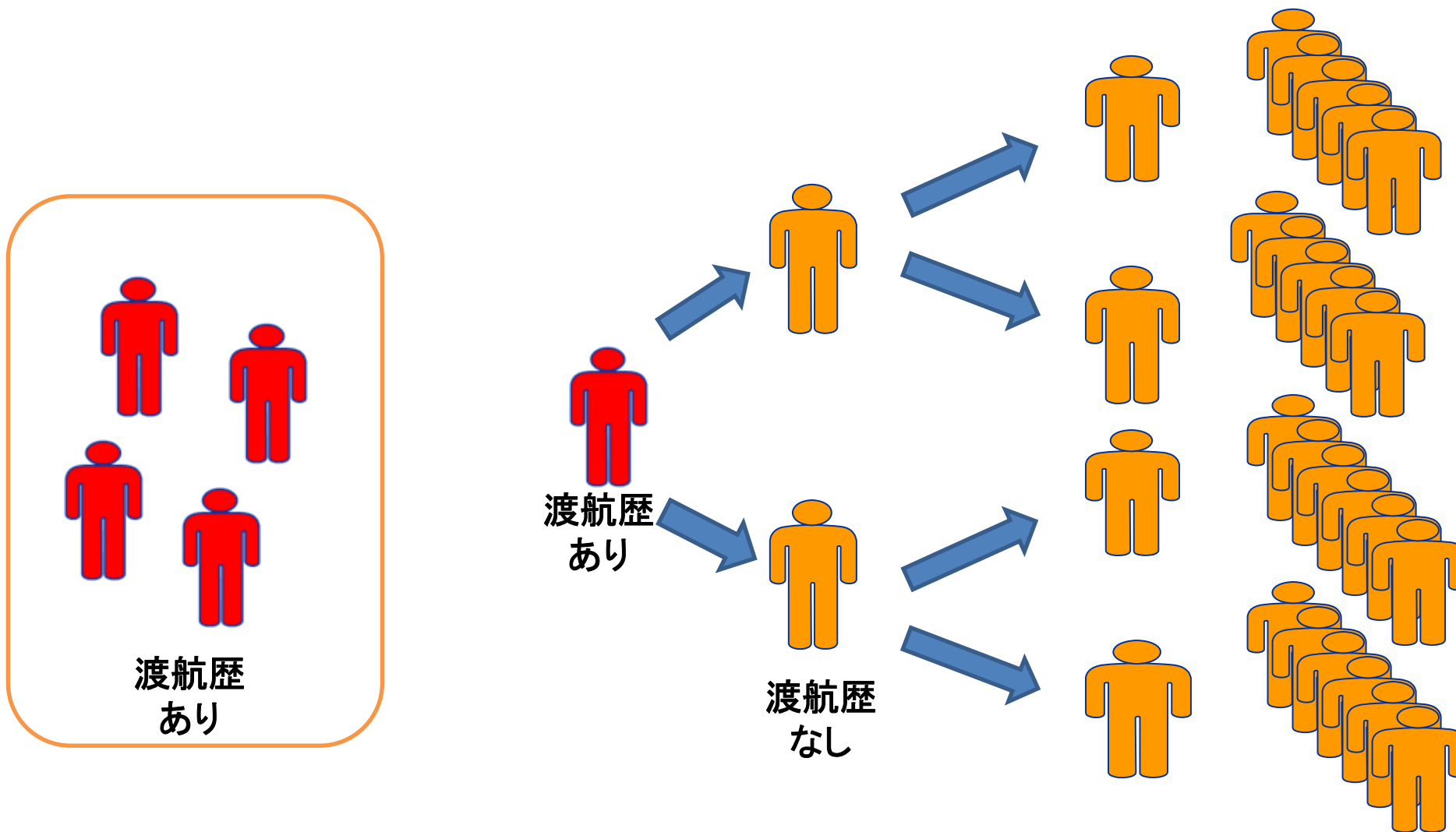
◀ Previous



現在の状況

- WHOの発表しているCase Countsは実際の状況を全く反映していない
 - メキシコ・アメリカ・カナダ
 - 急速に感染が拡大しすべての例を検査することは不可能
 - アメリカの公式の患者数:4714例、実際の患者数の推計10万人
 - メキシコでも地域によっては感染拡大が続いている
 - その他の国(多くは1桁の感染者数)
 - 渡航歴のある人を中心に調べているため
 - コミュニティーの感染が広がっている可能性はかなりある(関西のような例)

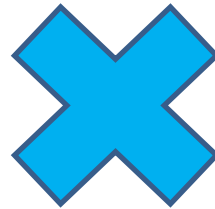
現在の患者検出システムの限界



日本で起きたことは他の国でも起きている可能性が高い

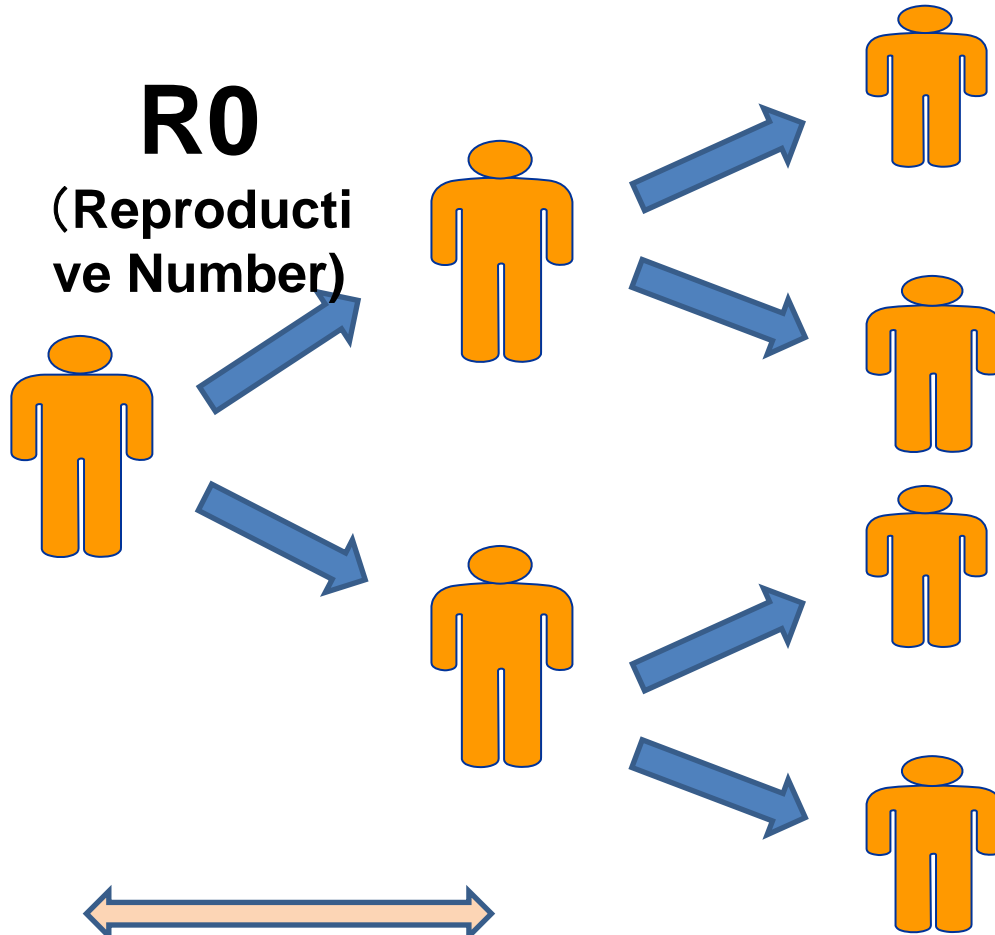
新型インフルエンザの被害

感染性
何人の感染者が出るか



**病原性
(毒性)**
感染した人のうちどのくらいの人が重症化し死亡するか

感染性を決める指標



Generation Time: 5日と仮定、
50日目 (10 Generations)

の感染者数

- R0=1.5の場合: 57人
- R0=1.8の場合: 357人
- R0=2.0の場合: 1024人

今回の新型インフルエンザの感染性

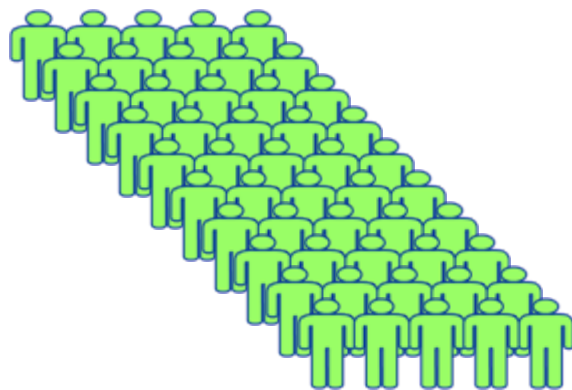
- 感染性の基本的な考え方
 - ほとんどの人が免疫を持っていないために感染は急速に広がる(感染性は高い)と考えるべき
- 感染性はどの程度か？
 - NY、関西の高校の例を見てもかなり感染性は高い
 - 全米への拡散のスピード
 - メキシコのPreliminaryなデータ
 - $RO=1.4-1.6$
- 10代で非常に高い罹患率

今後の日本での感染拡大

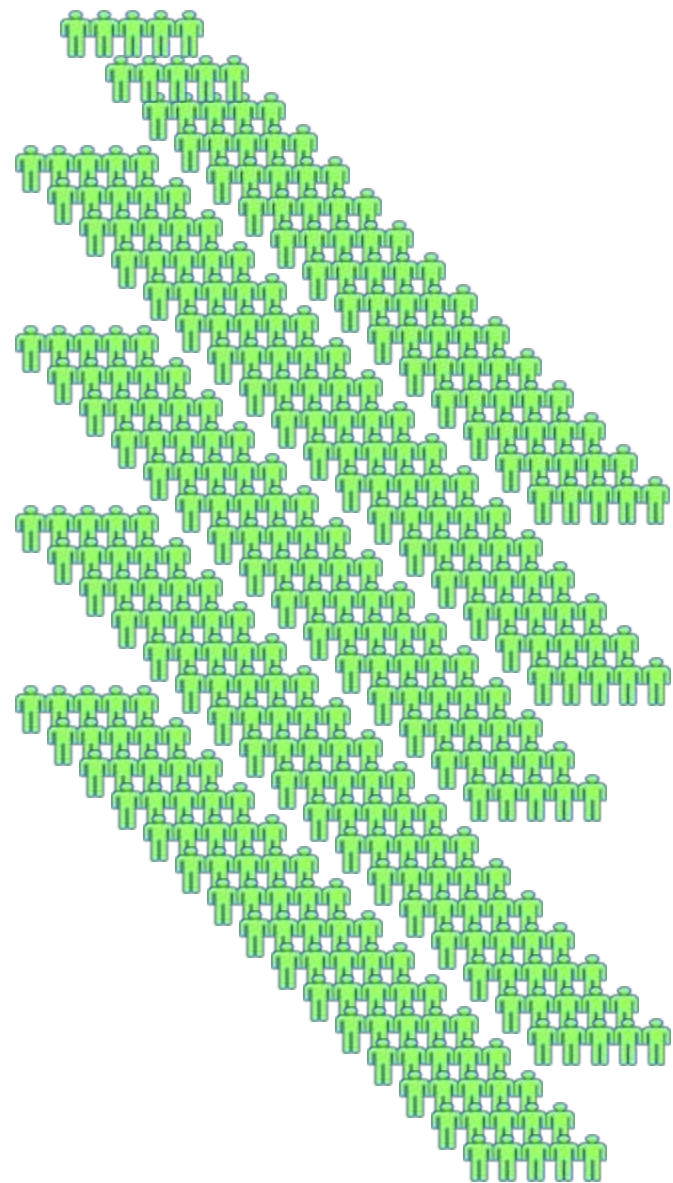


連休明け

2週間



2週間



今後予想される状況

- 日本でも確実に感染拡大は起こる
- 予想されるシナリオ
 - － このまま日本を含め大規模のパンデミックに突入
 - － 北半球では今回は「小流行」で終わる
 - スペインインフルエンザのパターン、アジアインフルエンザは日本では5-6月に大きな流行を起こしている
 - 「小流行」と言っても数千万の単位での患者がでないというだけ、数十万、数百万単位の患者発生はあり得る
- 少なくとも現在、感染性が減少し、感染拡大が収束に向かっていることを示唆するデータはない
 - － 短期的には感染拡大は継続する
 - － どこまで感染者数が広がるかはわからない
 - － 今の感染拡大への対応をまず考える必要がある

現在考えられる罹患率・感染者数のシナリオ (日本)

「小流行」
(罹患率<5%・感染者
数十万人～数百万人)

通常のインフルエンザ
と同程度
(罹患率5-10%・感染
者500-1000万人)

一気にパンデミック
(罹患率>25%・感染
者>3000万人)

今回の新型インフルエンザの病原性についてわかっていること

- ほとんどの感染者は軽症（通常のインフルエンザと変わらない症状）
- 感染しても発症しない、もしくは発熱しない感染者もいる
- 感染者の一部に非常に重症化する人が存在すること

低病原性(弱毒)ウイルスの意味

- ほとんどの人で感染は軽症、もしくは無症状
- 一部に重症化し死亡する例がある
- これまで想定されていた非常に致死率(=発症者に対する死亡者の割合)の高い新型インフルエンザ程の被害は起きない
 - 高病原性鳥インフルエンザ(H5N1): 致死率10-20%?
 - スペインインフルエンザ: 致死率2%
 - 現在想定されている致死率: 0.1-0.4%

どんな人が重症化しているのか？

- 高齢者の重症化例はほとんど見られていない
(感染者も少ない?)
 - 季節性インフルエンザと大きく異なるパターン
 - 若者から始まってまだ高齢者には感染していない?
(アメリカ・メキシコでは大規模なコミュニティでの感染)
 - 過去に流行していたウイルスとの交差免疫?
- 現時点で重症化しているのは子供(<5才)と20
– 50才代の成人

どんな人が重症化しているのか？

- 子供 (<5才)
 - 先天性疾患などの基礎疾患を持つ子供
- 成人 (20-50才代)
 - 糖尿病・心疾患・自己免疫疾患・喘息などの基礎疾患を持つ成人
- 妊婦
 - 妊娠後期の妊婦

(ここまでは通常のインフルエンザでもハイリスクグループ・高齢者が重症化しないとこのようなグループの人たちが重症化してくるのは理解できる)

どんな人が重症化しているのか？

- 成人(20-50代)
 - 全く基礎疾患を持たない健康な成人
 - メキシコでもアメリカでもある一定の割合で健康な成人が重症化している

重症化例の病態

- 少しずつだか実態が明らかになってきている
- 基本は重症のウイルス性肺炎＋ARDS
- サイトカインストーム？
- 2次性細菌性肺炎はおそらく主な重症化因子ではない？
- 基本的には高病原性鳥インフルエンザ(H5N1)と同じような病態(全身感染は？)

The NEW ENGLAND JOURNAL of MEDICINE

Emergence of a Novel Swine-Origin Influenza A (H1N1) Virus in Humans

Novel Swine-Origin Influenza A (H1N1) Virus Investigation Team*

ABSTRACT

BACKGROUND

On April 15 and April 17, 2009, novel swine-origin influenza A (H1N1) virus (S-OIV) was identified in specimens obtained from two epidemiologically unlinked patients in the United States. The same strain of the virus was identified in Mexico, Canada, and elsewhere. We describe 642 confirmed cases of human S-OIV infection identified from the rapidly evolving U.S. outbreak.

METHODS

Enhanced surveillance was implemented in the United States for human infection with influenza A viruses that could not be subtyped. Specimens were sent to the Centers for Disease Control and Prevention for real-time reverse-transcriptase-polymerase-chain-reaction confirmatory testing for S-OIV.

RESULTS

From April 15 through May 5, a total of 642 confirmed cases of S-OIV infection were identified in 41 states. The ages of patients ranged from 3 months to 81 years; 60% of patients were 18 years of age or younger. Of patients with available data, 18% had recently traveled to Mexico, and 16% were identified from school outbreaks of S-OIV infection. The most common presenting symptoms were fever (94% of patients), cough (92%), and sore throat (66%); 25% of patients had diarrhea, and

The members of the writing group (Fatmah S. Dawood, M.D., Epidemic Intelligence Service, Office of Workforce and Career Development; and Seema Jain, M.D., Lyn Finelli, Dr.P.H., Michael W. Shaw, Ph.D., Stephan Lindstrom, Ph.D., Rebecca J. Garten, Ph.D., Larisa V. Gubareva, M.D., Ph.D., Xiyun Xu, M.D., Carolyn B. Bridges, M.D., and Timothy M. Uyeki, M.D., M.P.H., M.P.P., Influenza Division, National Center for Immunization and Respiratory Diseases—all at the Centers for Disease Control and Prevention, Atlanta) assume responsibility for the overall content and integrity of the article. Address reprint requests to Dr. Dawood at the Influenza Division, Centers for Disease Control and Prevention, 1600 Clifton Rd. NE, MS A-32, Atlanta, GA 30333, or at fdawood@cdc.gov; or to Dr. Shaw at the Influenza Division, Centers for Disease Control and Prevention, 1600 Clifton Rd. NE, MS G-16, Atlanta, GA 30333, or at mshaw1@cdc.gov.

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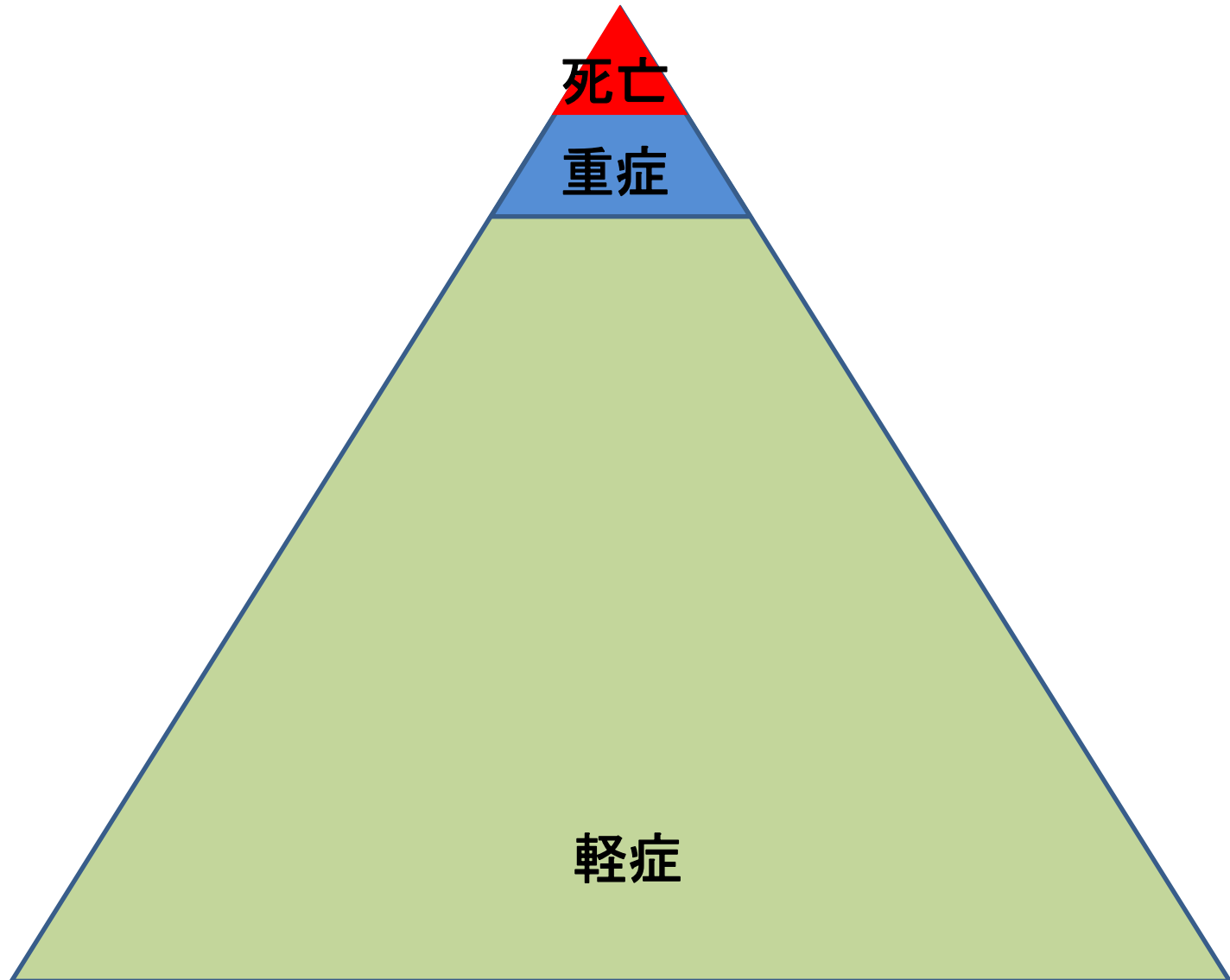
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ウイルス性肺炎

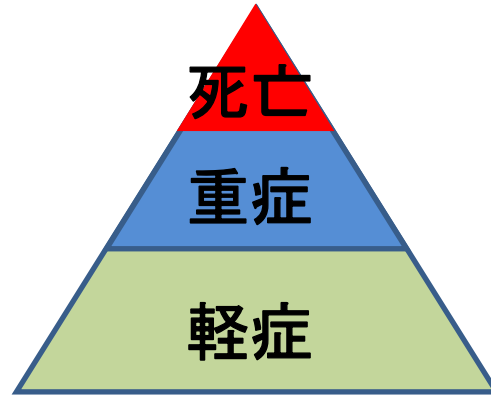
- 急速に進行し重症化するが多い
- ARDS(急性呼吸窮迫症候群)
- ICUで人工呼吸器を使用した呼吸管理が必要
- 呼吸不全で死亡
- 先進国でも救命することが難しい
- 重症化してからの抗ウイルス薬の治療効果は限定的



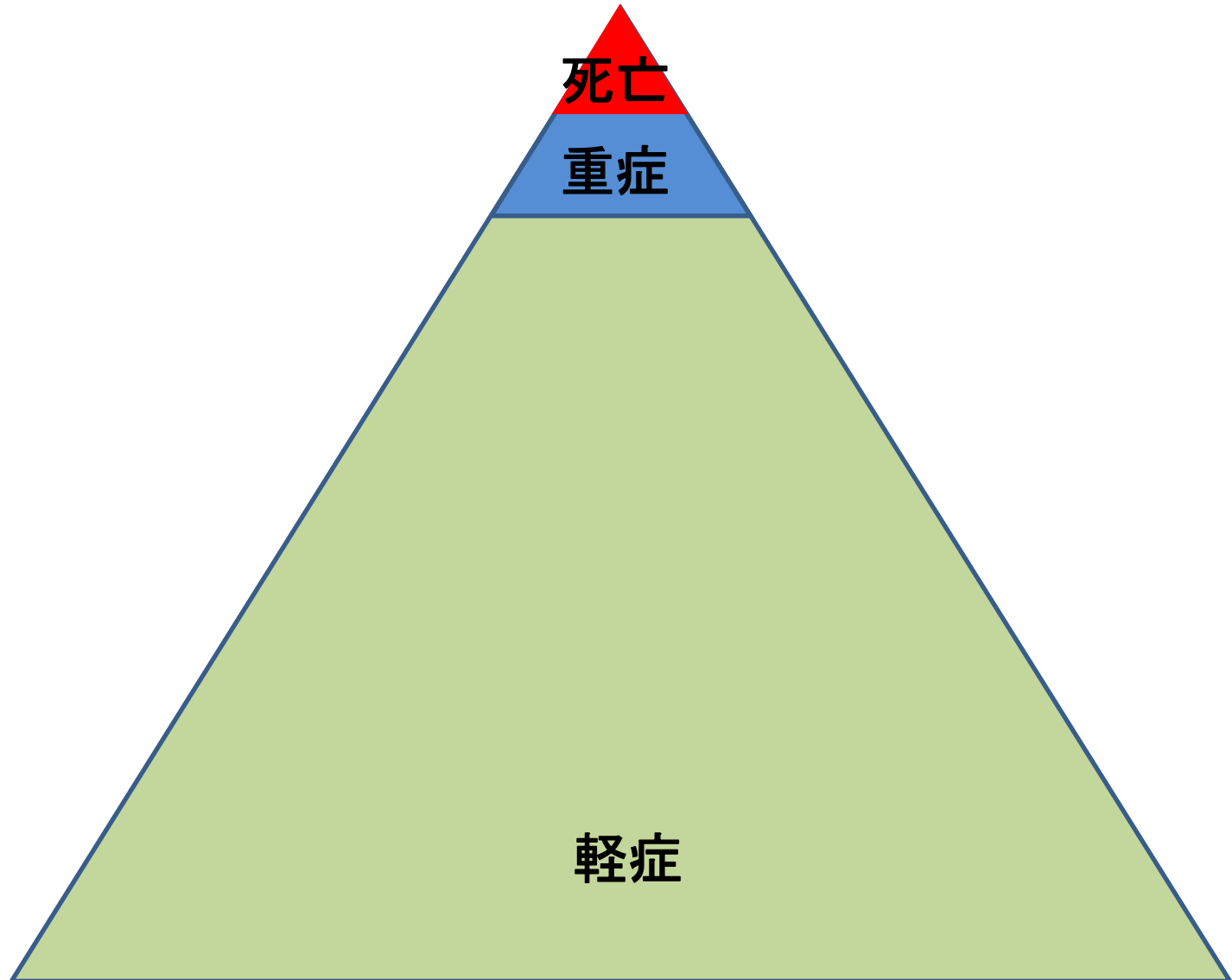
今回の新型インフルエンザの特徴



当初のメキシコの状況

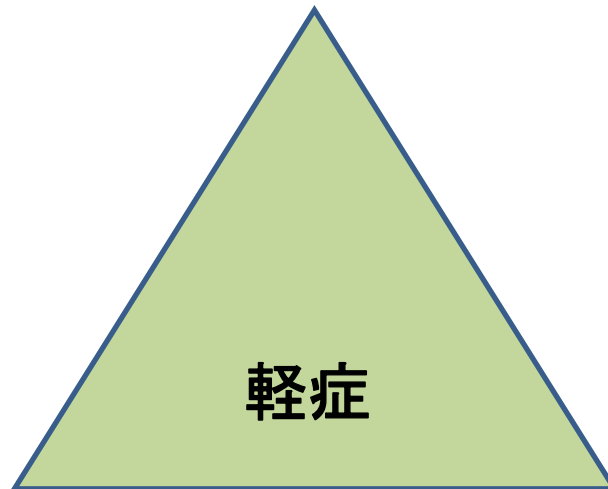


実際のメキシコの状況

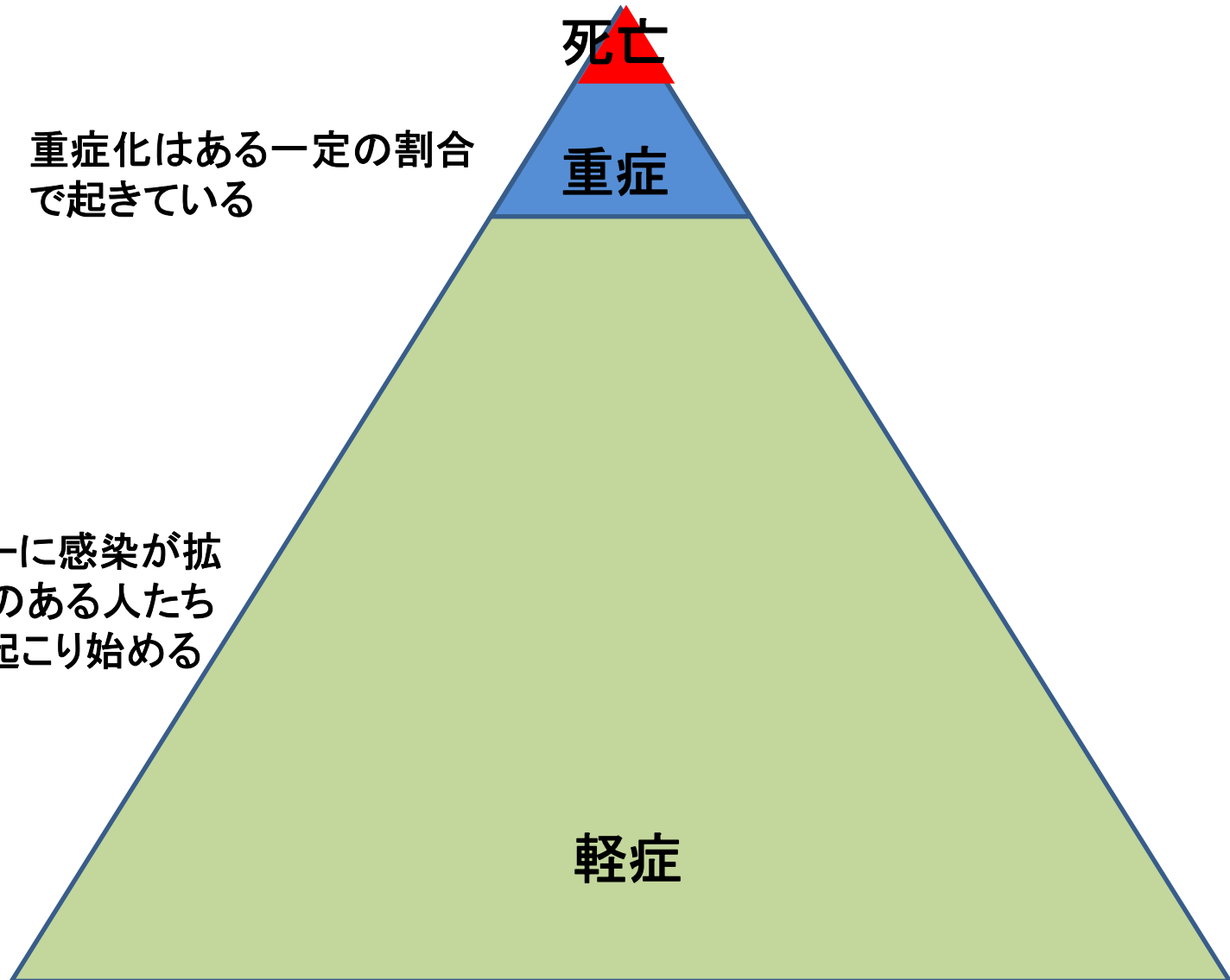


当初のアメリカの状況

健康な10代の高校生など
を中心に感染が拡大



現在のアメリカの状況



これからアメリカで起こること

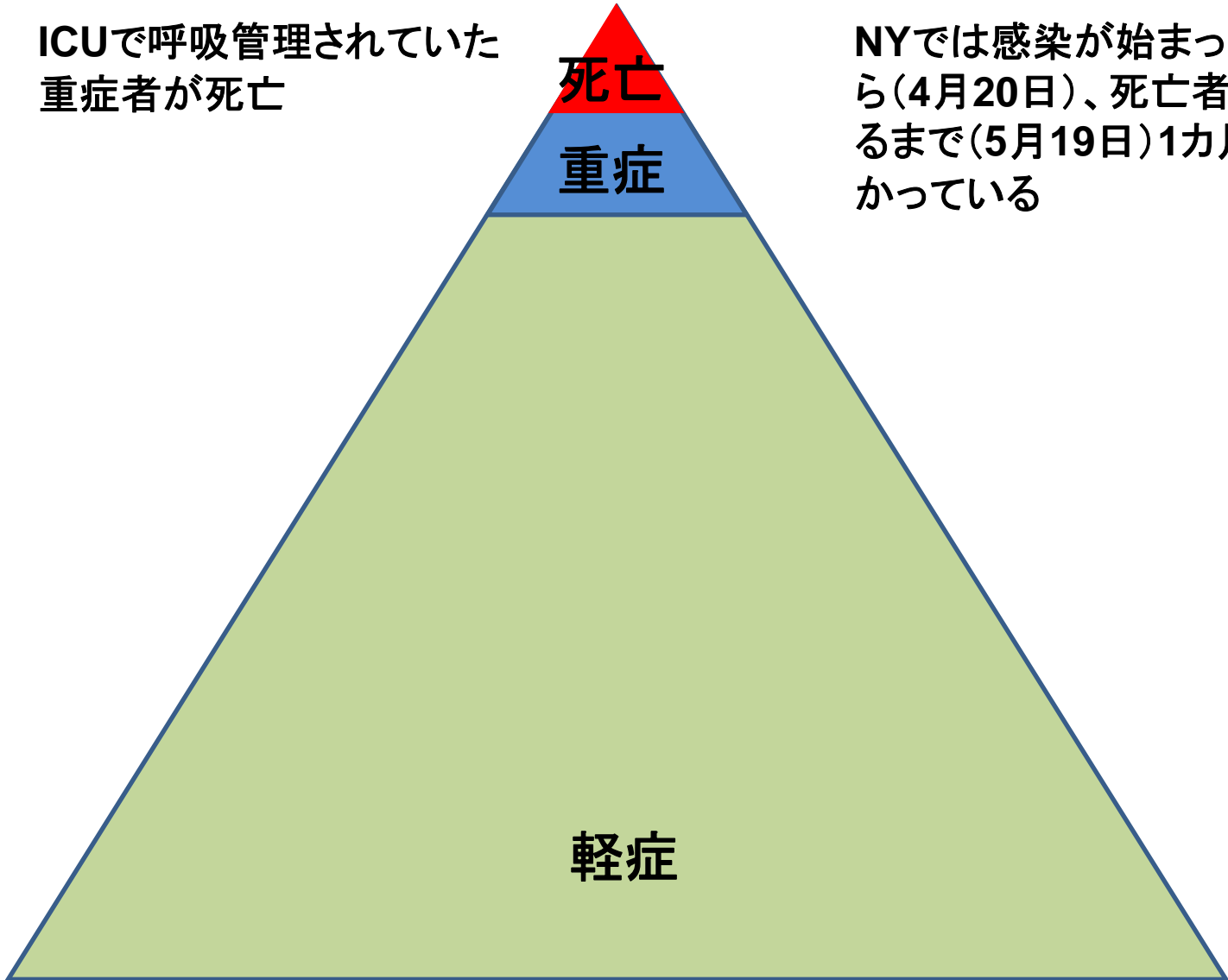
ICUで呼吸管理されていた
重症者が死亡

死亡

重症

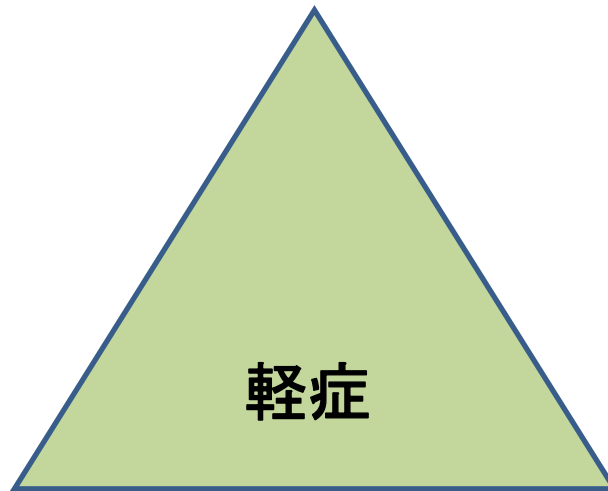
NYでは感染が始まってから(4月20日)、死亡者が出るまで(5月19日)1カ月かかっている

軽症



現在の日本の状況

健康な10代の高校生などを
を中心に感染が拡大



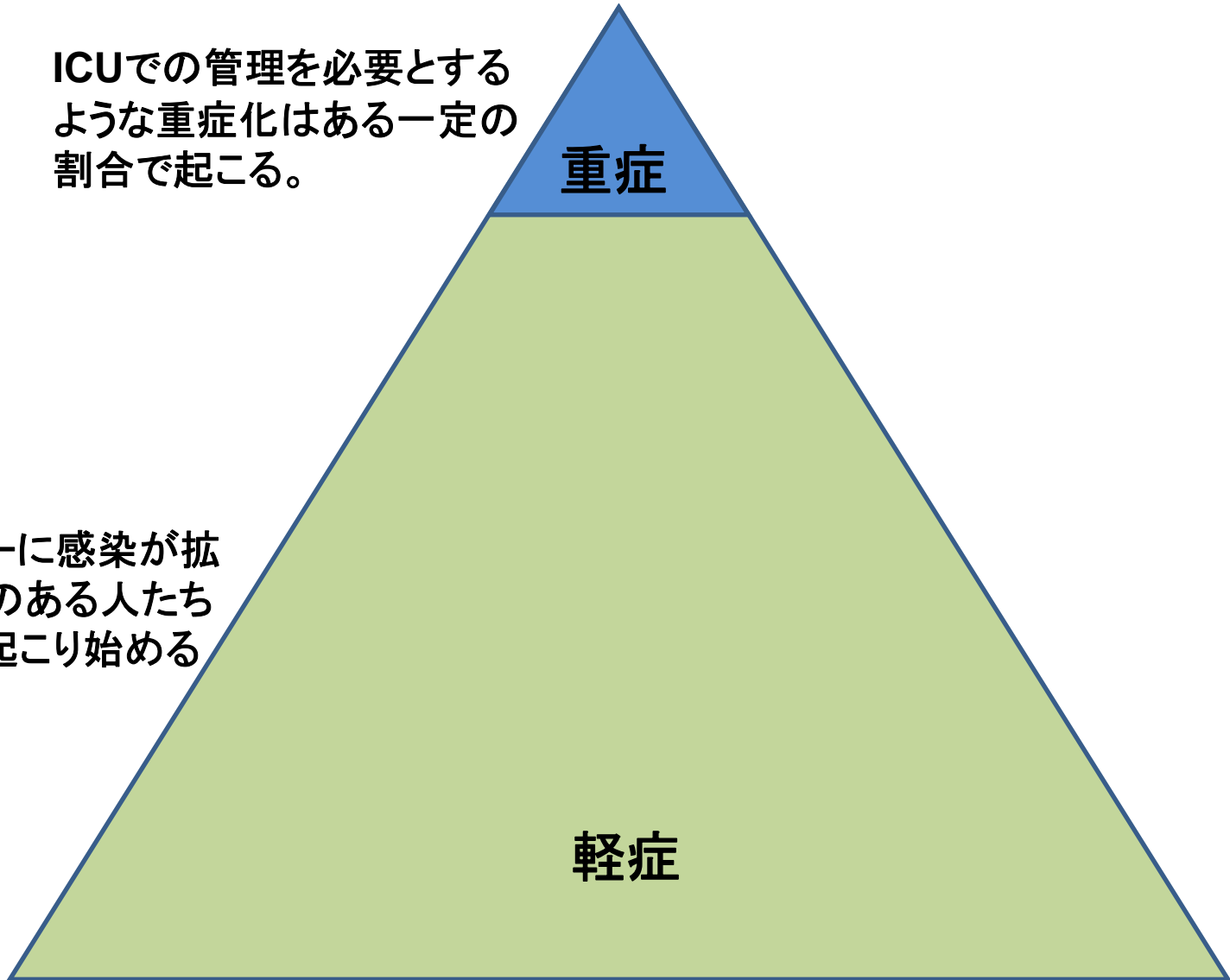
2-3週間後に日本で起こること

ICUでの管理を必要とする
ような重症化はある一定の
割合で起こる。

重症

コミュニティに感染が拡
大し、リスクのある人たち
にも感染が起こり始める

軽症



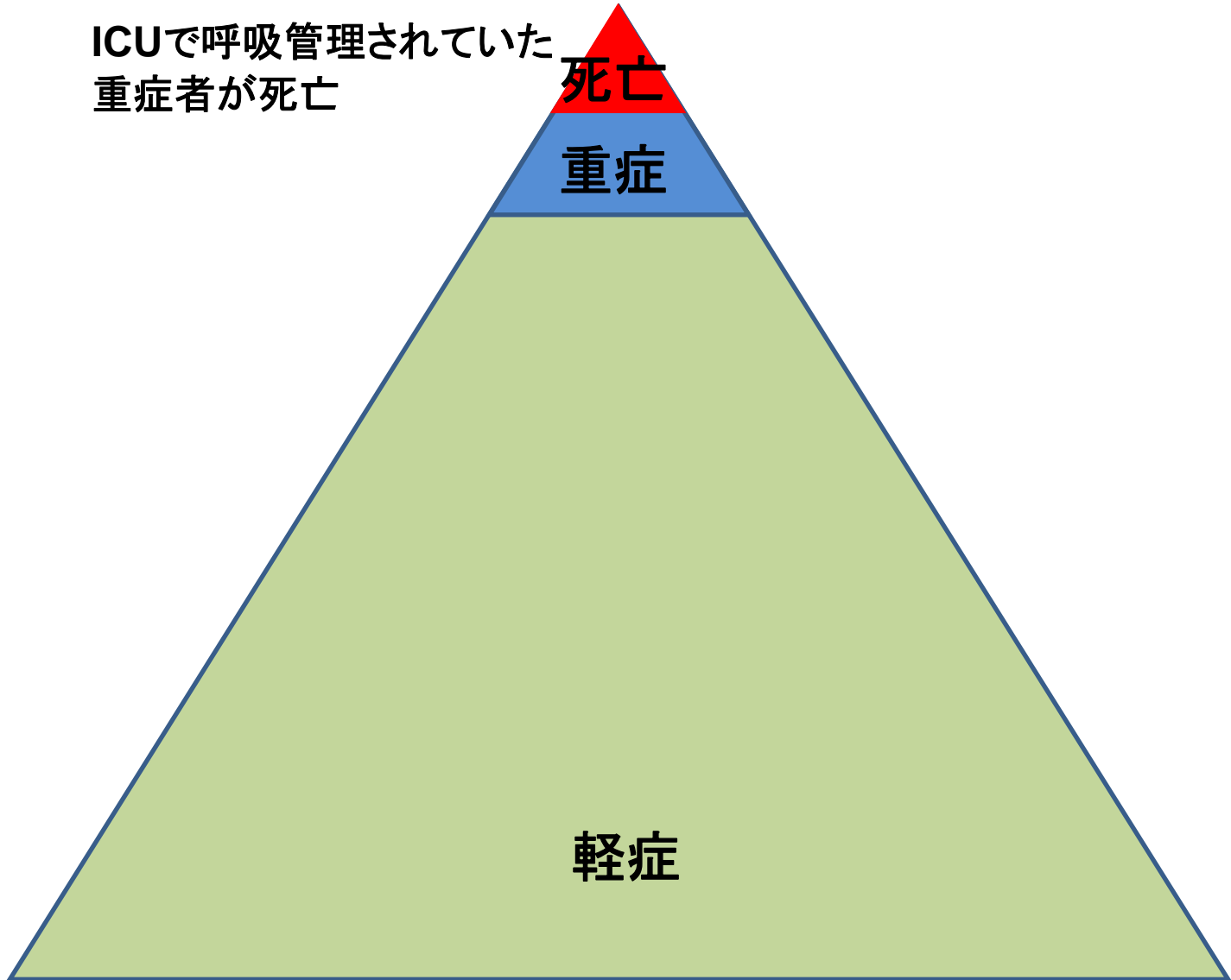
1カ月後に日本で起こること

ICUで呼吸管理されていた
重症者が死亡

死亡

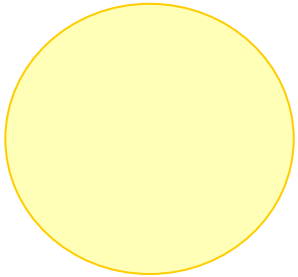
重症

軽症

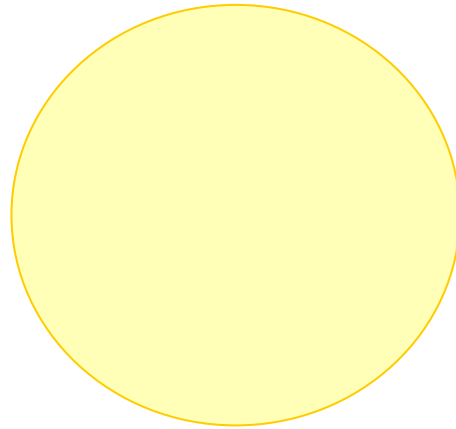


感染者数・致死率のシナリオ

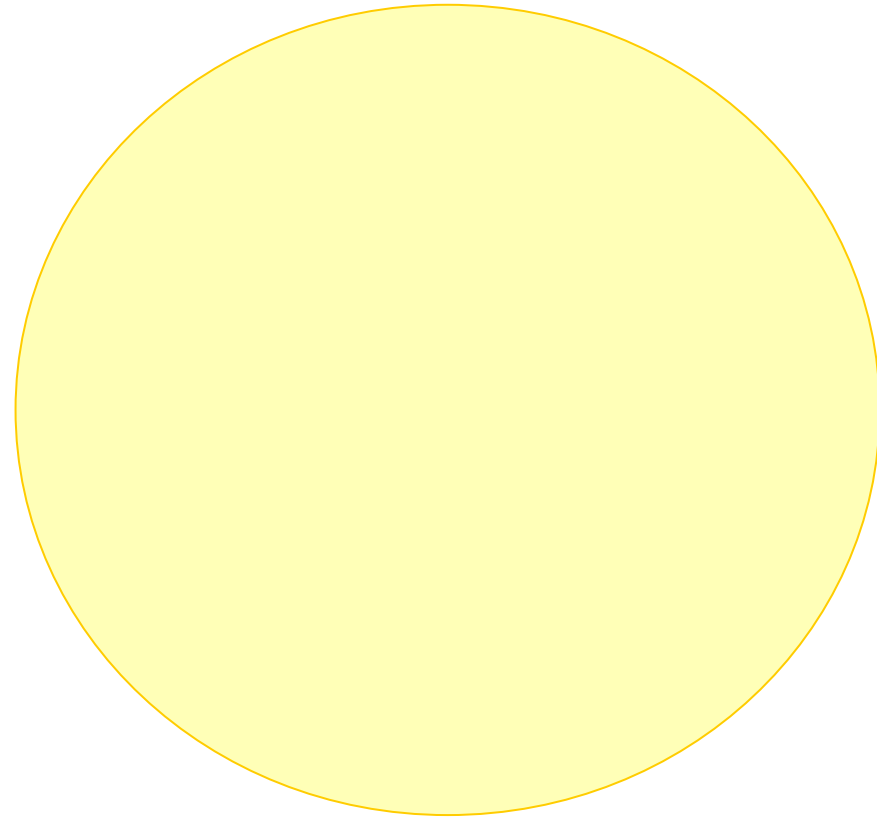
「小流行」
(感染者100万人)



通常のインフルエンザ
と同程度
(感染者1000万人)



一気にパンデミック
(感染者3000万人)



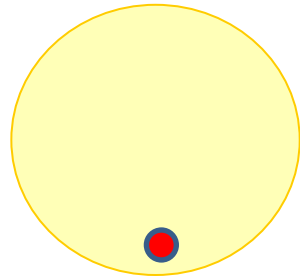
感染者数・致死率のシナリオ

(病原性が低い: 致死率0.1%)

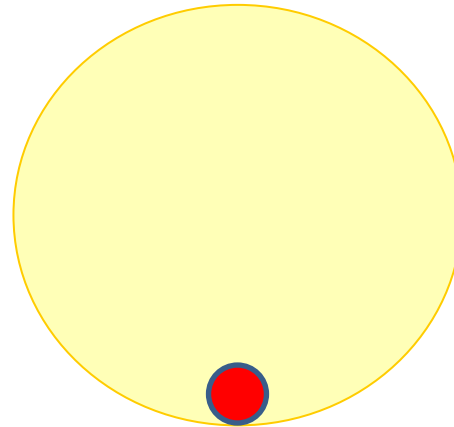
一気にパンデミック
(感染者3000万人)

「小流行」
(感染者100万人)

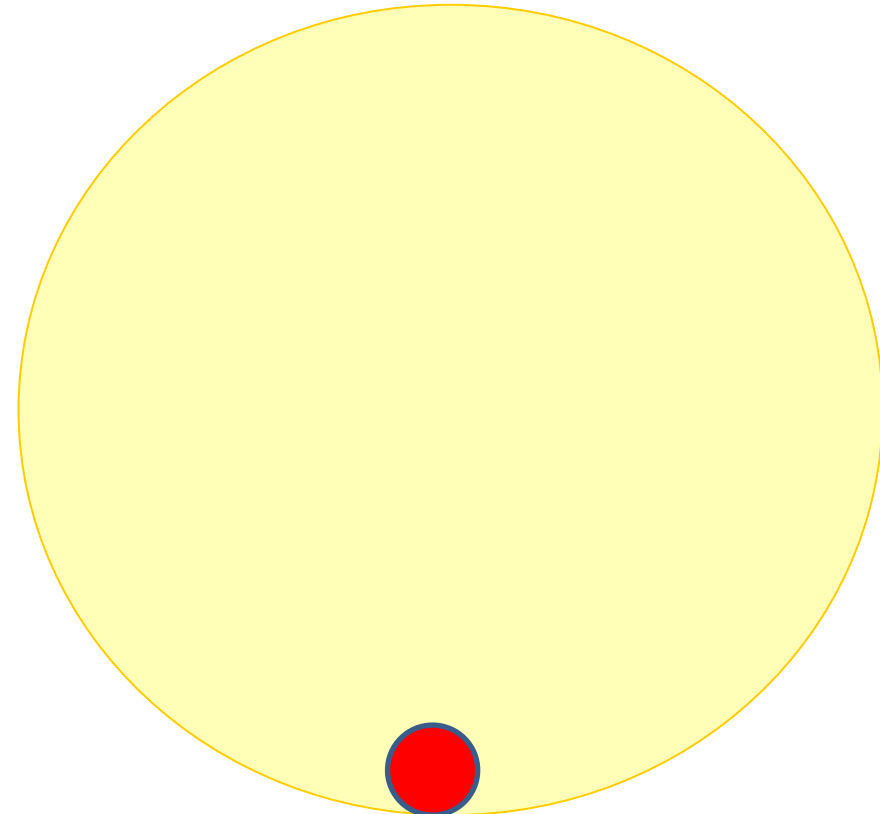
通常のインフルエンザ
と同程度
(感染者1000万人)



死亡者数:
1000人



死亡者数:
1万人



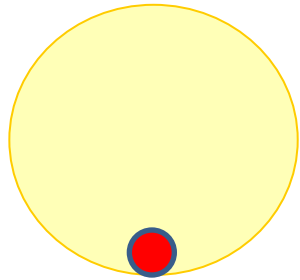
死亡者数:
3万人

感染者数・致死率のシナリオ

(病原性が中程度: 致死率0.4%)

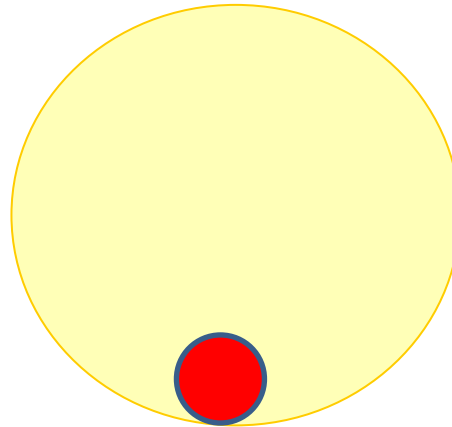
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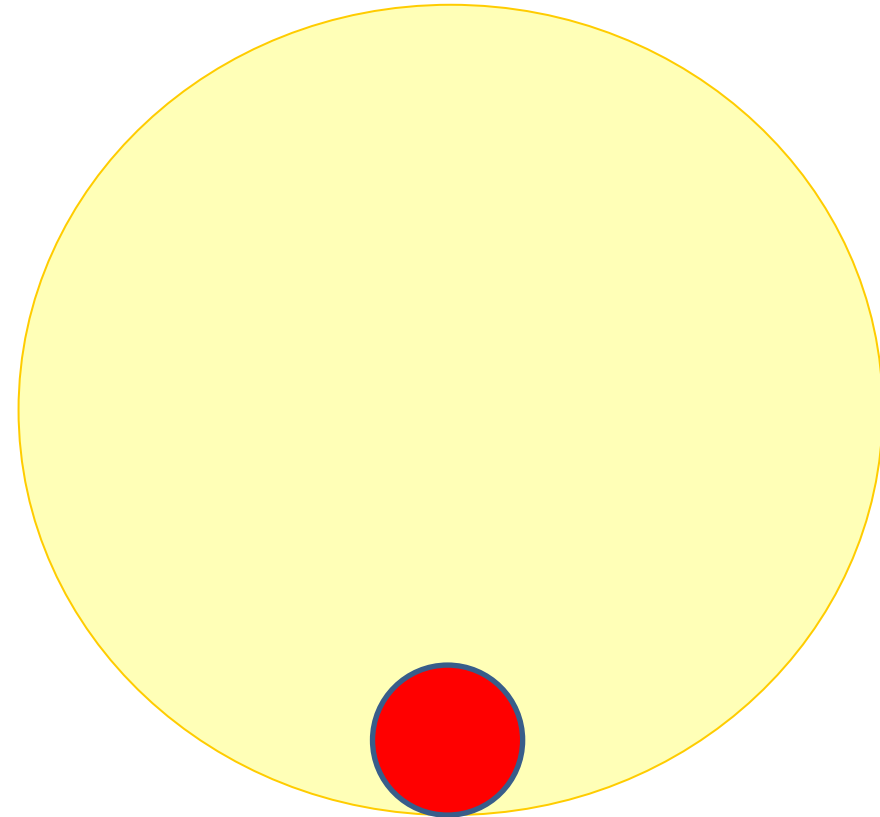


死亡者数:
4000人

通常のインフルエンザ
と同程度
(感染者1000万人)



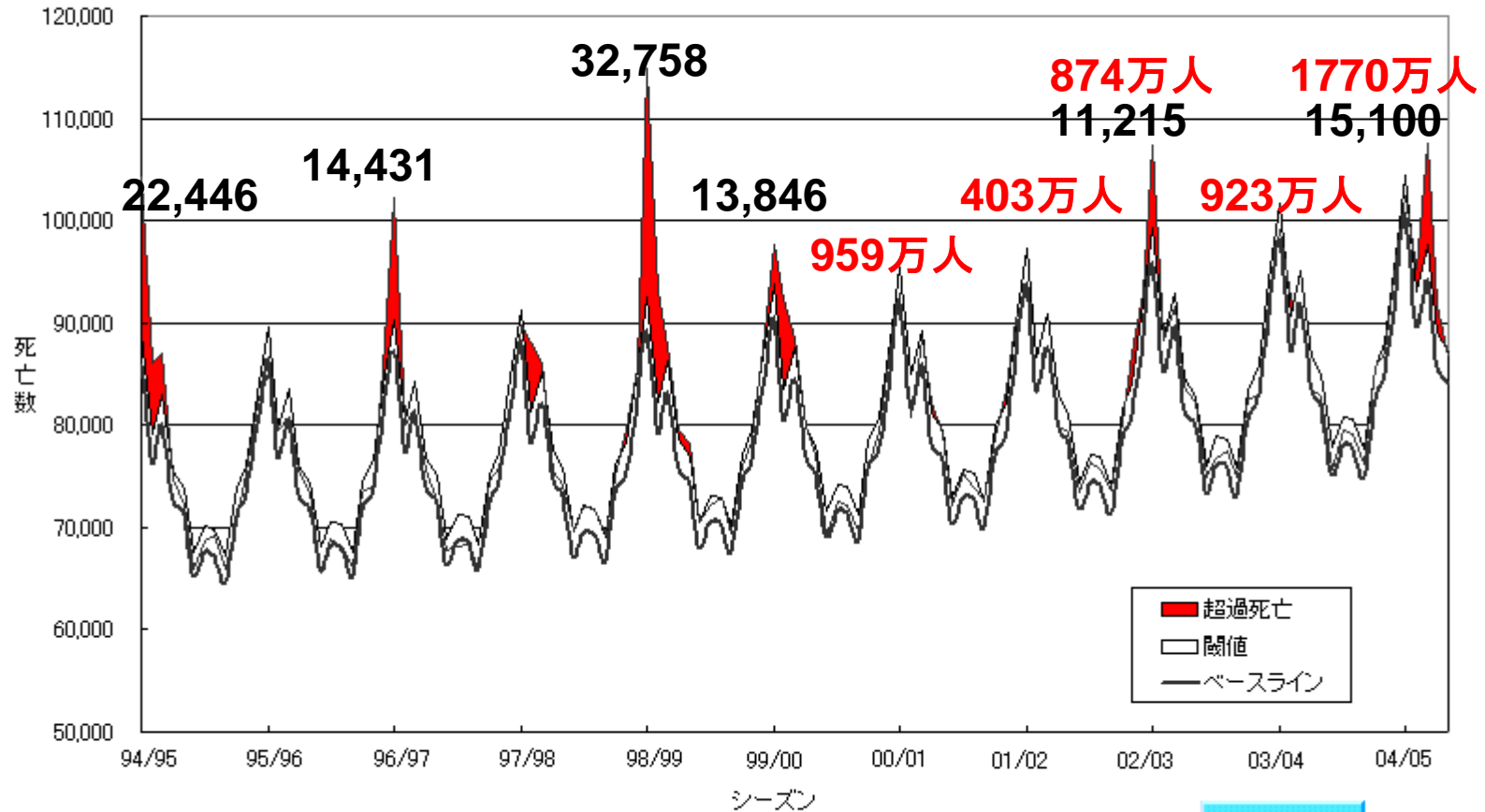
死亡者数:
4万人



死亡者数:
12万人

図2. インフルエンザによる超過死亡数(総死亡数)
Stochastic Frontier Estimationによる推計

推計患者数



IASR

Infectious Agents Surveillance and Report

(感染症研究所感染症情報センターのデータ)

今回の新型インフルエンザの被害想定

- このまま感染は確実に拡大する
- 最終的な感染者数・死亡者数はどの程度になるかは現時点ではわからない
 - 季節性インフルエンザより小さな被害
 - 季節性インフルエンザと同程度
 - 季節性インフルエンザより大きな被害

季節性インフルエンザと比べた場合の 社会的インパクト

- 通常の季節性インフルエンザ: 死亡するのはほとんど高齢者、死因はウイルスそのものでなくインフルエンザ関連死として超過死亡が見られる
- 今回の新型インフルエンザ: 死亡する人のほとんどは子供と20-50代の成人、死因はウイルス性肺炎による呼吸不全

重症化例の治療の課題

- 重症例が多発した場合の医療体制
 - 限られたICUベッド・人工呼吸器
 - 若い人・子供が重症化した場合には最後まで最善の医療を提供する必要がある
 - 医師不足などによりICUベッドが削減されている地域での医療体制
 - 妊婦が重症化した場合の産科病床・NICUを含めた医療体制

日本の医療の弱点が突かれて被害が拡大する可能性

- 医療の効率化(ICUベッドの削減)
- 医師不足・医療崩壊
- 産科医不足・産科医療の集約化
- NICUの不足

WHOの対応

- 現状の把握
 - 各国の感染者数・死亡者数・臨床像
- 今後の短期的(数週間)・中期的(～1年)展開の予測
 - 南半球・北半球・熱帯地域
 - 予想される被害
 - 途上国での被害拡大の可能性
- 今後の対策
 - 基本戦略(含公衆衛生対応)
 - 治療指針
 - ワクチン開発
 - サーベイランス



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Assessing the severity of an influenza pandemic

11 May 2009

The major determinant of the severity of an influenza pandemic, as measured by the number of cases of severe illness and deaths it causes, is the inherent virulence of the virus. However, many other factors influence the overall severity of a pandemic's impact.

Even a pandemic virus that initially causes mild symptoms in otherwise healthy people can be disruptive, especially under the conditions of today's highly mobile and closely interdependent societies. Moreover, the same virus that causes mild illness in one country can result in much higher morbidity and mortality in another. In addition, the inherent virulence of the virus can change over time as the pandemic goes through subsequent waves of national and international spread.

PROPERTIES OF THE VIRUS

An influenza pandemic is caused by a virus that is either entirely new or has not circulated recently and widely in the human population. This creates an almost universal vulnerability to infection. While not all people ever become infected during a pandemic, nearly all people are susceptible to infection.

The occurrence of large numbers of people falling ill at or around the same time is one reason why pandemics are socially and economically disruptive, with a potential to temporarily overburden health services.

Severity Assessmentの基本的な考え方

- 今回の新型インフルエンザの被害は国毎・地域ごとに大きく異なる
- それぞれの国・地域で影響を評価した上で対策を考える必要がある
- Severityの概念
 - 感染の重症度だけでなく経済・社会に与える影響を含め広く被害の程度を見極める必要がある
- Severityを決める要因
 - Virus: 抗原性・感染性・病原性
 - Population Vulnerability
 - Response Capacity

これまでの情報から考えられる途上国での 被害

- Virus
- Population Vulnerability
 - 高齢者は重症化しにくい？
 - 重症化するのには子供・若い成人・妊婦が中心、特に
 - 基礎疾患を持つ子供
 - 基礎疾患を持つ若い成人
 - 合併症のある妊婦
- Response Capacity
 - 途上国でのパンデミック対策は始まったばかり
 - 不十分な公衆衛生・医療体制
 - 抗ウイルス薬の備蓄はほとんどない
 - ワクチンの生産・供給体制もほとんどない

インフルエンザワクチンの現況

- 生産量：3億5千万Dose / year
- 先進国がほとんどを生産・消費
- 主な生産国
 - Australia, Canada, France, Germany, Italy, Japan, the Netherlands, the UK and USA

パンデミックに対応する医療資源の不足

- 医療機関の不足
 - 病院のベッド数
 - 病院・診療所の数
- 医療従事者の数
 - 医師
 - 看護師
- 基本的な医療物資
 - 抗生物質
 - マスク・手袋
- 人工呼吸器

Major Issues and Challenges of Influenza Pandemic Preparedness in Developing Countries

Hiroshi Oshitani,* Taro Kamigaki,* and Akira Suzuki*

Better preparedness for an influenza pandemic mitigates its impact. Many countries have started developing and implementing national influenza pandemic preparedness plans. However, the level of preparedness varies among countries. Developing countries encounter unique and difficult issues and challenges in preparing for a pandemic. Deaths attributable to an influenza pandemic could be substantially higher in developing countries than in industrialized countries. Pharmaceutical interventions such as vaccines and antiviral agents are less likely to be available in developing countries. The public health and clinical infrastructure of developing countries are often inadequate to deal with a widespread health crisis such as an influenza pandemic. Such an event will inevitably have a global effect. Therefore, improving pandemic preparedness in every country, particularly developing ones, is urgently needed.

Avian influenza, caused by influenza A virus (H5N1), continues to cause outbreaks among poultry and wild birds worldwide. It has spread from Asia to other regions, including Europe, the Middle East, and Africa. The number of cases of human subtype H5N1 infection also continues to rise. These historically unprecedented outbreaks have raised serious global concerns about the imminent arrival of an influenza pandemic. The World Health Organization (WHO) urges countries to develop and implement national pandemic preparedness plans to mitigate the health and social effects of a pandemic (1). However, the level of preparedness varies among countries. In general, developing countries have limited financial and technical resources to strengthen pandemic preparedness. They also face some unique and difficult issues, which make preparing for a pandemic more challenging. These have not been addressed adequately during planning. Effective and fea-

sible strategies are needed to mitigate the impact of the next influenza pandemic in developing countries.

Major Issues

Potential Impact of Next Influenza Pandemic in Developing Countries

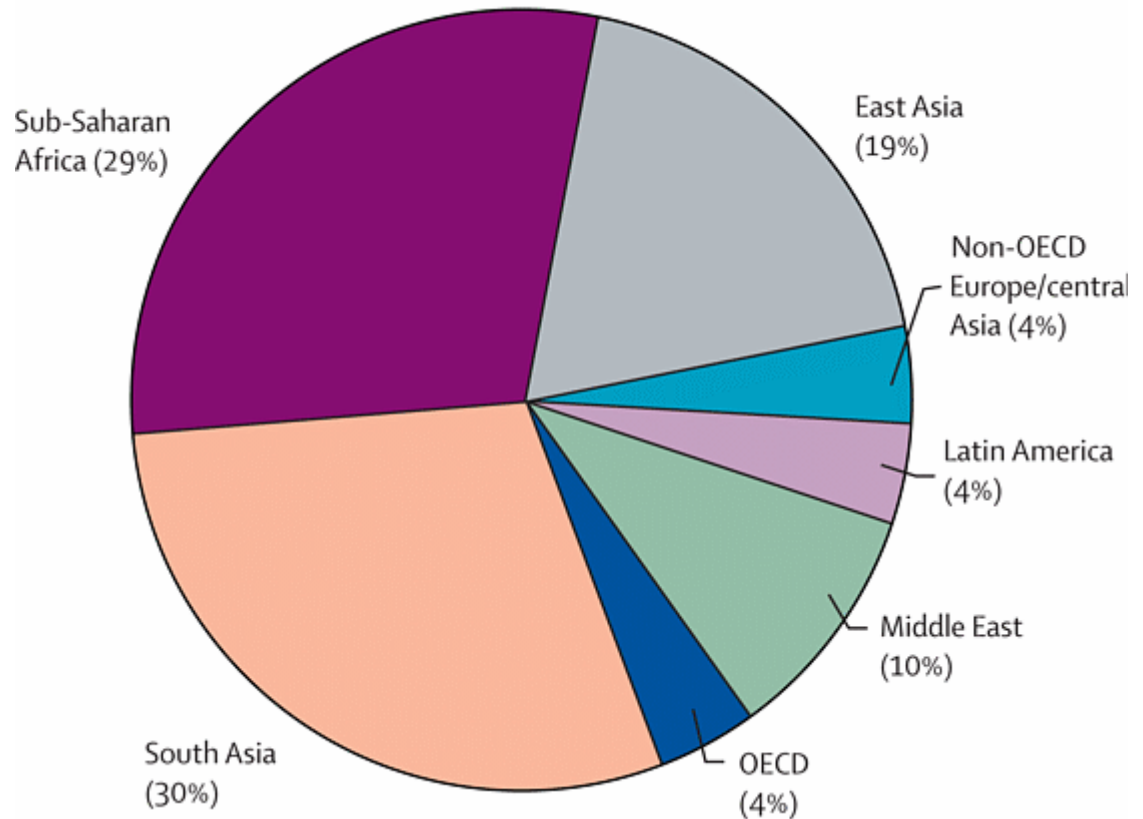
When an influenza pandemic emerges, all countries worldwide will inevitably be affected. However, the impact may vary both between and within countries. The estimated deaths for various countries during the Spanish flu pandemic from 1918 to 1920 shows that mortality rates in Europe and North America were significantly lower than those in Asia, Sub-Saharan Africa, and Latin America (2,3). A recent study that estimated the global impact of the Spanish flu pandemic indicated that a considerable difference in mortality rates was observed between high- and low-income countries (4). Why the pandemic caused such high mortality rates in developing countries is not entirely clear. Several factors may have been involved, including lack of access to adequate medical care, weak public health infrastructures, social factors such as housing conditions and population density, and host factors such as nutritional status and co-existing medical conditions. Another potential factor likely to influence mortality in a future pandemic is the high HIV/AIDS prevalence in some developing countries. Excess deaths attributed to pneumonia or influenza are significantly higher in HIV-positive persons during influenza seasons (5). HIV co-infection with a pandemic virus can be associated with more severe infections, which may further raise death rates in countries with high HIV/AIDS prevalence.

For these reasons, deaths associated with a future pandemic may be greater in developing countries than in industrialized countries. One study concluded that 96% of

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Estimated deaths in the next influenza pandemic

- Global estimate: 62 million deaths
- 96 % of deaths would occur in developing countries



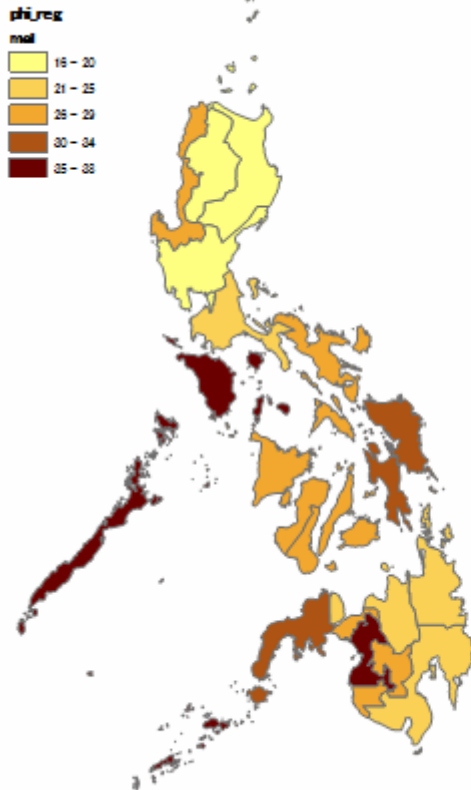
Christopher J L Murray et al. Lancet 2006; 368: 2211–18

フィリピン・レイテ島での新型 インフルエンザ対策強化

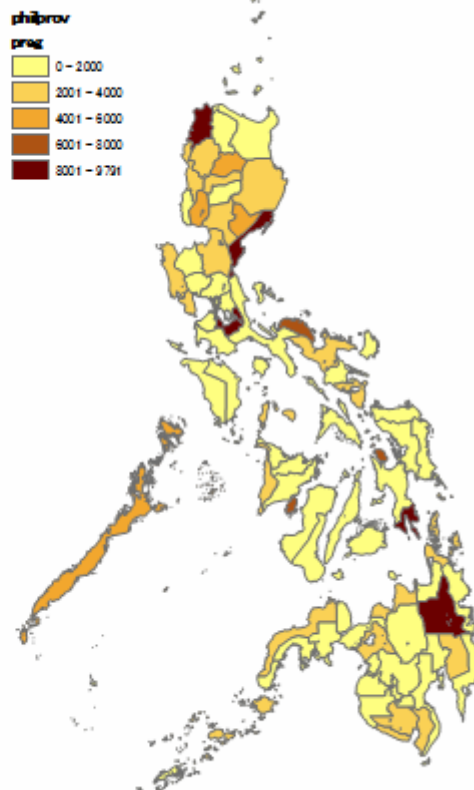
- Eastern Visayas Regional Medical Center レイテ島の三次救急医療施設
ベッド数：250(小児科52床)
- 生後8日から14歳の肺炎による入院患者
- 2008年5月1日から開始
- 617名の入院患者のうち61名死亡（死亡率10%）
- 病院には人工呼吸器は手術用以外にはなし



U5 Underweight rate (%)



妊産婦数/Province(2007)



Prevention and Protection from Novel Influenza A (H1N1)

29 countries affected; 22 hospitalized; 9-100 people sick; still spreading (as of May 27)

What is Influenza A (H1N1)?

Influenza A (H1N1) is caused by a novel flu virus that resulted from the reassortment of 8 viruses from pigs, humans and birds. This virus is spreading from person-to-person, probably in much the same way that regular seasonal influenza viruses spread. There is no vaccine yet to protect humans from the virus. But there are existing and experimental medicines that are effective in treating these influenza (H1N1) viruses.

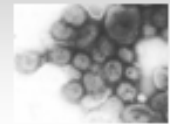


Image of Influenza A (H1N1) virus
Data by Mike Stillman

What are the symptoms and signs?

- ✓ Influenza like symptoms
- * Fever
- * Fatigue
- * Runny nose*/Nose or Joint Pains
- * Sore throat*/Lack of Appetite
- * Cough
- * Nausea Vomiting
- * Headache
- * Diarrhea

Who are the high risk individuals?

- ✓ Pregnant women
- ✓ 65N1 patients
- ✓ Children less than 5 years
- ✓ Persons 60 or older
- ✓ People with Chronic Illnesses, Cardiovascular Disease, Disease of kidney/liver/lungs and metabolism

Who can be infected?

Initial case can be a patient with Influenza like symptoms AND History of travel to Influenza A (H1N1) affected country OR residence in a community with confirmed cases of Influenza A (H1N1) OR close contact with a suspected human case of Influenza A (H1N1) within 10 days of symptoms onset

How is it transmitted?

Exposure to droplets from the cough and sneeze of the infected person.

* The novel H1N1 A (H1N1) virus is spread by using respiratory etiquette.

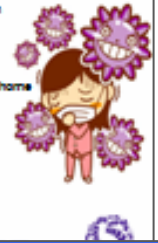
How can disease be prevented?

✓ Respiratory (cough) etiquette:

- * Cover your nose and mouth, and turn away from people when coughing and sneezing.
- * If you have a cough, wear mask not to transmit to other person.

✓ Wash hands with soap and water when you get home

- ✓ Avoid close contact with sick people
- ✓ Increase your immunity (power of resistance)
 - * Eat nutritious food
 - * Take enough rest
 - * Manage your stress
- ✓ Break away from the crowd
- ✓ Avoid extra gathering



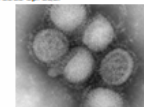
• What is Novel Influenza (H1N1)

• Seasonal influenza.

Influenza is an acute viral disease of the respiratory tract.

• Novel Influenza (H1N1) .

H1N1 (referred to as "swine flu" early on) is a new influenza virus causing illness in people. This virus is spreading from person-to-person, probably in much the same way that regular seasonal influenza viruses spread.



• Incubation period.

- Seasonal influenza : Average 2 days (range 1-4)
- Novel influenza : 2-7days

• Symptoms.

The symptoms of Novel Influenza in people are expected to be similar to the symptoms of regular seasonal Influenza.

- Fever
- Runny Nose
- Sore Throat
- Cough (usually dry)
- Headache
- Fatigue
- Muscle or Joint Pains
- Lack of Appetite
- Nausea Vomiting
- Diarrhea



• Mode of transmission.

Exposure to droplets from cough and sneeze from infected person. Hand/Face contact after touching a person or surfaces contaminated with the virus. Influenza virus may persist for hours on solid surfaces, particularly in lower temperatures and lower humidity.



Prevention

- Respiratory (cough) etiquette
 - * Cover your nose and mouth, and turn away from people when you cough and sneeze.
 - * If you have a cough, wear mask not to transmit to other person.
- Wash hands when you get home
- Break away from the crowd
- Avoid extra outgoing
- Avoid close contact with sick people
- Increase your power of resistance
 - * Eat enough food
 - * Take enough rest



まとめ

- 日本で世界で起こることについての分析・評価が必要
 - 必要なのは情報量の多さではない
 - 情報を分析・評価する基礎知識と基本的な分析能力
 - そして起こる得ることをイメージできる想像力
- 日本および世界の新型インフルエンザ対策に欠けているもの
 - 少し考えればわかることを、少しも考えてこなかった(そして今も考えていない)想像力の欠如