

## Riječ Uredništva

### STIGLA JE NOVA PANDEMIJA GRIPE

#### Pandemija gripe je među nama

Da, nastupila je nova pandemija gripe uzrokovana novim virusom A/H1N1. Svjetska zdravstvena organizacija (SZO) proglasila je 11. lipnja 2009. godine šesti stupanj pandemije. Novi virus gripe proširio se na sve kontinente. U Hrvatskoj je registrirano više stotina oboljelih, a to su zasad uglavnom mlađi ljudi koji su bolest stekli u inozemstvu.

U ožujku 2009. godine, dakle 40 godina nakon posljednje pandemije influence (hongkoška gripa 1968. godine) u Meksiku se pojavio novi virus influence. Novi virus nastao je kao rezultat preslagivanja (engleski: *reassortment*) čak četiri tipa virusa A/H1N1 (dva svinjska soja, jedan ptičji i jedan humani) u organizmu svinje. Zato se u početku pojavio naziv svinjska gripa, iako se bolest ne prenosi sa svinja na ljude, nego s čovjeka na čovjeka, a po mjestu prve pojave virusa bolest je nazivana i meksičkom ili sjevernoameričkom gripom. Za neke zemlje je naziv svinjska gripa bio neprihvatljiv, a ni Meksiko se nije zalagao da zadrži naziv po svojoj zemlji pa se iskristalizirao naziv nova gripa A/H1N1, a najnoviji naziv prihvaćen od SZO-a jest – pandemijski virus H1N1/2009.

Za razliku od drugih infektivnih bolesti, zbog stalnih promjena virusa, pojedinac i čovječanstvo su stalno izloženi i podložni influenci. Da bi virus influence uzrokovao pandemiju mora posjedovati nekoliko pandemijskih karakteristika, a to virus H1N1/2009 ima: a) posve novi virus (čovječanstvo se do sada nije susrelo s njim), b) lak prijenos s čovjeka na čovjeka (poput virusa sezonske gripe, respiratornim putem i dodirnom), c) uzrokuje bolest u ljudi (koja sada nije osobito teška), d) proširio se na mnoga područja (do sada je bolest registrirana u više od 190 zemalja).

#### Bolest nije osobito teška

Prema prvim podacima iz SAD-a, Meksika i Kanade, a sada i iz europskih zemalja nova gripa je po kliničkoj prezentaciji vrlo slična sezonskoj. Najvjerojatnije je očekivanje da će takva i ostati i da neće devastirati svijet i pisati novu povijest. Sadašnja bolest ima smrtnost manju od 0,5 %. Sada se zna da mnogo češće obolijevaju djeca i mlađi ljudi, a da se bolest u starijih rjeđe pojavljuje, pa je stoga broj komplikacija i njihova težina manji u usporedbi sa sezonskom gripom. Postoje dokazi da starija populacija ima neki stupanj unakrižno zaštićujuće imunosti od ranije preboljelih epizoda gripe.

No, zabrinutost postoji zbog najmanje dva razloga. Prvi je u nemogućnosti prevencije bolesti cjepivom na početku pandemije. Drugi je razlog u nepredvidivosti kretanja pandemije i težine bolesti, pa se još ne zna hoće li to uistinu i ostati blagi oblik bolesti tijekom sljedećih mjeseci ili godina. Naime, moguće su daljnje promjene virusa, odnosno rekombinacija s virusima sezonske ili ptičje gripe sa izazivanjem mnogo teže bolesti, odnosno komplikacija.

U svakom slučaju, nova je pandemija gripe "utješna nagrada" za čovječanstvo. Naime, ne smije se zaboraviti da je virus ptičje gripe A/H5N1, za koji se do jučer mislilo da je najvjerojatniji novi pandemijski virus, uzročnik izrazito teške bolesti u ljudi s vrlo visokom stopom smrtnosti (više od 60 %).

#### Svijet nije bespomoćan

Za razliku od većine drugih infektivnih bolesti, svijet nije izrazito napredovao u mogućnostima borbe protiv influence jer se epidemije pojavljuju svake godine pri čemu obolijeva i umire veliki broj ljudi. No, u sučeljavanju s novom pandemijom ipak više nismo bespomoćni kao npr. 1918. ili 1957. godine. U borbi protiv influence općenito, sa stajališta pojedinca, te za ublažavanje epidemijskog i pandemijskog pohoda sa stajališta država i ukupnog čovječanstva, najvažnije oružje jest cjepivo. No, proces definiranja pandemijskog soja, namnožavanje virusa za proizvodnju, sama proizvodnja na oplodjenim kokošjim jajima, te postupak ispitivanja na životinjama i ljudima jesu izuzetno složeni i odgovorni postupci. Zbog toga cjepivo može biti dostupno tek za nekoliko mjeseci, odnosno krajem ove godine. Pandemijsko cjepivo će sadržavati samo

## Editorial

### THE NEW INFLUENZA PANDEMIC HAS ARRIVED

#### Influenza pandemic is here

The new influenza pandemic caused by new A/H1N1 virus has arrived. The World Health Organization (WHO) has proclaimed the sixth level of pandemic on June 11, 2009. The new influenza virus has spread to all the continents. In Croatia so far several hundreds of cases have been reported, mostly young males who acquired the disease abroad.

In March 2009, 40 years after the last influenza pandemic (Hong Kong flu in 1968), a new influenza virus occurred in Mexico. The new virus has developed as the result of reassortment of as much as four types of A/H1N1 viruses (two swine strains, one bird and one humane) in swines. Therefore, the term swine flu was used at the beginning of pandemic, although the disease is not transmitted from swine to humans, but from humans to humans, and according to the location of the first occurrence of the virus, the disease was also named Mexican or North American flu. For some countries, including Mexico, the term swine flu/Mexican flu was unacceptable, so the new term A/H1N1 came into use, and the latest term accepted by the WHO is – pandemic virus H1N1/09.

As opposed to other infectious diseases, and due to constant changes of the virus, individuals and mankind have constantly been exposed and subject to influenza. In order for influenza virus to cause a pandemic, it must exhibit several pandemic characteristics, which H1N1/2009 virus already has: a) a completely new virus (that mankind has never seen before), b) easy transmission from humans to humans (like seasonal flu virus, via respiratory route and contact), c) causes disease in humans (which for now is not very severe), d) has spread to many areas (until now the disease was registered in more than 190 countries).

#### The disease is not particularly severe

According to currently available data from the USA, Mexico, Canada and now from European countries as well, the new influenza is similar to seasonal influenza by its clinical manifestation. It is most likely to expect that it shall remain such and that it will not devastate the world and write new pages in history. Current illness has the mortality rate of less than 0,5 %. It is known that children and younger people are more frequently affected, and since the disease occurs less frequently in the elderly, the number of complications and their severity is smaller compared to the seasonal flu. There is evidence that older population has some level of cross-immunity from previous episodes of flu.

However, the concern still exists for at least two reasons. The first one is the impossibility to prevent the disease with vaccine at the beginning of pandemic. The second is the unpredictable growth of pandemic and severity of disease, so that it is still unknown whether the disease will remain mild during the next several months or years. Namely, further mutations of the virus are possible, that is recombinations with seasonal flu or bird flu viruses, thus causing more severe illnesses, especially complications.

In any case, the new influenza pandemic is a "consolation prize" for mankind. Namely, we must not forget that bird flu A/H5N1 virus, until recently considered the most likely new pandemic virus, has caused extremely severe disease with high mortality rates (more than 60 %).

#### The world is not helpless

As opposed to the majority of other infectious diseases, the world has not made a particular progress in finding possibilities to fight against influenza, because epidemics are occurring every year and affecting and killing many people. However, in confronting the new pandemic, we are not as hopeless as in 1918 or 1957. In the fight against influenza, in general, from individual point of view, and in order to relieve epidemic and pandemic advances, for countries and mankind in general, the most important weapon is the vaccine. However, the process of defining pandemic strain, replication of the virus for production, the production itself on embryonated chicken eggs, conducting research on animals and humans are extremely complex and

jedan soj virusa (monokomponentno), za razliku od sezonskog koje je trokomponentno. Ali za nastanak potpune imunosti pandemijsko cjepivo će najvjerojatnije trebati primijeniti u dvije doze s razmakom od nekoliko tjedana.

U ovom času nije moguće predvidjeti sve mogućnosti širenja novog virusa i težinu bolesti, odnosno točno vrijeme dostupnosti cjepiva, pa nije moguće sada donijeti konačne stavove o distribuciji cjepiva i primjeni u određenim populacijskim ili profesionalnim skupinama. Primjerice, moguće je da se pandemija brzo proširi i da veliki dio pučanstva postane prirodno imun prije dostupnosti pandemijskog cjepiva. Ako se, npr. novi virus bitno promijeni u sljedećih šest mjeseci ili godinu dana i počne izazivati težu bolest u ljudi, tada će i novo cjepivo biti slabije učinkovitosti. Pandemijsko cjepivo prioritetno će trebati dobiti ugrožene populacijske skupine, a to su mala djeca i trudnice, te bolesnici s kroničnim bolestima i imunokompromitirani. Starija djeca i mlađi odrasli, izgleda, da će imati prednost pred starijima koji nemaju kroničnih bolesti.

Osim cjepiva, čovječanstvo sada raspolaže i učinkovitim antivirusnim lijekovima za liječenje i sprječavanje bolesti. To je posve nova mogućnost, koja nikad u prošlosti nije postojala, za ublažavanje prvog pandemijskog vala dok ne bude dostupno pandemijsko cjepivo. Zato SZO u svojim preporukama već godinama potiče vlade zemalja svijeta za nabavu i skladištenje antivirusnih lijekova. Inhibitori neuraminidaze (oseltamivir, zanamivir) nisu do sada našli širu primjenu u liječenju ili sprječavanju sezonske gripe. Temeljni je problem u potrebi primjene lijekova u samom početku bolesti, poželjno prvi dan nakon pojave simptoma, a učinkovitost imaju samo pri primjeni u prvih 48 sati.

### **Hrvatska je spremna**

Hrvatska ima dobro organiziranu javnozdravstvenu službu, primarnu i bolničku zaštitu, te dugu tradiciju i dobru organizaciju cijepljenja. To su preduvjeti za dobro funkcioniranje zdravstva i u izvanrednim situacijama. Hrvatska ima uskladišteno i naručeno 800000 pakiranja antivirusnih lijekova, a to pokriva 20% pučanstva, što je u europskom prosjeku. Osim antivirusnih lijekova, osigurano je i 1,5 milijuna doza pandemijskog cjepiva kada ono bude dostupno.

No, osim pandemijske gripe, u sljedećoj zimskoj sezoni susrest ćemo se s novom, uobičajenom epidemijom sezonske gripe. U ovom času se čini da bi bilo praktično provesti cijepljenje protiv sezonske gripe već početkom jeseni, dakle barem mjesec dana prije uobičajene primjene. Tako bi se dobilo potrebno vrijeme za organizaciju novog cijepljenja pandemijskim cjepivom.

*Urednički odbor*

demanding procedures. Therefore, we can expect the vaccine to be available only in several months time, that is by the end of this year. Pandemic vaccine will contain only one strain of the virus (monocomponent), as opposed to seasonal that is tricomponent. However, in order to achieve complete immunity, the pandemic vaccine will most likely have to be administered in two doses with several weeks apart.

At this moment it is not possible to predict all possibilities of spread of the new virus and the severity of the disease or the exact time of vaccine availability, so therefore it is not possible to reach the final decision on the distribution of vaccine and its administration among particular population or group of professionals. For instance, it is possible that the pandemic spread is fast and that a large part of the population will develop natural immunity before pandemic vaccine is available. If, for instance, the new virus significantly changes in the next six months or year and starts causing severe disease in humans, then the new vaccine will be less efficient. Pandemic vaccine should, as a priority, receive those groups of people who are at utmost risk, such as small children and pregnant women, as well as patients with chronic illnesses and immunocompromised. Older children and younger adults, apparently, will have the advantage over older people with no chronic diseases.

Besides vaccine, the mankind now has at its disposal effective antiviral drugs for the treatment and prevention of diseases. This is an entirely new possibility that never before existed, for relieving the first pandemic wave until pandemic vaccine is available. Therefore the WHO in its guidelines recommends governments of all countries to purchase and store antiviral drugs. Neuraminidase inhibitors (oseltamivir, zanamivir) have not so far been widely used in the treatment and prevention of seasonal flu. The basic problem is the need to use the medication at the very onset of disease, preferably on the first day after the symptoms occurred, and their efficiency is valid only if taken within the first 48 hours.

### **Croatia is ready**

Croatia has a well organized public health service, primary and hospital care and a long tradition of successful vaccination program. These are prerequisites for good functioning of the health care system even in extraordinary situations. Croatia has stored and ordered 800.000 packages of antiviral drugs, covering 20 % of the population, which is the European average. Apart from antiviral drugs, our government has ensured 1,5 million doses of pandemic vaccine once it becomes available.

However, besides pandemic flu, in the upcoming winter season, we shall experience the usual epidemic seasonal flu. At this moment it seems practical to start with vaccination against seasonal flu at the beginning of autumn, meaning at least one month prior its usual application. In this way, required time would be gained for organization of new vaccination with pandemic vaccine.

*Editorial Board*