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Cost-benefit analysis of vaccination against paratuberculosis in dairy cattle

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Paratuberculosis is an infectious and incurable disease which causes considerable economic losses in dairy cattle, due mainly to premature disposal and losses of milk production. In 1984 the Animal Health Service North-Netherlands started a vaccination trial in which young calves were vaccinated once, to test whether vaccination reduced the production losses and whether the overall costs of vaccination were outweighed by the benefits. Vaccination against paratuberculosis reduced the number of clinically infected animals by almost 90 per cent. It also reduced the numbers of subclinically infected animals and animals with a positive histological and/or bacteriological test result. Although vaccination did not prevent losses in milk production, it reduced the infection pressure and the clinical signs of the disease. Partial budgeting showed that vaccination against paratuberculosis was highly profitable. The costs of vaccination were US$15 per cow and the benefits (total returns minus costs) were US$142 per cow.

PARATUBERCULOSIS is an infectious and incurable disease which particularly affects cattle, sheep and goats. The bacterium *Mycobacterium paratuberculosis* causes a thickening of the intestinal lining which reduces the efficiency of feed absorption. In the clinical form, paratuberculosis causes a considerable loss in milk production and the cows lose weight in spite of the fact that their appetite remains good. The disease manifests itself most often in cows which are between four and five years old (Benedictus 1985).

The animals most susceptible to the infection are young calves, which can be infected by contact with manure or milk, or in utero (Benedictus 1985). The severity of the infection depends primarily on the age of the animal and the concentration of the pathogen present. The older the animals and the lower the infection pressure, the less often an infection will cause clinical signs of paratuberculosis (Benedictus 1985). When *M paratuberculosis* is present on a farm, all the animals will usually come into contact with it (Benedictus 1985).

Paratuberculosis causes considerable economic losses which are due mainly to premature disposal and a reduction in milk production. In dairy cattle, reductions in milk production were reported to range from about 5 per cent in cows with subclinical forms of the disease to 20 per cent in clinically affected cows. Moreover, affected cows were culled earlier and had a reduced slaughter value. The average losses per animal culled were found to be US$1250 and US$1000 for clinically and subclinically infected animals respectively (Benedictus and others 1987).

In the Netherlands, an eradication programme based on the voluntary disposal of infected cows was ineffective, and the number of cases of paratuberculosis did not decline over the years. In 1984 the Animal Health Service North-Netherlands started a field vaccination trial in which young calves were vaccinated once (Kalis and others 1991). The goals of the trial were to investigate the effect of vaccination on the numbers of animals with the clinical or subclinical form of paratuberculosis, and to test whether vaccination reduced the production losses and whether the benefits of vaccination outweighed the overall costs. This article gives the results of the cost-benefit analysis of the trial. A comparison was made between the situation before and after vaccination, taking into account a vaccinated and a control group.

Materials and methods

Data

The vaccination trial was conducted on 12 farms in the northern part of the Netherlands, where more than 5 per cent of cows were culled anually as a result of paratuberculosis. The unvaccinated cows which were culled between 1982 and 1984 were tested for paratuberculosis. In 1984 the vaccination trial started and all the calves on the farms were vaccinated once before one month of age with a heat-killed water-in-oil emulsion vaccine. The vaccinated animals left the farms between 1984 and 1992 and all those which were culled were examined by the Animal Health Service for clinical signs of paratuberculosis. Material from the intestines was collected for histological, bacteriological and cultural tests to check whether an animal was infected. The histological tests used staining techniques and the material from the intestine was cultured to investigate whether *M paratuberculosis* was present. The presence of *M paratuberculosis* was tested microscopically in the animals which were positive in the histological or bacteriological test and if the organism was identified the animals were considered to be subclinically infected. *M paratuberculosis* was often not identified microscopically in animals with a positive cultural test result and these animals were considered to be latently infected. After five years the rate of disposal of animals because of the clinical form of paratuberculosis was reduced from 11 per cent in 1984 to less than 1 per cent in 1989. However, the subclinical form of the disease was still present to a considerable extent (Kalis and others 1991).

Data on 652 cows were available for economic analysis. Data on 573 cows, 304 of which were vaccinated and 269 of which were unvaccinated controls, could be used to calculate the reduction in milk production. The cows from the vaccinated and control

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groups were subdivided into the following four groups on the basis of clinical and laboratory tests:

(a) healthy, uninfected animals in which no bacteria were found;
(b) subclinically infected animals which tested positive for paratuberculosis in the bacteriological and/or histological test, but which had no clinical signs;
(c) animals with clinical signs of paratuberculosis which were confirmed by laboratory tests and were culled;
(d) latently infected animals which were positive only in the cultural tests, and which were free of clinical signs.

In the vaccinated group the numbers of animals in groups a, b, c and d were 162, 27, 18 and 97 respectively, and in the unvaccinated group the numbers were 124, 45, 50 and 50.

The empirical data were evaluated statistically with Statistix 4.0 (Siegel 1992) and tested for significance by the least significant difference method, with $P<0·05$.

Cost-benefit analysis

The possible benefits of vaccination for the farmer would be reduced culling and lower losses in production. However, the farmer must meet higher costs for vaccination and sampling.

The costs and benefits of vaccination were calculated by partial budgeting, which meant that only the changes produced by the vaccination programme were calculated. The economic losses for each animal consisted of the following components (Dijkhuizen and others 1991): first, the losses before disposal, which consist of the reduction in milk production and the costs of examination and treatment; secondly, the losses at disposal, which consist of the lower slaughter value and the costs of open places; and thirdly, the loss due to disposal, which is the loss of future income.

The sum of these components gives the total losses per animal at farm level. The benefits of vaccination will be the reduction in the losses due to one or more of these components.

Results

Losses before disposal

The production of milk, fat and protein in the cows' last lactation before disposal and in their first (heifer) lactation were compared, after adjustment for differences in age, season, year and length of lactation (Wilmink 1987). This calculation gave the loss or gain in milk production for a cow in its last lactation compared with its expected milk production capacity as a heifer. The percentage reduction in milk production multiplied by the average production of heifers of the corresponding subgroup gives the absolute reduction in kg of milk, fat and protein. The results for the subgroups are summarised in Table 1.

In the subgroup of uninfected animals the vaccinated animals had a greater reduction in milk production than the unvaccinated animals, 316 kg compared with 28 kg of milk. In the subgroups of subclinically and latently infected animals the vaccinated animals also had a greater reduction in milk production, respectively 706 – 199 = 507 kg and 382 – (–248) = 630 kg. However, the vaccinated clinically infected animals had a smaller reduction in milk production, 1089 – 631 = 458 kg milk, than the unvaccinated animals. In each group, similar trends were apparent for the reduction in the production of fat and protein.

The costs of examination and treatments included the visit by a veterinarian at a rate of about US$20 and possible faeces and blood tests costing about US$5. Some animals were also treated for scour at an average cost of US$3. The total costs were estimated to be US$25 per clinically infected cow. The costs of vaccination were US$15 per animal.

Losses at disposal

Clinically infected animals had a lower slaughter value at disposal, owing to weight losses, which was estimated at about 30 per cent. Considering a normal slaughter value of US$1085 per culled cow, this loss was US$325 per clinically infected cow. According to Benedictus and others (1987), replacement animals will not always be available immediately, and a cost of US$47 was therefore assumed for two weeks of open places per culled cow.

Losses due to disposal

The economic losses due to premature disposal can be defined as the difference between the income a particular animal could earn during its remaining expected life, and the expected income over the same period of a replacement animal. These losses vary, particularly with the productive quality of the cow and her age at disposal, and were taken from the dynamic programming model of Houben and others (1994). The cows in the various subgroups produced on average 6·5 per cent above herd level in their first lactation and were culled on average after 3·3 lactations. The losses due to disposal averaged US$815 per case, and ranged from US$614 for vaccinated, latently infected cows to US$919 for unvaccinated, clinically infected cows (Table 2).

Profitability of vaccination

The profitability of vaccination is the difference in costs before, at and due to disposal, compared with the unvaccinated group. The total costs for the vaccinated and unvaccinated groups were determined by multiplying the frequency of uninfected, subclinically, clinically and latently infected animals in each group by the costs at each stage. The costs of disposal of an average cow from the unvaccinated and vaccinated group are the standard of comparison. It was assumed that the total rate of disposal at farm level remained the same. The total losses calculated for the periods before, at, and due to disposal are summarised in Table 2.

As might be expected the total losses were highest for clinically infected cows. Vaccination reduced the losses for these animals by US$106 per cow. For subclinically and latently infected cows the opposite occurred; in the case of subclinically infected cows, mainly because of a high lost future income, and in the case of latently infected cows because of a greater reduction in milk production before disposal. The total losses for uninfected animals were lower, despite a greater reduction in milk production,

TABLE 1: Reductions in milk, fat and protein production (% and kg)

	Uninfected		Subclinically infected		Clinically infected		Latently infected	
	unvaccinated	vaccinated	unvaccinated	vaccinated	unvaccinated	vaccinated	unvaccinated	vaccinated
Number of cattle	124	162	45	27	50	18	50	97
Milk								
(%)	0·5	5·7	3·9	13·1	20·6	13·1	–4·5	7·0
(kg)	28	316	199	706	1089	631	–248	382
Fat								
(%)	0·6	4·9	2·0	13·5	13·2	14·2	–4·1	7·9
(kg)	1·5	12·2	4·5	32·7	29·7	32·4	–10·1	19·5
Protein								
(%)	–1·2	4·2	2·0	13·5	21·8	13·6	–5·3	5·3
(kg)	–2·3	7·9	3·4	25·0	33·4	23·3	–9·8	9·9

TABLE 2: Total losses (US$) before, at, and due to disposal per subgroup

	Uninfected		Subclinically infected		Clinically infected		Latently infected	
	unvaccinated	vaccinated	unvaccinated	vaccinated	unvaccinated	vaccinated	unvaccinated	vaccinated
Number of cattle	124	162	45	27	50	18	50	97
Before disposal (%)	–14	42	44	352	407	363	–96	139
At disposal	47	47	47	47	47	47	47	47
Due to disposal	831	624	831	907	919	857	768	614
Total	864	713	922	1306	1698	1592	719	800

because of a smaller lost future income. Clinically infected animals had a smaller reduction in milk production and a smaller lost future income, which also resulted in smaller losses for clinically infected animals in the vaccinated group.

In Table 3 the costs per subgroup have been multiplied by the number of animals in the unvaccinated and vaccinated groups. Vaccination against paratuberculosis decreased the frequency of subclinically and clinically infected animals. In the unvaccinated group 26 per cent and 11 per cent of the animals were subclinically and clinically infected, respectively, whereas in the vaccinated group the percentages were 11 per cent and 0·8 per cent, respectively. This means a reduction of 86 per cent in the numbers of clinically infected animals. The number of latently infected animals increased considerably from 15 to 26 per cent. However, the number of uninfected animals increased after vaccination from 48 to 62 per cent.

Taking into account the frequency distribution shown in Table 3, the total losses were US$949 per cow in the unvaccinated group and US$807 in the vaccinated group. The benefits of vaccination, that is the total returns minus the costs, were on average US$142 per culled cow. It is true that the costs for the uninfected and latently infected cows were higher in the vaccinated group (US$444 and US$210 respectively versus US$410 and US$111 in the unvaccinated group), but the frequency of subclinically and clinically infected animals was considerably lower in the vaccinated group, which is the major reason that vaccination was profitable.

Discussion

Paratuberculosis is difficult to diagnose in the various stages of the disease (Sprangler and others 1992) and a combination of tests was used to increase the reliability of detection.

The unvaccinated and vaccinated groups were made comparable for age, calving season, month of lactation, and lactation length by correcting the lactations by factors derived from the Dutch Cattle Syndicate (NRS) (Wilmink 1987). Nevertheless it has not been proved that all the differences in milk production and lost future income could be explained by an infection with paratuberculosis. Among the uninfected animals there were differences in costs between the unvaccinated and vaccinated group; the losses due to lost future income should be interpreted with caution.

Benedictus and others (1987) observed a reduction in milk production of 16 per cent in subclinically infected animals whereas, in this investigation, the reduction was only 4 per cent in the unvaccinated group and 13 per cent in the vaccinated group. One explanation might be that the subclinically infected animals used by Benedictus and others (1987) were at a later, almost clinical, stage of the disease. The 20·5 per cent reduction in milk production for the clinically infected animals was similar to the 19·5 per cent observed by Benedictus and others (1987). The 13 per cent reduction in the milk production of the vaccinated clinically infected animals may not have been due entirely to the vaccination. These animals were culled, on average, before their third lactation, that is before the influence of paratuberculosis on milk production reaches its maximum (Collins and Nordlund 1991).

TABLE 3: Costs per average culled animal

	Cows per subgroup (%)	Total costs per cow (US$) (see Table 2)	Average costs within group (US$)
Unvaccinated			
uninfected	47·5	864	410
subclinically infected	26·1	922	241
clinically infected	11·0	1698	187
latently infected	15·4	719	111
total	100		949
Vaccinated			
uninfected	62·3	713	444
subclinically infected	10·7	1306	140
clinically infected	0·8	1592	13
latently infected	26·2	800	210
total	100		807

The vaccination of the uninfected and latently infected animals appeared to reduce their milk production by 5·7 per cent and 7·0 per cent, respectively, whereas there was hardly any reduction in the uninfected (0·6 per cent) and latently infected (–4·5 per cent) cows in the unvaccinated group. The reduction in milk production in the vaccinated group may have been due to the fact that older animals, like heifers, can still experience an infection with *M paratuberculosis* without getting the clinical form when they are older (Rossiter and others 1994). The vaccinated heifers which were infected may not have had any difficulty in resolving the infection and remaining uninfected or becoming latently infected, unlike the unvaccinated heifers, which may have had more difficulty in resolving an infection, and suffered a reduction in milk production. As a result, the vaccinated heifers had a higher milk production than the unvaccinated heifers (C. H. J. Kalis, personal communication). The correction of the last lactation of a vaccinated, uninfected or latently infected cow in relation to its lactation as a heifer thus seems to result in a greater reduction in milk production in the vaccinated group.

Vaccination did not seem to reduce the incidence of infection with *M paratuberculosis*, as was shown by the large number of latently infected animals in the vaccinated group. However, vaccination did reduce the incidence of severe clinical infections. Subclinically and clinically infected animals had much higher costs than latently infected animals, US$203 and US$979 respectively, in the unvaccinated group, and US$506 and US$792 respectively, in the vaccinated group. Since vaccination reduced the incidence of subclinically and clinically infected animals considerably, the eradication of paratuberculosis would be highly profitable, and vaccination could contribute to the process.

On the farms used in this investigation 11 per cent of the animals were clinically infected before vaccination. Even if the level of infection had been only 5 per cent, the benefits of vaccination would still have been US$83 per head.

Farms that vaccinate are not allowed to export live animals. The calculated benefits of vaccination will, however, on average easily outweigh the potential losses from such a restriction. For example, if 10 per cent of the heifers were exported at an average price of US$1390, then the US$142 benefit from vaccination would outweigh the losses from the export restrictions.

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Short Communications

Synovial sarcoma in a ferret

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A-TWO-and-a-half year old stock male fitch ferret (*Mustela putorius furo*), kept group housed in an enriched environment for biomedical research, presented with an abnormal gait. This was found to be caused by a swelling 4 cm across and 6 cm long around the right stifle joint, which had apparently developed over a 48-hour period.

On clinical examination, the animal was otherwise well. There was no evidence of respiratory or cardiovascular disease, and no loss of weight or condition. Recent screening indicated the animal was free from Aleutian disease virus. The swelling was firm, immobile and apparently not painful. It extended to the distal third of the tibia and proximally to the middle of the femur. It thus prevented movement of the stifle joint, although the animal was able to move around by swinging the leg out from the hip joint to compensate.

The animal was sedated with 100 µg/kg medetomidine given by intramuscular injection (Domitor; SmithKline Beecham Animal Health), and radiographs were taken of the swelling (Fig 1). These showed a circular mass with soft tissue density centred around the proximal tibia, and a second ovoid mass extending from the stifle to the distal tibia. Two areas of mineral density were visible within the soft tissue masses. There was sclerosis in the proximal tibia, particularly in the epiphysis, and increased density within the medulla with loss of the corticomedullary junction, extending to the proximal third of the tibia. In the region of the tibial crest, there was periosteal new bone giving a 'sunburst' effect, with areas of marked sclerosis caudal to this. No radiographic changes were visible in the distal femur, and the joint space was clear.

A diagnosis of malignant neoplasia arising from the proximal tibia was made on the basis of these clinical and radiological findings. The animal was euthanased and a post mortem examination carried out. Examination of the chest cavity revealed numerous, well defined white foci within the parenchyma of the lungs. The swelling on the leg consisted of a well encapsulated mass of firm, pale tissue with two lobes: a spherical part around the joint, with an oval part extending distally down the tibia. The bony pathology in the proximal tibia was visible grossly within this mass (Fig 2). No other abnormalities were present.

Histological examination of the mass around the joint revealed that it consisted of broad sheets of dark-staining epithelioid cells separated by wide bands of fibro-collagenous tissue. There were also clusters and short rows of epithelioid cells ranged alongside small clefts and interspersed by narrow bands of fibrous tissue (Fig 3). In a few areas there were scattered single epithelioid cells within fibrous tissue. The epithelioid cells had clearly defined cell borders and dark-staining, sometimes vacuolated, cytoplasm. The broad sheets of cells were anaplastic with nuclear pleomorphism and many mitotic figures. Giant cells and multinucleate cells were also present. The fibro-collagenous tissue included large pale-staining cells with fibrillar cytoplasm and uniform nuclei with very few mitoses. Sheets of anaplastic epithelioid cells were infiltrating periosteum and bone and there was associated non-neoplastic new bone formation and periosteal and cartilage hyperplasia in these areas. The tumour also appeared to be expanding into the surrounding subcutaneous connective tissue and was bordered by a capsule of the fibrous tissue component. These findings were consistent with a diagnosis of synovial sarcoma.

FIG 1: Lateral radiograph of right stifle. Note marked soft tissue swellings, radiodense foci, sclerosis and sunburst effect in proximal tibia

The lesions in the lungs were those of focal histiocytosis, consisting of accumulations of foamy macrophages with multinucleate giant cells, cholesterol clefts and lymphocytes. There was no evidence of tumour metastasis.

Spontaneous neoplasms in ferrets have been reported as being rare, although the incidence is hard to determine. Several authors have postulated that the paucity of reports is due to the relatively short lifespan of ferrets in the laboratory, but there is no increase in incidence in pet or zoo ferrets which are longer lived (Dillberger and Altman 1989). Others have suggested a genetic resistance to neoplasia, but reviews of pathological findings in ferrets have shown that neoplastic diseases have been reported in all

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