Predictive Models and FMD: the emperor’s new clothes?

R.P. Kitching, Chief Veterinary Officer and Director, Animal Health Branch

Science is as much a victim of fashion as any other human endeavor. Research funding is frequently directed towards the most recent high profile threat to public health, safety or way of life, which in the field of biology is usually the appearance of a new pathogen or an old pathogen in a new guise. The constant stream in the last 20 years, including Salmonella, Listeria, Escherichia coli 0157, bovine spongiform encephalopathy (BSE) and foot-and-mouth disease (FMD), has developed its following of scientists eager for grants. Having prior knowledge of these organisms is often less of an advantage than having a high scientific profile and useful connections. But to achieve a public profile and have exposure in the press, it is necessary to have something interesting to say that is understandable and with which the reader can in some way identify.

Certain discoveries, such as the organization of the DNA molecule or Dolly the cloned sheep have instant appeal, but these can be few and far between. In the absence of real scientific discovery, some may feel it necessary to make something ordinary look more interesting, and if that requires a little exaggeration, or not making clear that the results being reported are dependent on the reader understanding a series of sometimes hidden assumptions, this is no different to what the public is exposed to daily by the advertising industry. But of course scientific integrity must be different from commercial integrity, particularly when the funding for the research comes from the public purse.

During the 2001 FMD epidemic in the UK, and following the appearance of Professor Roy Anderson on the BBC Newsnight programme, public perception was that the outbreak was “not under control” (Anderson, 2002). Government reaction was to take the control policy away from the Ministry of Agriculture, Fisheries and Food (MAFF; subsequently replaced by DEFRA) and lay it in the hands of Science Group, under the chairmanship of the Government Chief Scientist, which reported directly to the Cabinet Office Briefing Room (COBR) set up during the crisis. The Science Group had no formal organization, but was dominated by four teams of modelers, whose predictions...
Predictive Models and FMD: the emperor’s new clothes?

for the future of the outbreak usually took up the majority of each meeting. There is uncertainty about whether their advice included the three kilometer cull, but the “24/48 h” policy, whereby all FMD susceptible animals on premises contiguous to the infected premise were to be slaughtered within 48 hours, was a direct result of their predictions, and the resulting mass slaughter is now history.

Those who explain the disagreements between the modelers and the veterinarians responsible for carrying out the policy as being due to different cultures (Anderson, 2002) ignore the obvious fact that if the input data into the models is wrong, then the output will also be wrong. In 2001, much of the input was based on assumptions derived from previous outbreaks of FMD, but the 2001 outbreak was very different in many ways from the last major FMD outbreak in the UK in 1967/68. However when these differences were pointed out by those of us with experience with FMD, our views were largely ignored.

So how could the control policy for a major disease outbreak be based on models which had never been validated? If the predictions for the number of new variant Creutzfeld-Jacob disease (vCJD) cases in the UK made in the late 1990’s had not been sufficient to undermine the credibility of the predictive modelers, surely the FMD experience should have made the modelers appreciate the limitations of their science and accept at least some responsibility for the misery and expense that their models initiated. Predictive modeling has become fashionable but, often without much evidence that it serves any useful purpose, is the science based too much on reputation?

Of course models have a place in all science and particularly in medical and veterinary science, they can be extremely useful in developing scenarios, identifying bottlenecks in biological processes, directing research towards answering specific questions, addressing resource issues and in a multitude of additional applications. But all models require relevant and accurate input data and cannot be expected to be oracles. Such data is frequently not available at the start of a disease outbreak, but then it is usual to use a series of assumptions and, when hard data become available, the assumptions can be replaced.

Models, like any diagnostic test, require validation to show that they work before they can be used in decision support. However, it would seem almost impossible to validate fully a predictive model for an FMD outbreak, as no two outbreaks are ever the same. The causative agent and the susceptible population are constantly evolving; the way the two interact changes due to different farming practices and population dynamics, and there is no possibility of anticipating chance encounters with any certainty.

In the right circumstance, and in the hands of someone who knows its limitations and understands the assumptions that have been made, a predictive model does have a place in a FMD outbreak control program. Undoubtedly predictive models are here to stay, but with no veterinary knowledge or input to avoid the pitfalls that were so apparent in 2001, models will only serve to provide weight and justification for indefensible decisions.

An interesting footnote to the disastrous use of models to define policy during the 2001 FMD outbreak in the UK is the claim that some of the financial institutions that precipitated the current global economic crisis also relied on predictive models to develop their lending and risk strategies. What next?

References:

Avian Influenza in British Columbia, 2009

On January 21, 2009, an H5 subtype of Avian Influenza (AI) virus was identified by PCR testing at the Animal Health Centre in samples from a flock of 12-week-old turkeys. CFIA was notified that evening and the premise was placed under quarantine. The following day all poultry premises within a 3 Km radius of the index farm were placed under quarantine and subjected to movement restrictions. On the same day, the Joint Emergency Operations Centre, directed by both CFIA and BC Ministry of Agriculture and Lands, and the Poultry Industry Emergency Operations Centre were activated. Direct communication was established among government and industry representatives.

Five days later, AI virus was confirmed in a second flock of turkeys that was housed in a barn on an immediately adjacent property. Because of the close proximity of the affected flocks, the two barns were managed as a single infected premises. Birds in the first barn were euthanized on January 26 and those in the second barn on January 27. Flocks on 22 farms within the 3 Km zone were subjected to sampling for movement permits and surveillance. An additional 12 farms outside of the 3 Km zone with epidemiological connections to the index premise were also quarantined and sampled. The implicated virus was an H5N2 subtype, genetically similar to a virus from a wild duck in California.

On Feb 10, surveillance sampling detected a second farm of chickens with the H5 AI virus. A second 3 Km zone overlapping the first added 10 new quarantines with 2 additional farms discovered through epidemiological trace-outs. Two days later the birds on this farm were euthanized. Over the entire AI event, a total of 52 premises were placed under quarantine, including four that were a result of pullets being moved from a quarantined farm to another outside of the 3 Km zone.

To minimize the possibility of spreading avian influenza, infected flocks were euthanized and the carcasses and litter underwent a composting process in the barn called ‘biological heat treatment’. Once the entire mass has reached the time/temperature requirements for influenza virus destruction, the material is moved outside for full composting and the buildings are thoroughly cleaned and disinfected. Twenty-one days after the second flock completed the biological heat treatment process, the quarantines for uninfected flocks/premises were lifted and unrestricted movement of birds and products, such as eggs was resumed. The infected premises remained under quarantine until 21 days after the barns were cleaned and disinfected.

During the seven weeks of sampling for movement, licensing, and surveillance, 10,944 oral and cloacal swabs representing 52,489 chickens, turkeys, and ducks were tested for AI virus by PCR at the Animal Health Centre Laboratory and no further AI virus was detected.

After the final quarantine was completed, a 3-month post outbreak surveillance period was initiated. Samples are being collected throughout British Columbia from approximately 230 poultry flocks, including layer and breeder chickens, turkeys, and long-live meat birds such as Taiwanese Chicken. The post outbreak surveillance will be completed by June 11, 2009. The purpose of this surveillance is to demonstrate to Canada’s trading partners, and the world, that BC is now AI-free. The International Organization for Animal Health (OIE) will be notified of the surveillance results upon completion of the testing.

The Animal Health Centre offers more than 400 laboratory diagnostic tests for agents that may be found in wild and domestic birds, mammals, fish, reptiles and amphibians. Submission forms and a list of our laboratory tests are available at http://www.agf.gov.bc.ca/ahc/ahclist.htm or http://www.agf.gov.bc.ca/ahc/poultry_health/lab_services.htm
Short cuts from the post mortem room

Equine:

An unusual cause of equine epistaxis: A 20 year old horse was submitted for chronic unreleenting progressive bilateral epistaxis (nose bleed). The condition was refractory to treatment and euthanasia was elected. Abnormalities were found in the thorax where a large unilateral encapsulated pulmonary mass was observed in the left lung field. Upon incision, the mass was firm to cystic with gritty areas. Large foci of hemorrhage continuous with the bronchus were found. The mass caused significant destruction and hemorrhage of the pulmonary parenchyma with secondary suppurative bacterial bronchopneumonia. As the mass was unilateral, and no other masses were found, a tentative diagnosis of granular cell tumour was made. Surprisingly, on histopathology, large numbers of duct like structures with frequent papillary projections lined by tall columnar epithelium were observed and the mass was interpreted to be a primary pulmonary papillary adenocarcinoma. This tumour is rarely reported in the horse. Most adenocarcinomas diagnosed in the equine lung are reported to be metastatic from the kidney and, as such, present with a multifocal distribution. Primary single focus tumours of the equine lung are most often granular cell tumours.

What body condition score cannot tell us about equine nutritional status:
Evaluation of body condition score is widely used as a general indicator of equine health and nutritional status. This scoring is particularly valuable in the winter when temperatures decline and horses may be off work, blanketed, off pasture and fed hay of varying quality. Body condition score is an excellent measure of energy balance based on the degree of subcutaneous fat deposition. However, the status of other essential nutrients such as vitamins and trace minerals cannot be evaluated on the basis of body condition score.

Two miniature donkeys were submitted to the AHC this winter for necropsy. Both donkeys were in good to fat body condition. White muscle disease associated with selenium deficiency was diagnosed in both animals on the basis of marked myocardial and skeletal muscle degeneration in association with deficient levels of selenium in the liver. One donkey also had lesions suggestive of Vitamin E deficiency in abdominal fat stores. Due to valid concerns for weight gain, these donkeys had been removed from pasture and fed non lush hay. However, despite having a body score slightly above the optimal, these donkeys were malnourished.

Summer pasture is the best source of vitamin E for horses. While lush hay can be a good source of vitamin E, the non lush, ‘diet’ varieties of hay are generally cut at a later stage and tend to be lower in vitamin content. With the exception of some restricted areas in British Columbia, most soils are deficient in selenium and thus hay is not generally considered a good source of dietary selenium.

Excessive weight gain is as undesirable in horses as is weight loss. To ensure adequate nutritional status while maintaining optimal bodyweight, owners are advised to formulate diets for their horses and donkeys starting with analysis of the hay. Hay should form the basis of the diet and once nutrient levels have been established, any further concentrate or vitamin/mineral supplementation needed can be calculated based on the individual needs of each horse. If there is concern regarding the overall nutrient status of a horse, serum testing for vitamin A and E plus trace minerals can be conducted by the AHC. For more information on body condition scoring, the following website provides a very good explanation with pictures http://www.omafra.gov.on.ca/english/livestock/horses/facts/98-101.pdf
**Domestic cats:**

In the past 6 months two cats from two separate animal shelters in the lower mainland have been submitted for necropsy. Both of the cats were Felv and FIV negative and had been ill and died despite treatment. Significant post mortem findings included rhinitis and meningitis. Gram positive cocci in pairs and chains were demonstrated in the meningitis. *Streptococcus equi zooepidemicus* (Sez) was cultured from nasal passages, brain and other organs. One cat was PCR positive for feline Herpesvirus but demonstrated no microscopic lesions compatible with viral disease. The other cat was negative for virus.

To our knowledge, Sez has not previously been reported in association with disease in cats. This organism has been reported in shelter dogs where it has caused severe hemorrhagic pneumonia. Sez is a widespread opportunistic bacterium which is most commonly isolated from horses. Disease in shelter cats may be due to stress associated immunocompromise which favours proliferation of Sez in the oropharynx leading to rhinitis. Spread to the brain may occur hematogenously or via the cribiform plate.

**Fish:** Two barred spinefoot (*Siganus doliatus*) captured from the wild were submitted for histopathology from the quarantine facility of the Vancouver Aquarium. The cerebral meninges of both fish contained several polysporic plasmodia of myxosporean parasites (*Kudoa* sp., arrowheads; Twort’s Gram stain). Plasmodia varied from 150 to 300 µm in diameter, and each was filled with spores that contained 6 or 7 polar capsules (inset).

Myxosporeans are multicellular organisms that are common in most fish species; their life cycle involves an invertebrate host. Significance to their host is often limited to that of a space-occupying mass. Because the invertebrate host is unlikely to be in the Aquarium, presence of this parasite in these fish did not prevent clearance of their cohorts from quarantine.
Shortcuts from the Post Mortem Room

Wildlife: The BC Interagency Wild Bird Mortality Investigation Protocol is a partnership between the Canada Wildlife Service (CWS), the BC Ministry of Environment and the BCMAL Animal Health Centre in which publicly reported cases of wild bird mortality are investigated and a cause of death is determined. A single dead Glaucous-Winged Gull in Richmond was reported through the hotline, retrieved by a CWS biologist, and submitted for necropsy.

The most common causes of mortality in gulls submitted to the AHC in the past have been trauma, gunshot and pesticide toxicity. At necropsy this bird was in excellent body condition and had no palpable fractures or visible signs of hemorrhage. The crop was distended with a thick brown pasty material that had the unmistakable and enticing odour of chocolate. Upon closer examination there were also small bits of pink candy and licorice. This material extended into the proventriculus which had moderate flaccid distension. There were no other visible lesions. A presumptive diagnosis of chocolate toxicity was made based on the gross findings.

Chocolate toxicity in gulls in BC was previously diagnosed in 2002 in a mortality event on Annacis Island in which 26 seagulls were found dead with no visible lesions and abundant sweet-smelling brown pasty material in the crops and throughout the entire digestive tract. Toxic levels of theobromine were present in the liver and kidney. It was the day after Valentine’s Day and the field investigation revealed a large amount of dark baking chocolate had been disposed of in an open dumpster accessible to the scavenging gulls.

Theobromine is an alkaloid in chocolate with caffeine-like properties. Death by chocolate is a consequence of lethal overstimulation of the heart and CNS and smooth muscle relaxation. There is wide species variability in sensitivity to theobromine toxicity with dogs having a particularly low toxic threshold.

Blackleg (Clostridium chauvoei necrotizing myositis) in British Columbia cattle: a perennial hazard

Dr. John Coates, Veterinary Pathologist

During the summer months, calves and yearlings in B.C. have an increased risk of contracting the bacterial disease commonly referred to as ‘Blackleg’. Blackleg, or acute bovine clostridial necrotizing myositis, was recently diagnosed on gross necropsy in a pastured four month-old beef calf from the Fraser Valley. The diagnosis was confirmed by the Fluorescent Antibody Technique (FAT).

At time of submission, the owner stated that the calf was lame the previous day, and it was found dead the next morning. Necropsy showed that the calf was in good body condition and the ‘blackleg’ lesion was within the deep adductor muscles on the medial aspect of the femur, just below the hip joint. The affected muscle was ‘black’ in colour, appeared dry, and had a distinct rancid or butyric (‘buttery’) odor. Microscopically, there was acute, severe, necrotizing and suppurative myositis, or inflammation of the muscle tissue.

Clostridium chauvoei is the bacterial agent responsible for bovine blackleg. The disease is enzootic in many areas of BC, especially where land is subject to flooding. The animal in this case was from a farm east of Mission, where there are many low-lying areas subject to seasonal or periodic flooding from Fraser River tributaries. Although the disease may strike younger stock anywhere, and at any
time of year, outbreaks are most common in summer and early fall. When the disease occurs, it usually affects several animals over a short period of time. Beef and dairy cattle under two years of age are most susceptible.

Although skeletal muscle lesions – such as in this calf – are present in most cases of blackleg, they may be very localized and difficult to find. However, there is often focal or diffuse hemorrhagic and fibrinous pericarditis (inflammation of the heart sac) and pleuritis. Where these lesions are present in the absence of severe pneumonia, blackleg should be suspected (1). Unlike Clostridium septicum and other clostridia that may infect cattle, Clostridium chauvoei does not proliferate rapidly after death, and smears from muscle or other lesions can be submitted from even partially decomposed tissues for diagnostic testing (1).

In consultation with the veterinarian, the owners in this case immediately vaccinated the remaining young stock with a multivalent clostridial vaccine. Fortunately, at last report, the owners had not suffered any additional losses.


**Dr. John Coates, pathologist at AHC retires**

Dr. John Coates (OVC 66) recently retired from the Animal Health Centre (AHC), after more than 21 years of service as a veterinary pathologist. Prior to studying for his MVSc degree in pathology and cytogenetics at the Western College at Saskatoon, Dr Coates spent many years practicing veterinary medicine on the Canadian prairies, and in New Zealand. In 2002, he published a book on his experiences in clinical practice, entitled Catgut, Crocuses and Cows: a Prairie Veterinarian’s Journey into Practice. John’s background in mixed practice served him well in diagnostic pathology.

Dr. Coates was actively involved in the Western Conference of Veterinary Diagnostic Pathologists, and the Canadian Association of Veterinary Pathologists (CAVP). While CAVP president, John was senior author of a commentary entitled Crisis in our midst (Can Vet J 1997;38:75-77). The essay lamented erosion of government support (at that time) for veterinary diagnostic laboratories in Canada, while documenting their practical relevance to both animal and human health.

John’s work in diagnostic pathology led to numerous interesting cases, some of which were published in refereed journals, as abstracts of the Western Conference, at the annual B.C. Symposium on Zoonotic and Communicable Diseases, within Diagnostic Diary, or presented elsewhere. A few notable cases included vitamin A toxicity with subsequent premature growth plate closure in the bones of pigs fed fish offal (solution: remove the fish livers); and a two-year study on congenital lordosis (swayback) in a group of purebred Haflinger horses that supported evidence of an autosomal recessive trait.

In addition to his work as a pathologist, Dr. Coates devoted much of his own time as managing editor of the laboratory’s newsletter Diagnostic Diary. John considered the newsletter a vital communications link between the Laboratory and its clientele of veterinarians and livestock owners, and he lent invaluable advice and support to the recent effort, now known as the Animal Health Monitor. The Animal Health Centre staff are privileged to have worked with John for so many years. He was a role model for others, and we wish him and his wife Robin a happy and healthy retirement.
In the News

Scientists at the U.S. Department of Agriculture’s Agricultural Research Service have uncovered genetic evidence about the evolutionary path that transformed Salmonella enteritidis from an innocuous bacterium into a virulent pathogen. To distinguish between the apparently identical genomes, researchers used a technique called “whole-genome mutational mapping” to analyze multiple strains. Through these analyses, the researchers developed a timeline of when S. enteritidis first became capable of transmission from a hens reproductive organs to eggs--approximately 36 years ago. It appears that a large-scale swap of DNA created a hybrid strain of S. Enteritidis with ability to contaminate the internal contents of eggs. Later, two lineages emerged and continued to evolve with varied ability to contaminate eggs and to survive on the farm. Read more about this research in the April 2009 issue of Agricultural Research magazine http://www.ars.usda.gov/is/AR/archive/apr09/salmonella0409.pdf

H1N1 Influenza

Not surprisingly, the novel circulating strain of H1N1 influenza, previously called “swine flu”, has been identified in residents of British Columbia. Most of the cases in the U.S. and Canada have been mild or moderate, self-limiting respiratory infections. H1N1 influenza viruses have been occasionally detected in pigs, however this new version has a unique genetic profile that has not been found previously in swine, bird or human influenza strains. The new virus has an animal origin and it has adapted so that transmission from human to human is efficient. While public health officials are monitoring the impact of H1N1 influenza on human health, livestock producers should be vigilant for respiratory illness in their herds and maintain high levels of biosecurity.

For more information see the Public Health Agency of Canada website: http://www.phac-aspc.gc.ca/


We are always pleased to receive feedback from our readers. Suggestions on future topics and potential contributions are encouraged. You can find past and current issues of these bulletins on our website: http://www.agf.gov.bc.ca/ahc/ahcwho.htm.

To receive this newsletter electronically, contact Lynette.Hare@gov.bc.ca

Send correspondence to:
Mira J. Leslie, DVM, MPH
BCMAL/ 1767 Angus Campbell Road
Abbotsford, BC V3G 2M3

Email: Mira.leslie@gov.bc.ca
Phone: 604-556-3066 Fax: 604-556-3015