MUCOSAL DISEASE:

Fighting back

by John Leitch

DR Joe Brownlie leads a research team that is working on Mucosal Disease.

Their priority has been to understand the disease and then to develop a dead vaccine. Early indications are that they now have a product that offers some effective protection.

A live vaccine against Mucosal Disease is commercially available, but results in America and Europe show that two weeks after vaccination some cattle develop the disease and die.

So a dead vaccine is the only safe solution.

It is reckoned that in the UK, losses caused by Mucosal Disease run to a staggering £49m.

This stems from deaths, ill thrift, and stillbirths.

Mucosal Disease is fatal. It is caused by bovine virus diarrhoea virus (BVDV), a

Dr Joe Brownlie.

minute organism that has the most damaging effect (like German Measles in humans) when it infects an unprotected dam (ie, one with no antibodies) in the first 120 days of pregnancy.

At this early stage, her young foetus is unable to make an immune response.

The calf is unable to make the specific antibody to combat the virus. It is infected throughout its life. It tolerates the unwelcome organism, and goes round shedding great quantities of virus, putting other animals at risk. Eventually it will develop Musocal Disease and die.

Joe Brownlie work at the Institute for Research on Animal Diseases, Compton, Berks.

"The clinical picture is that an animal with Mucosal Disease stops feeding," he explains. "There are ulcers in the mouth, and the animal has diarrhoea. Once the disease has started you can't stop it.

"We find the incubation period to be 16-17 days here at Compton. The typical figure for farm outbreaks is 20 days.

"It can cause so much damage in a herd. I went to one farm in Berkshire where 40 out of 60 replacement cattle died. I've also visited herds in Hertfordshire and Buckinghamshire where 50 out of a total of 100 animals died."

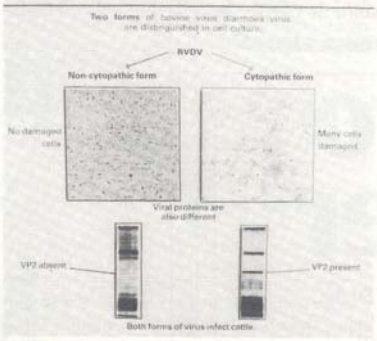
The disease has been known for the past 40 years, but it was only 18 months ago when it was first induced experimentally. That was at Compton.

Dr Brownlie reports: "Animals are usually 6-24 months old when they get Mucosal Disease. The virus destroys their lymphoid tissue, the very tissue that should attack it. Normally when a virus invades an animal you would expect lymphocytes to come pouring out from lymph nodes, spleen, thymus, and (most important) from raised areas of the gut called Peyer's patches.

"But with Mucosal Disease there is no lymphocyte attack. Instead there is ulceration of the gut, abcesses, and a collapse of the Peyer's patches."

The four-man team working on Mucosal Disease at Compton comprises of Joe Brownlie, Michael Clarke, Chris Howard and Dave Pocock.

Fig 1. The Cause



They have found that there are two forms of BVD virus (Fig 1) responsible for causing Mucosal Disease. The less aggressive one is non-cytopathic (ie, it doesn't damage or kill the host animal's body cells), while the other is cytopathic. Close examination of the two reveals that a certain viral protein (VP2) is absent in the non-cytopathic form.

Both forms of the virus infect cattle.

This discovery led Joe Brownlie and his colleagues to put forward a hypothesis which accounts for the pattern of Mucosal Disease outbreaks on farms.

They looked at all the 60 animals on the Berkshire farm mentioned earlier. The cattle fell into four groups (Fig 2).

Group 1: *Healthy. Neither antibody nor virus.*

Group 2: *Healthy. Antibodies, but no virus.*

Group 3: *Viraemic. Had the non-cytopathic form of the virus (V1) but no antibodies.*

Group 4: *Mucosal Disease. Had both non-cytopathic (V1) and cytopathic (V2) forms of BVDV. No antibodies.*

"The Group 3 animals are like the cow Theresa who featured in the *Dairy Farmer* story on Mucosal Disease in May 1985 (p22).

"Every animal we have examined so far that has had Mucosal Disease has had both V1 and V2 forms of the BVDV," reports Dr Brownlie.

He admits: "Our theory about there being two forms of BVDV — a non-cytopathic V1 and a cytopathic V2 causing Mucosal Disease — were contentious for a while. However, it has now been accepted, as other research teams in America, New Zealand, and Scotland have confirmed our original findings.

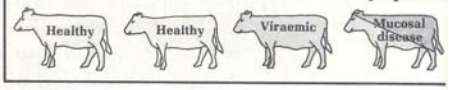
"As a young calf develops in the cow's womb, it takes 110-120 days before its immune system is fully functional. Only then does it have the ability to make antibodies to defend it against viruses. After this time it recognises the difference between its own tissues (heart, lungs, etc) — which it doesn't reject — and potentially-dangerous invading organisms. But if the virus is already there before the calf is 110-120 days old, then the developing immune system is tricked into saying 'This is my own; this is not foreign; this is me!' "

When such calves are born they are said to be viraemic because they shed virus all the time.

The IRAD team kept calves with the non-cytopathic form of Mucosal Disease in isolation for over a year, during which time they learned how to purify the V1 and V2 forms separately. When calves were exposed to V2 on top of the V1 already carried, then they went down with Mucosal Disease within three weeks of exposure.

"Which further proves our hypothesis," insists Joe.

Fig 2. In outbreaks of mucosal disease, four combinations of virus and antibody were found.



Which leads to the question why do we get so many outbreaks of Mucosal Disease? Why is it that so many cows come into contact with BVDV when they are in early pregnancy; when they are at greater risk?

In order to provide the answers, Dr Brownlie and his team did a survey of commercial herds. They fell into two groups:

- Open herds. Cattle bought in.
- Closed herds. Only used AI. No females ever brought in.

"We consistently found that cows and youngstock in closed herds had no antibodies," discloses Joe. "There was no evidence of BVD virus. In other words, these were highly-susceptible groups of cattle with no immunity.

"The open herds, on the other hand, contained animals with antibodies, so they were protected. The virus was there on the farm, spreading from animal to animal. Youngstock were being exposed to infection long before they reached breeding age, so antibodies developed. The consequence was that any further virus attack during the first

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This is Theresa, two weeks away from calving, for the fourth time. She was bought as a healthy-looking Friesian bulling heifer in Taunton Market. It was only after she had produced her third calf that the Somerset farmer and his vet suspected that something was wrong. Tests showed that she was persistently infected with the virus that causes Mucosal Disease. She was spreading it continuously. Full details of Theresa were included in the article *Growing menace (Dairy Farmer May 1985, P22).*

120 days of pregnancy, the big danger period, was successfully warded off.

"It is in closed herds where outbreaks of Mucosal Disease are occurring. It is unfortunate, but the fact that more herds are becoming closed means that Mucosal Disease outbreaks are more likely.

"The problem is that in most closed herds, the owner eventually brings in a bull or some young heifers. They are mixed with the rest of the farm's cows and bulling heifers. Very often it is such bought-in stock that bring BVDV with them, the virus arriving right at the very time when the farm's own females are highly susceptible.

"Owners of closed herds should be very aware of this problem. They are at great risk.

"They ought to get newly-bought cattle checked before mixing them with their own stock."

"The result of such a test takes two weeks.

"The animal should preferably be tested before it leaves the seller's farm. If it has already arrived at the buyer's farm, then it should be kept in isolation until the test result is available.

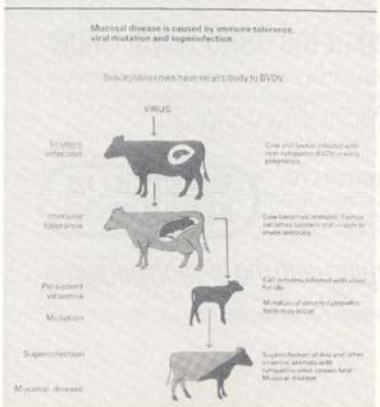
"Anyone with a closed herd should contact his vet before introducing stock from another farm. The vet should test the animal for both antibodies and virus.

"You do not want an animal with no antibodies but with a viral infection. This is your 'Theresa' type animal again. Such animals are menaces.

"I find that once Mucosal Disease occurs on a farm, the herdsman can normally think back and can start recalling a recent history of stillbirths, abortions, weakly calves, and infertility (caused by early embryonic loss)."

After finding that the hypothesis about there being two strains of BVDV (V1 and V2) was borne out by further research, Dr Brownlie and his team extended their thinking once again.

Fig 3. Hypothesis



They now suggest that the virus V2 arises from the population of V1 virus, most probably by mutation.

"You get one mutation at every 10^3 multiplications of the V1 virus," reveals Joe. "Just remember that there are a staggering number of virus present — every 1 ml of blood contains 10^6 virus, and a bulling heifer has about 10^7/ml of blood. So there are obviously a lot of mutations occurring.

"So many mutations, in fact, that you would think it would only be a matter of hours before a freshly-calved animal progressed from V1 to the deadly cytopathic V2 form. But animals can be anything up to two years old before Mucosal Disease develops.

"The explanation for this is that most mutations don't survive. Those that are significantly different from the V1 are immediately gobbled up by the calf's immune system. So it takes 6-24 months before a V2 emerges that is sufficiently close to the original V1 that the immune system is fooled."

Dr Brownlie's team are now linking with Belgian researchers in Liege in the hope of producing a genetic sequence similar to that of the virus. Such genetic engineering work could then lead to the production of a synthetic vaccine.

Fig 3 shows Dr Brownlie's current interpretation of the Mucosal Disease pattern.

A susceptible cow has no antibody to BVDV. She is in early pregnancy when the virus comes along. This is the non-cytopathic form (V1), and both cow and foetus are infected.

The cow develops immune tolerance and protects itself, but the foetus is unable to make antibody because it is too young. It becomes tolerant.

Eventually at nine months the cow produces a live calf. It might look normal, but it is persistantly viraemic. It remains infected for life. It sheds virus every day.

Many months later there is a mutation of the virus. The cytopathic V2 form is produced, and this spreads to all viraemic animals on the farm. The cytopathic virus causes Mucosal Disease and this is fatal.

The theory is that whenever you have viraemic calves there is a chance that a mutation in any one of them will produce V2 at any time and Mucosal Disease will then occur a couple of weeks later.

"So if you are fattening animals and you know they have BVDV, it is better to get them slaughtered as soon as you know they are infected, because once V2 arrives it will go through the herd very quickly indeed," suggests Joe. "It would be immoral to sell the animals to another farmer."

If a closed herd is only buying in semen then is it safe? "You are unlikely to get BVDV from semen because AI centres do check for this," replies the Compton researcher.

Is it best to mix stock as much as possible in open herds, to ensure that infection spreads to all youngstock before they are old enough to start breeding?

"No, this is too unreliable," warns Dr Brownlie. "The best thing is to get all newly-purchased animals checked.

"Any animal that has no virus can be safely mixed. Others that show the presence of non-cytopathic form of BVDV, but no antibody, should be retested two weeks later. If the result is still the same, you should get rid of them. Don't bring them onto the farm." **D**