THE ROYAL SOCIETY

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Summary of oral evidence: Dr Ilaria Capua

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Dr Capua is head of the Virology Department at Istituto Zooprofilattico Sperimentale delle Venezie, Padova, Italy and Head of the National, FAO and OIE (World Organisation for Animal Health) Reference Laboratories for avian influenza and Newcastle disease. Her team consists of three units: one that carries out diagnostic activity; one that produces diagnostic reagents and evaluates vaccines; and one that performs research at an international level. Dr Capua spoke to the working group via teleconference.

Members of the working group present were: Sir John Skehel, Professor Glynis Breakwell, Professor Neil Ferguson, Dr John McCauley, Professor Andrew McMichael, Professor Karl Nicholson and Professor Robin Weiss.

Key points

Data sharing

Dr Capua was asked by the working group about her recent experiences with obtaining and sharing data on the H5N1 virus. Dr Capua does not handle human samples but has received avian samples from many of the affected areas. Dr Capua told the group that the National Centres are not provided with international guidelines to manage the sequence/clinical data.

Dr Capua received and sequenced the first samples of the H5N1 virus from Nigeria. She was approached by several people from the World Health Organization (WHO) network to ask if she'd like to deposit the Nigerian sequence data in their limited-access database. In return she was offered the password for the database and access to the other information it stores. However, Dr Capua declined the offer and deposited the sequence data for the Nigerian H5N1 virus in GenBank, a publicly accessible database. Dr Capua told the group that she believes that questions remain unanswered about how the virus reached and is spreading in Africa, and that sharing data openly is a vital tool in addressing this and other unanswered issues. Dr Capua also commented on the extensive media coverage of the issue. She believes that if H5N1 is genuinely the greatest threat to human health, then researchers must collaborate more actively to learn more about it, and sharing information is instrumental to this. However, the issue should not be over-hyped by the media.

Dr Capua has not seen any changes in the numbers of international specimens sent to her laboratory following the publication of the Nigerian sequence. She has received specimens from approximately 15 African and Middle Eastern countries and diagnosed High Pathogenic Avian Influenza (HPAI) and Newcastle Disease in about six or seven of those. The relevant Government Minister of each country was asked permission to publish the sequence data and all have agreed. She has also published sequence information from Iran, Afghanistan and Vietnam with permission from their Governments.

Dr Capua told the working group that after publishing the Nigerian sequence data in GenBank, she wrote letters to colleagues internationally urging them to do the same. Subsequently, she has been told by the administrator of GenBank that more sequences have been made available.

She believes that veterinarians and veterinary virologists are not accustomed to their research being such high profile and may have lost perspective. Having sequenced the H5 haemagglutinin gene of the samples they receive, they need to think about sequencing other genes and sharing the data with experts in related fields.

There are hundreds of avian influenza isolates in repositories worldwide that have not been sequenced which may contain significant information which could contribute to increasing our knowledge.

Dr Capua told the group that she is leading the FLUID project which was established within the OFFLU Network (OIE/FAO network of expertise on avian influenza) and the NIH. Virologists are asked to submit H5 samples, together with historical samples to the database to advance the field. Virologists are able to send RNA to the Institute for Genomic Research, Rockville, to be sequenced free of charge. NIH will also refund any costs involved such as shipping, staff time etc.

Poultry vaccination policy in Italy

Vaccination in poultry in Italy started after an outbreak of low pathogenic AI (LPAI) H7N1 in 1999-2001. Within 9 months the virus mutated to HPAI and more than 13 million birds died or were destroyed. After the outbreak had been eradicated LPAI H7N1 re-emerged and other 3-4million birds were killed. No financial compensation was foreseen at the time for LPAI in Italy and the economic consequences of another AI epidemic would have caused the collapse of the poultry industry.

The so-called DIVA (Differentiating infected from Vaccinated animals) system was developed to control the re-emergence of LPAI H7N1. This is based on the administration of a vaccine with a heterologous neuraminidase (H7N3) to act as a marker and differentiate vaccinated from infected birds. Birds at high risk were vaccinated over a year, including turkeys, layers (chickens) and some breeders in densely populated areas. Following vaccination the second wave of LPAI I H7 infection was eradicated and vaccination was discontinued.

Shortly after, an outbreak of H7N3 followed in the same area and birds were vaccinated with an H7N1 vaccine to eradicate the virus. Subsequently a bivalent H5N7 vaccine programme has been introduced. Dr Capua told the group that she considers the programme a success as previous outbreaks resulted in the infection of approximately 300 flocks, whereas following vaccination this has been reduced to 15 outbreaks as the programme has reduced secondary spread.

Dr Capua was asked about how they chose the vaccine strain and she told the group that ideally vaccines with rare neuraminidases should be, but at the time (2000) the H7N3 strain from Pakistan was the only strain available at that time. Later an H7N1 strain of vaccine became available and that was used. The vaccine is a natural isolate which had been shown to be efficacious and was only used for a limited time of 12-18 months so there was no need to update the H7 component.

Dr Capua stressed that vaccination in poultry can be a useful tool providing that an effective monitoring programme is in place in the field. Good biosecurity is also needed. The monitoring programme is targeted to identifying field infection, vaccine efficiency etc. Sentinels are also used in flocks. Only a small area at high risk of infection is vaccinated in Italy, and the 'fast reporting system' for the early identification of an outbreak in place guarantees the identification of ant viral incursions in the vaccinated population. Backyard flocks are also monitored, and in the past H7N7 has been found in domestic goose and mallard. Approximately 5000 wild birds have also been tested for the H5N1 virus but it has not been found.

There was a discussion of virus shedding following vaccination and this is known to differ between birds. For example, the vaccine works extremely well in chickens and they are resistant to challenge even with high doses of virus. In the field, vaccinated chickens (layers) never developed infection, despite active viral circulation. Vaccination works less well in turkeys and may become infected even after vaccination, but they shed less virus than unvaccinated birds.

There have been discussions within Europe about what is an acceptable test for vaccine efficacy, discussions about mechanisms for assessing the quality of avian vaccines and the dose to be used. No guidelines exist currently for testing avian vaccines and they are not in the European Pharmacopoeia. Dr Capua told the group that the FLUAID project is looking at the quality of vaccines across a range of poultry species.

In developing countries, decisions on vaccination are often left to the interpretation of the Minister for Agriculture. The group discussed the problem in Indonesia where several vaccines are being used without a harmonised approach and an eradication strategy.

Dr Capua was asked about how the vaccination strategy in organised and implemented. In Italy it is the Ministry of Health that liases with the EU Commission for the details on the implementation of the vaccination policy. The central authority makes decisions, but decisions on the logistics of implementation are made at a regional level. The vaccination programme in Italy has been running for 5 to 6 years and has evolved to improve the efficiency of the programme. Dr Capua told the group that Italy has been challenged by several incursions of AI viruses and that the situation is difficult to follow for the external observer. However, the AI control strategy was deemed successful by the European Commission. Exports of meat and eggs were initially suspended by the European Commission for the first year of vaccination but since the DIVA test has been used to show no circulating virus, exports have begun again and Italy is now trading meat and eggs from vaccinated flocks freely.