ADVISORY COMMITTEE ON THE MICROBIOLOGICAL SAFETY OF FOOD

(i) Norwalk-like calicivurus genes in farm animals and (ii) Molecular epidemiology of rotaviruses in the UK between 1995 and 1999

1. For the Committee's meeting in March 2000, Members received for information an abstract (see ACM/466 : Annex I attached for ease of reference) reporting that viruses closely related to Norwalk-like caliciviruses had been found in animal stools, sparking discussion about the potential for zoonotic transmission.

2. MAFF commissioned an assessment of the research from the Veterinary Laboratories Agency (VLA). This is at Annex II.

3. VLA were also asked to make an assessment of the zoonotic implications of a molecular typing study of human rotaviruses (Annex III). VLA's assessment is at Annex IV.

4. Members' comments are invited on these papers. David Paton of VLA's Virology Department will attend to introduce his assessments and respond to Members' questions.

Secretariat
November 2000

ANNEX I

ACM/466

Ref : van der Poel W H M, Vinje J, van der Heide R, Herrera M-I, Amparo V, Koopmans M P G. Norwalk-like calicivirus genes in farm animals. Emerg Infect Dis 2000; **6(1)**.

ANNEX II

NORWALK-LIKE CALICIVIRUS GENES IN FARM ANIMALS : VLA ASSESSMENT

1. The key points, largely made by the authors, are :-

- most human cases of small round structured virus (SRSV) infection are acquired from other people. However, epidemics of new variant strains have been noted, and this phenomenon could be consistent with viral introduction from a non-human host.

- it is now known that pigs and calves can be infected with related viruses. However, it is common to find related virus species affecting humans and animals independently. Near identical viruses have not been demonstrated in animals and humans and therefore the sequence data do not prove an epidemiological interspecies link. Studying more viruses might reveal that such identities do occur.

- the new information provided by this paper is that infection of calves with this type of virus is rather common and that pigs can also be infected (in Europe as well as in Japan).

- the prototype Norwalk virus of humans does not readily infect domestic animals experimentally, arguing against it having derived recently from one of the tested species.

2. In summary, zoonotic transmission remains an unproven hypothesis. Further comparisons of more animal and human strains are warranted to test this hypothesis, and this type of surveillance could readily be accomplished. If very closely related viruses were found in animals and humans, it would be worth repeating the attempt to infect animals with such a human isolate.

David Paton

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Veterinary Laboratories Agency
June 2000

ANNEX III

PHLS Human Rotavirus Molecular Epidemiology Unit. Molecular Epidemiology of Human Rotaviruses in the UK 1995-1998.

Report available from :-

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ANNEX IV

MOLECULAR EPIDEMIOLOGY OF HUMAN ROTAVIRUSES IN THE UK 1995-1998 : VLA ASSESSMENT

1. The report by Gray *et al*. describes the characterisation of rotaviruses from patients in the UK, collected during the 3 years between September 1995 and August 1998. Approximately 3,000 viruses were typed, representing about 7% of recognised cases, or 0.2% of the likely number of total incidents. Fifteen different combinations of G and P genotypes were detected. It was found that the most prevalent genotypes were the same ones reported as being most prevalent from human cases in other parts of the world. However, a small proportion of isolates (<5%) were of more uncommon genotypes, some of which include types previously reported in pet or livestock animals. Sequence data on animal rotaviruses are few, and phylogenetic comparisons between the human data and animal data were not attempted. In the report, particular emphasis is given to the G9 type (1-2% incidence). Rotaviruses with this form of VP7 gene have been previously identified in lambs and pigs, including animals from the UK. Certain features of the human epidemiology of these viruses appear different to those of other types. Their occurrence appears to have a slightly different seasonality, and they appear to occur more readily in older age groups of person. Furthermore, the number of cases was somewhat higher in the last year of the study than in the earlier two years. Possibly, this form of rotavirus is relatively new in humans, and may become more common due to the opportunity afforded by a low level of population immunity. It is suggested that livestock are a possible source of these virus infections of humans. This variant has become increasingly common in humans elsewhere, such as in Bangladesh, and the UK cases could also have arisen due to introduction from abroad by other humans. The other genetic type found at a very low level of incidence (<0.5%) in the present study in people, and also previously reported in pet animals, was G3.

2. The rotavirus story is reminiscent of influenza. In both cases, the disease is common in humans and animals, and in both cases, reassortment of viral genes can occur following dual infection with different virus variants. For both diseases, there seems to be no doubt that most human infections are acquired from other humans. In the case of influenza, occasional infection of humans from animals

can occur but, usually, this leads to asymptomatic and poorly transmissible infections, since the viruses involved are not adapted to replicating in the new host. However, dual infection of humans with a human-adapted and another influenza virus has the potential to produce a chimaera which is both novel to humans and able to replicate and spread efficiently. The lack of population immunity to the new variant may then lead to a serious pandemic.

3. For rotaviruses, one would like to know whether the virus is able to spread from animals to humans and, if so, whether it replicates efficiently and causes disease. Does it cause isolated incidents or can it spread from person-to-person and even alter the dynamics of rotavirus infection in humans ? Even on the first question, the available data are circumstantial and rather inconclusive. The principle deficiency is the lack of sequence data from animal rotaviruses, which prevents close comparison between human and animal strains. No such comparison is offered by the study of Gray *et al*. The question of the significance of such a zoonosis, should it occur, is also difficult to answer since rather little is known about the long-term molecular epidemiolgy of rotavirus infections of humans or animals, and the replicative and pathogenic potential of animal rotaviruses in humans is unclear. There is some evidence provided by the current three year study that prevailing human genetic types fluctuate, but it is not clear that sudden and dramatic shifts in prevailing rotavirus antigenicity occur or are associated with more serious consequences that were seen with the previous collection (ie. no equivalent to pandemics as in influenza). It is not known that rotaviruses of different genotypes differ widely in virulence, and it is also unclear what role population immunity plays in the selection of different variants. Even if the unusual rotavirus types found in humans were originally from animals, it is not clear whether this occurred by way of multiple introductions from animals, or a small number of zoonotic incidents followed by human-to-human amplification. Therefore, the significance of occasional human infection by rotavirus variants of animal origin, if it occurs, cannot be properly judged. However, there is no available evidence that it leads to pandemic disease, as in influenza.

4. If it is assumed that :-

- rotavirus infections can occasionally spread from animals to humans, and therefore from humans to humans, and

- that such infections are not more serious than infection with human-adapted strains

then the main likelihood of harm is that vaccines targeted at human types might not give protection. The probability of introducing vaccination for rotavirus in humans is therefore an important consideration in the need for more work on the zoonotic aspects of the disease.

5. In summary, the study of Gray *et al*. demonstrates a low prevalence of human infection with strains of rotavirus that could have a zoonotic source. There is some evidence that some of these strains are becoming more prevalent, but it is rather tentative and, considering the small size of previous surveys, these isolates could previously have been overlooked. Further human data showing a more convincing rise in the incidence of atypical rotavirus cases would certainly strengthen the argument for investigating animal cases. The study provides little additional evidence for animals as a reservoir for human infection (the existence of similar viruses in animals and humans was already known), but it has established an excellent database of human strains in the UK. If a database of sequences from animal rotaviruses in the UK were established, this would enable meaningful phylogenetic comparisons to be made. This should answer the question as to whether the viruses are being exchanged between host species. However, rotavirus surveillance might have to be continued for several years therafter before it would be clear what, if any, significance this had.

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