RE-FLECTIONS
Underwriting Newsletter

LETTER FROM THE EDITOR

Dear Readers:

This month, *Re-flections* features two articles that I hope will stimulate your interest. The first, written by Dr. Oscar Cartaya, provides an in-depth analysis of the risk related to a possible Avian Flu epidemic. This article discusses the specifics of the H5N1 virus' characteristics and sheds insight into pandemic projections.

The second article, written by Dr. Sharylee Barnes, provides very practical information on a cardiac test that is expected to be used more often in the near future. This is the Coronary Computed Tomography Angiogram (CTA) test. Dr. Barnes discusses the value of this test and compares it to other more traditional cardiac tests.

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is a major factor that prevents easy transmission of this virus between humans.

Once the current H5 influenza virus has reached its target cells and infected a human host, it has a number of genetic characteristics that makes it lethal. Among these, it has resistance to interferons; it codes for thick and tenacious mucus production; and it is able to attach easily to other nearby target cells. Hemorrhage, edema, and widespread cell bursting have not been characteristic features of this virus, and its reproductive rate is within the normal range for human influenza viruses and is not close to the rate of reproduction of the 1918 virus.

The results of an infection with either the H1 or the H5 virus are quite different. The 1918 virus spread very rapidly and caused respiratory failure through a complex mechanism including production of an overwhelming level of infective particles, cellular edema, and hemorrhages. Large numbers of people were infected because of the extraordinary level of viral production, the easily reachable cell types targeted by this virus, and its strong attachment to target cells. An abnormally high proportion of those infected developed respiratory failure and secondary bacterial infections. Both the transmission rate and the mortality rate were very high with the 1918 pandemic virus.

The current H5 avian flu virus cannot be transmitted effectively between humans because of the location of the cells it targets. Once established, this virus causes respiratory failure through a mechanism including fluid pooling in the lower respiratory tract. With this virus, the transmission and rate of infection are low, because of the poor accessibility of the target cells; once infected, however, a large percentage of the patients may die from this disease.

Genetic Change

It is clear that the current H5 avian influenza virus may not spread rapidly among humans because of the inaccessibility of its target cells. However, it is well-known that influenza viruses mutate and change, sometimes quite rapidly. This process of change is well-studied and involves either genetic mutation or genetic reassortment. Genetic mutation is an actual change in the genetic material of the virus. Minor genetic changes (called antigenic drift) are the most common types of mutations, but produce only minor changes in the characteristics of the virus. Major mutations (antigenic shift),

Azerbaijan	0	0	0	0	0	0			8	5
Cambodia	0	0	0	0	4	4			6	6
China	1	1	0	0	8	5	12		21	14
Djibouti	0	0	0	0	0	0			1	0
Egypt	0	0	0	0	0	0	15		15	7

ment is not likely to produce the kind of changes needed to increase the transmissibility between humans of the current H5 avian influenza virus.

It must be understood that for the current H5 avian influenza virus to become easily transmitted between humans, its target cell location must change to an easily accessible location. Since genetic reassortment is not a likely mechanism to cause this to happen, and antigenic drift is not likely to cause such a major change, it is only through antigenic shift that such a change may occur. As described above, this would be a rare and unpredictable event.

A new strain of the H5 avian influenza virus that does not respond to experimental vaccines made against the current H5 avian influenza virus has been reported in China. This virus is reportedly capable of infecting humans but cannot be transmitted between humans. It is thought that this new strain resulted from a process of antigenic drift. Other such strains with relatively minor genetic changes must be expected in the future. Until a major genetic change occurs in the H5 avian influenza virus, the review presented in this paper is valid.

Conclusions Regarding the H5 Avian Influenza Virus

Currently, we have effective influenza vaccines capable of providing protection against death (even if "non-matched"); effective antibiotics to control secondary bacterial infections; adequate techniques for life support and fluid balance; and an elaborate knowledge of cardiac physiology and arrhythmias together with effective treatments for such. It is not reasonable to project a mortality rate comparable to that experienced in the 1918 pandemic for any new influenza pandemics treated with modern techniques.

Conclusions

We have valid reasons to be cautiously optimistic about the prospects for the outcome of a possible new pandemic caused by the present H5 avian influenza virus. Given the data presented about the current virus in comparison with the 1918 virus, it is not at all certain that the present virus will cause a major pandemic. Even if the present H5 avian influenza virus were to mutate and become readily transmissible among humans, there is no convincing indication that it will be as lethal as the 1918 pandemic virus. Should an outbreak occur, numerous factors will impact the final outcome, including the combined effects of the measures in place to identify an H5 avian influenza outbreak and take early action; preparations for mass vaccinations (possible with "non-matched" vaccines); restrictions of congregation and travel aimed to lower the spread of the disease over a longer amount of time; and the marked advances since 1918 in our capacity to medically care for this condition and provide adequate ventilatory support to infected persons.

Based upon this review of the available data and preparations to deal with this outbreak, it is likely that we will be able to keep the overall mortality in line with the mortality observed during other pandemics in the later years of the 20th century (an overall mortality of 0.1% of the infected group). Furthermore, if such an H5 avian influenza pandemic were to occur, it is likely that peak mortality will occur among the very young and the very old and infirm; in addition, persons living in isolated areas or not having access to adequate medical care may experience a higher mortality rate. The evidence suggests that the disaster scenarios outlined in today's news media predicting a very high mortality rate equal to or higher than the mortality rate recorded in the 1918 pandemic for this new potential H5 avian influenza pandemic are not supported by the available data, and have a very small likelihood of becoming true.

References

Sometimes in an APS received for underwriting, only a few letters (CTA) alert the underwriter that a cardiac evaluation is planned for the proposed insured. To add to the confusion, the newer CT scanning machines may be used to assess cerebral, carotid, pulmonary, and renal vasculature, so the term angiography needs context.

Computed tomography is not new, but its technology is continually being refined. The basic X-ray consists of a focused image being made at a particular tissue depth in order to create a thin cross-sectional view (slice) of the tissue to be studied. Serial cross-sections are done creating multiple images. In addition, the X-ray tube rotates around the tissue in a spiral pattern so the cross-sections are from a multitude of angles. From all this X-ray data, the computer generates high-resolution, 3-D images that resemble a photograph.

Each rotation performs a number of images. Within the past few years, machines have been developed that obtain 16 slices per rotation, the number needed to get clear images of the coronary arteries. The advent of 64-slice machines achieves remarkable detail. At three rotations per second, a multi-slice CT creates up to 192 slices per second!

Speed is important because the scanner captures an image of a moving object, the beating heart. Speed *freezes* the image, like a fast shutter speed on a camera. The resolution possible is amazing and important when looking at the sub-millimeter-sized anatomy of the coronary arteries.

Multi-slice scanners can visualize more than just hard plaque in the coronary arteries. Artery caliber, lumen, course, soft plaque, wall thickness and the presence of dissection, vasculitis, myocardial bridging or aneurysm can be seen by the trained eye. Excellent visualization of the aorta, valves, cardiac chambers and walls, pericardium, and intra-cardiac masses is possible. We think that Cardiac CTA information might supplant that from Echocardiography and Coronary Artery Catheterization in some clinical settings.

The initial image produced in Cardiac CTA is done without contrast and is basically equivalent to EB42824(i28 Tm[-slice)-24pl0(a7(t)]TJn 1 Tf10 0 0.Beam36 37.428 Tm[contrast)-23(and d d d d

and therefore Cardiac CTA will not work for them—at least not in the arteries that are known to have calcium. If an obstructing lesion is found during a traditional coronary artery catheterization, it can be treated on the spot. This is not possible with Cardiac CTA. It cannot be used with tachycardia, atrial fibrillation, or frequent ectopy because the movement will blur the image. Cardiac CTA does not give a good image of the smaller branches (obtuse marginal, diagonal, septal perforators, etc.).

The disadvantage of contrast use still exists. One must be concerned with possible allergy to iodine or shellfish and the kidney toxicity of cumulative contrast doses, especially in the elderly and people with previous radiation therapy near the kidneys. The radiation dose is higher than with coronary artery catheterization, and is similar to the radiation used for a technetium nuclear stress test. Cardiac patients are at risk for high cumulative radiation exposure.

Given the information above, who are good candidates for the test? A person who is being considered for a catheterization, but whom the attending cardiologist believes is unlikely to need an intervention or for whom he expects to "rule out" coronary disease, is a good candidate. This might include worried asymptomatic people with abnormal lipids, diabetes, or a bad family history, as well as people with atypical chest pain or suspect syndrome X'. Another group would be symptomatic patients with equivocal or discordant traditional cardiac testing, such as: "false-positive" exercise ECG, mildly positive stress ECHO, or diaphragmatic attenuation defects on stress Perfusion scans.

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