Scientific Committee on Vector-borne Diseases

An Assessment of Japanese Encephalitis Vaccination in Pigs in Hong Kong

Background

This paper provides an assessment of vaccinating pigs with Japanese encephalitis vaccine in Hong Kong.

2. It must be remembered that JE is not a contagious disease and this message needs to be made clear to the public. It will only be transmitted by biting from a competent infected mosquito. The virus source may be from the pig-mosquito-pig or bird-mosquito-bird cycle but spill over to dead-end hosts like humans and horses only occurs via mosquitoes. Vaccination Epidemiology

3. From testing on the AFCD Pig Breeding Centre at Ta Kwu Ling, breeding sows in Hong Kong that have been exposed to mosquitoes have been exposed to JE virus (all adult sows and boars in HK) and most have protective antibody to JE virus. (This is why we don't see any abortions or male reproductive problems from JE infection)

4. Sows pass maternal antibody to piglets that protects them from JE infection until the maternal antibody gradually disappears. This takes until 8 to 14 weeks of age in the piglet from our sequential testing of litters at the Government Pig Farm.

5. The duration of maternal antibody from natural exposure or from vaccination of sows will be the same so vaccination of sows to produce maternal antibody is not going to produce different levels of
maternal protection in young pigs.

6. Slaughterhouse monitoring studies with JE show that natural infection occurs in pigs throughout the year in Hong Kong. As soon as piglets lose their maternal immunity and are exposed to JE carrying mosquitoes they become infected, produce protective antibodies within 14 days and thereafter they will not become infected with, or transmit JE after that time. JE infection confers life-long immunity for the pigs.

7. Mosquitoes in effect provide an active JE vaccination programme of pigs as they lose their maternal antibodies. The biology of the system prevents sudden large build up of susceptible pigs that could be infected leading to spill-over to humans.

8. With continuous breeding of pigs throughout the year there will be a 'continuous supply daily of young pigs losing their maternal antibody, becoming susceptible to infection, seroconverting to JE and becoming immune to further JE infection. Unfortunately the time that maternal antibody declines varies from litter to litter and the optimum time for the first man-made vaccination also varies. With man-made vaccination the time of recommended vaccination is a compromise so that not all litters are likely to be optimally vaccinated.

9. Man-made vaccinations of pigs against JE in Taiwan and Japan are done to prevent reproductive failure problems in environments where the disease occurs epidemically in pigs. In these situations pigs require 2 doses a month apart and it takes 1-2 weeks after the second vaccination before good antibody protection is present. Thailand, which has a significant JE problem in humans, does not vaccinate pigs against JE for public health purposes.

10. Giving the first vaccination while maternal antibody is present reduces the primary vaccination response and results in poorer protection after 2 doses, so the first vaccination must be given after maternal antibody falls. However the exact timing of the decline in maternal antibody will vary from pig to pig (8-14 weeks of age).

11. If no JE infected mosquitoes were present and pigs were vaccinated at 3 months it would take until 4.5 months before they were protected. But with JE mosquitoes present, as is the case in Hong Kong, these pigs will have been exposed and protected at 3.5 to 4 months, irrespective of vaccination.

12. At times of year when mosquito numbers are low the risk of any spill-over to humans is also very low. At times when mosquitoes are abundant the unprotected pigs quickly become antibody positive and protected as they lose their maternal antibody cover. Due to variation in maternal antibody levels and age of the pigs this infection is staggered and does not result in large numbers of pig infections at any point of time so the risk of spill-over to
humans is also very low given normal mosquito precautions at that time of year.

13. There is a risk from relying on vaccination. Protection in sows from natural infection is life-long whereas with vaccination long term protection depends on regular booster vaccination. Unless booster vaccination is regularly provided to sows before antibody levels fall there is increased risk that unprotected litters will occur and this means large numbers of susceptible piglets at one point of time. If they all become infected at one time there is increased risk of spill-over to humans.

14. Vaccination of animals with a live virus whilst there is continuously circulating field virus is not recommended. Japanese encephalitis is a flavivirus which has been demonstrated to recombine with other strains of flaviviruses. Simultaneous infection with two live flaviviruses, which has most certainly be the situation if pigs are vaccinated, will provide the greatest opportunity far recombination and subsequent creation of a novel virus with unknown pathogenicity. Since migratory water birds are the main reservoir of JE, this novel virus would be expected to spread to our neighbours.

15. The live virus used in the vaccine has been attenuated for pig use but its pathogenicity for humans is unclear. The manufacturers recommended caution when using the vaccine to prevent accidental human injection.

16. Vaccination of pigs will have no effect on the transmission cycle of the virus. Ardeid birds (e.g. egrets and herons) play an important role as virus reservoirs with pigs acting as amplifying hosts. The bird mosquito-human cycle will continue even without a (theoretical) immune pig population.

Centre for Health Protection
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## Pros and Cons for JE vaccination of local pigs for human JE prevention

<table>
<thead>
<tr>
<th></th>
<th>Natural exposure (“Mosquito” vaccination.)</th>
<th>Man-made vaccination (MMV)</th>
<th>Remarks</th>
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</thead>
<tbody>
<tr>
<td>Level of antibody protection</td>
<td>High</td>
<td>Low-moderate</td>
<td>Igarashi (2002) Current Topics in Microbiology and Immunology 267: 139-152 showed that antibody titer in vaccinated pigs were significantly lower than pigs exposed naturally.</td>
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<tr>
<td>Lag phase before antibody protection</td>
<td>1-2 weeks after maternal antibody gone</td>
<td>5-6 weeks after maternal antibody gone</td>
<td>Two doses are month apart protection 1-2 weeks after second dose for MMV.</td>
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<tr>
<td>Duration of antibody protection</td>
<td>Life long</td>
<td>Needs annual boosters</td>
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<tr>
<td>Risk in recombination to give highly pathogenic virus</td>
<td>Nil</td>
<td>New genes in the live attenuated JE vaccine will be continuously exposed to genes of circulating JE field viruses raising the possibility of recombination to give a new JE virus with unknown properties</td>
<td>Seligman and Gould (2004) The Lancet 363: 2073-75 recommend caution with use of live-attenuated vaccines in endemic situations.</td>
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<tr>
<td>Risk to vaccinator</td>
<td>Nil</td>
<td>Possible.</td>
<td>The vaccine virus has been attenuated for pigs but its pathogenicity status for humans is not clear. The manufacturers recommend caution to prevent accidental human injection.</td>
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<tr>
<td>Timing of vaccination</td>
<td>See remarks</td>
<td>Must wait for maternal antibody to fall before pigs are vaccinated</td>
<td>Mosquitoes repeatedly &quot;vaccinated&quot; as maternal antibody falls. Timing of MMV is very difficult in endemic situation, too early - poor vaccine coverage, too late - susceptible pigs.</td>
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<td>Impact on other transmission cycles</td>
<td>nil</td>
<td>nil</td>
<td>The wild bird-mosquito-human cycle will still continue.</td>
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