



Arthralgia and early cutaneous purpura in a pig with acute PDNS

PMWS and PDNS – two recently recognised diseases of pigs in the UK

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THE clinicopathological manifestations of postweaning multisystemic wasting syndrome (PMWS) and, in particular, porcine dermatitis and nephropathy syndrome (PDNS), have caused considerable concern owing to their similarities to those of classical swine fever (CSF) and African swine fever (ASF). This has led to a dramatic increase in the number of notifiable disease investigations, triggered mainly by outbreaks of PDNS. The significance of these similarities was apparent when cases of CSF were confirmed in East Anglia in August 2000 – the first to occur in Great Britain since 1986. However, even before this outbreak occurred, it was clear, once CSF and ASF had been ruled out, that a new disease to the UK, namely PMWS, was affecting pig herds in the south and east of England and that PDNS was being seen as a common sequela to this syndrome. This article describes the clinical signs associated with PMWS and PDNS. In addition, it discusses the epidemiological findings to date and provides some guidelines on control.

PMWS

Clinical signs

PMWS is believed to be a primary disease process. Herds affected with this syndrome are also thought to be much more likely to have pigs with the epidemic form of PDNS.

The clinical signs of PMWS show a very precise age distribution. Adults and newborn piglets are not susceptible to the disease and, generally, piglets immediately after weaning are also unaffected. However, exceptionally, transient postweaning diarrhoea has been noted in some herds. The syndrome often first appears when piglets are six to eight weeks of age. After this age, mortality rates can rise dramatically and are associated with



PMWS: severe extensive oedema of the mesocolon

Historical perspective

PDNS was first described in Chile in 1976 and has occurred sporadically in the UK for a number of years. However, since late 1999 it has become more prevalent in the UK, with both the sporadic and epidemic forms of the disease having been reported on farms in England. PMWS, meanwhile, was first described in Canada in 1991 and was first reported in the UK in Northern Ireland in 1998, and in England in late 1999. Outbreaks of PMWS in East Anglia and the south of England have closely paralleled the descriptions of the disease in Canada, France and Spain and have also been reported in several other countries around the world.

The actual numbers of farms affected by PMWS and PDNS in the UK is not known. However, a survey of pig practitioners suggested that, by mid-April 2000, 191 premises had been affected by PMWS and 251 premises by PDNS. This equates to about 9.6 per cent of the number of larger pig holdings (those with 100 or more sows and/or 200 or more growers) which were recorded in the June 1999 census in England and Wales. In many incidents, PDNS progressed from being only a sporadic disease, affecting small numbers of pigs, to an epidemic form, where much larger numbers of cases were seen.

CLINICAL SIGNS OF PMWS SEEN IN ENGLAND SINCE AUGUST 1999

	Frequency of occurrence (%)
Onset at 6 to 8 weeks/2 to 3 weeks postweaning – usually very precise	85
Enlarged subcutaneous lymph nodes	80
Depression	70
Loss of condition	64
Inappetence	60
Dyspnoea	52
Rough hair coat	50
Pallor	43
Diarrhoea	21
Jaundice	21
Sudden death	7
Neurological signs	5

striking loss of condition, pallor and generalised illthrift. Subcutaneous lymph nodes of affected pigs are frequently enlarged and the superficial inguinal lymph nodes are often visibly and palpably enlarged. Dyspnoea, diarrhoea, jaundice and neurological signs are seen in some cases. These signs may be influenced by other predominant endemic diseases present on the farm.

In growing herds (with animals of up to about 30 kg bodyweight), mortality is in the range of 8 to 20 per cent. In finishing herds, mortality tends to be lower – typically between 5 and 10 per cent – some of which may be due to PDNS. (For comparison, in unaffected herds, overall mortality rates in average rearing and finishing herds generally range between 3 and 4 per cent.) It is noticeable that there is very variable distribution from pen to pen – some pens have no affected pigs while others may contain many affected animals. Interestingly, allowing for dead and dying pigs that often have to be culled on welfare grounds, the growth rates and feed conversion efficiency of unaffected pigs in a group seems to be as good as the herd would expect to achieve under normal conditions.

Diagnosis

The diversity of lesions found in cases of PMWS makes it difficult to achieve a definitive diagnosis of the condition. However, the clinical picture and history are highly suggestive and, when a large number of affected animals (at least six to 10 pigs) are examined, typical post-mortem findings tend to point towards the disease. The

Findings required to confirm a diagnosis of PMWS

- High mortality rate in weaned pigs, starting from six weeks of age
- High incidence of 'wasting pigs', combined with a lower incidence of dyspnoea, pallor, jaundice, neurological signs and scour
- Clinically affected pigs that are unresponsive to antibiotic therapy
- Typical postmortem findings when a number of pigs are examined
- Lymphocyte depletion, histiocyte infiltration, typical inclusion bodies and possibly syncytia on histological examination

diagnosis becomes more certain if typical histological findings are detected.

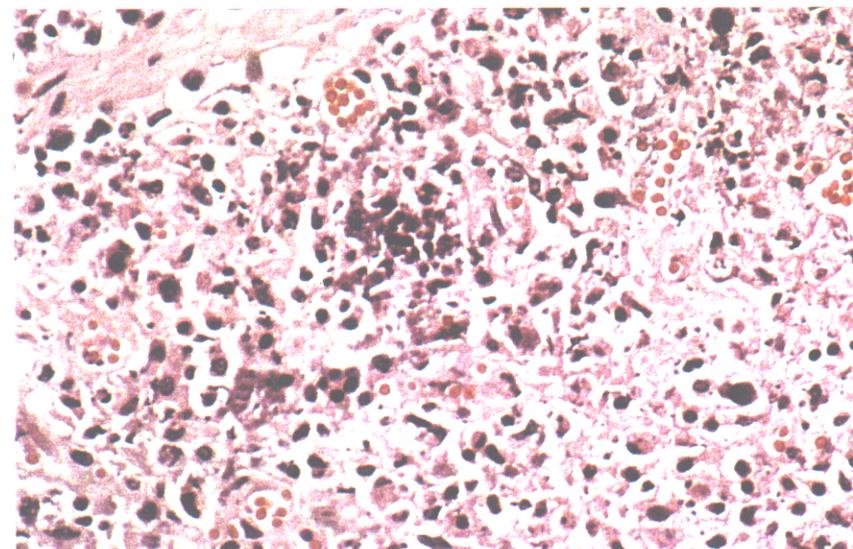
Pathological findings in cases of PMWS are described in the box overleaf. All of these postmortem findings are unlikely to occur in one pig, but postmortem examination of six to 10 pigs will show the distribution and variability of the lesions. The gross lesions are



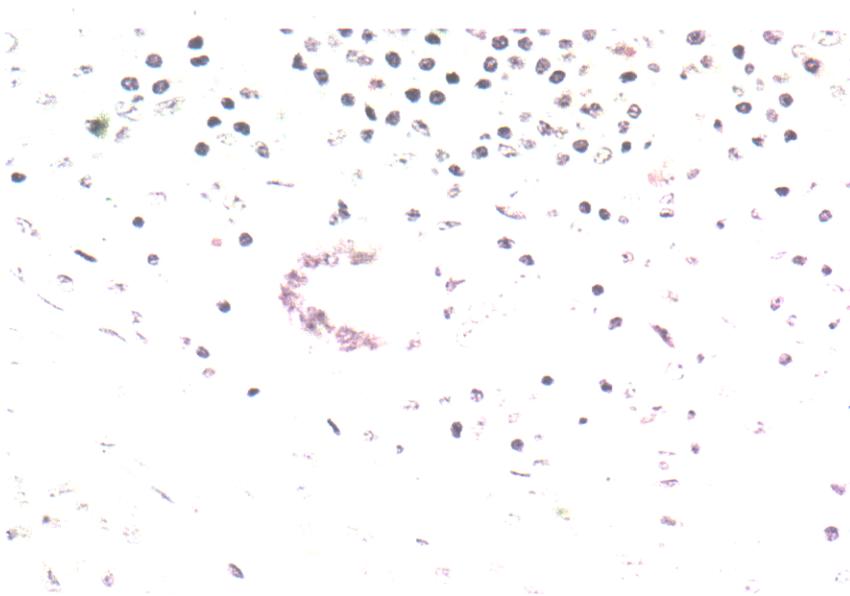
PMWS: enlarged pale mandibular lymph node



PMWS: severe pulmonary oedema, showing lobular septae



PMWS: lymph node showing lymphocyte depletion, histiocyte infiltration, inclusions and oedema



PMWS: lymph node showing lymphocyte depletion, histiocyte infiltration, oedema and a giant cell

primarily restricted to the lymph nodes, lungs, liver, kidneys and intestines. The histological lesions are primarily of lymphoid depletion, which is most prominent in follicular areas, and histiocyte infiltration, which is often most prominent in parafollicular areas, with syncytia and intracytoplasmic inclusions.

Pathological findings in PMWS cases

Gross lesions

- Enlarged lymph nodes (usually non-haemorrhagic), particularly inguinal, tracheobronchial and mesenteric
- Heavy oedematous lungs, which are non-collapsible, sometimes with marked interlobular oedema
- Enlarged kidneys with small (1 to 3 mm) pale white foci in the cortices
- Carcase jaundice/liver atrophy (uncommon)
- Ulceration of the gastric pars oesophagea may be present but the incidence of this is no greater than in pigs unaffected by PMWS
- Carcase oedema – occasionally severe pericardial, thoracic and mesenteric effusion and ascites

NB There may be no obvious gross lesions

Histological lesions

LYMPHOID TISSUE

- Lymphoid cell depletion
- Histiocyte infiltration
- Amphophilic intracytoplasmic inclusions
- Syncytia

LUNG

- Interstitial pneumonia
- Sloughing of bronchial and bronchiolar epithelium, leading to stenosis
- Lymphoid lesions, as described above

LIVER

- Hepatitis – periportal lymphoid infiltrates
- Occasional hepatocyte necrosis
- Parenchymal collapse and lobular atrophy

KIDNEY

- Interstitial nephritis associated with lymphocytic infiltration, although fibrosis is rarely a feature. In chronic cases, 'end stage' kidneys may be seen

INTESTINE

- Lymphoid lesions, as described above, particularly in Peyer's patches

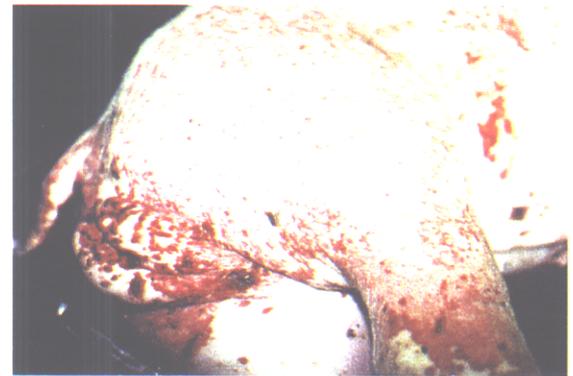
In many cases, secondary infections may confuse the diagnosis. Common secondary diseases found in outbreaks of PMWS in England are Glässer's disease, enzootic pneumonia, streptococcal infections, salmonellosis, pasteurellosis and spirochetel colitis.

PDNS

Clinical signs and diagnosis

Epidemic PDNS tends to affect older pigs, particularly animals ranging from 12 to 14 weeks of age, although the disease has occurred in pigs of between about seven and 20 weeks of age. Cases of sporadic PDNS have been reported to occur in animals of between five weeks and nine months of age.

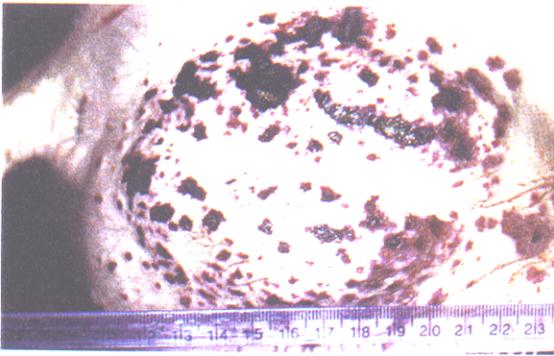
Typically, the morbidity in outbreaks of epidemic PDNS in England has ranged between 0.5 and 14 per cent, with a case mortality rate of 25 to 30 per cent. Between 60 and 80 per cent of pigs which show cutaneous purpura die. Owing to the similarities between



PDNS: acute purpural rash on the hindquarters

Clinical signs of acute epidemic PDNS cases seen in England since August 1999

- Cutaneous purpura – petechiae/ecchymoses over the hindlimbs in particular and also the perineum. These may coalesce. The lesions darken and, if extensive, may become necrotic. Purpura may also be seen elsewhere on the body, particularly on the flanks, ventral abdomen, forelimbs, head and ears
- Most pigs clinically affected with skin lesions die, the rest usually have to be culled
- Animals may be pale, dull, depressed and anorectic, and are often febrile in the early stages of the disease
- Animals may have dyspnoea and transient cyanosis
- Many pigs have oedema of the lower limbs and eyelids; sometimes conjunctivitis and diarrhoea may occur
- Many animals are reluctant to move
- Many pigs have elevated blood urea and creatinine levels, indicating kidney dysfunction
- Superficial lymph nodes, particularly the superficial inguinal (mammary or scrotal) and subiliac (pre-femoral), which are not normally visible or palpable, may be seen and felt



PDNS: subacute coalescing skin lesions on the scrotum of a boar



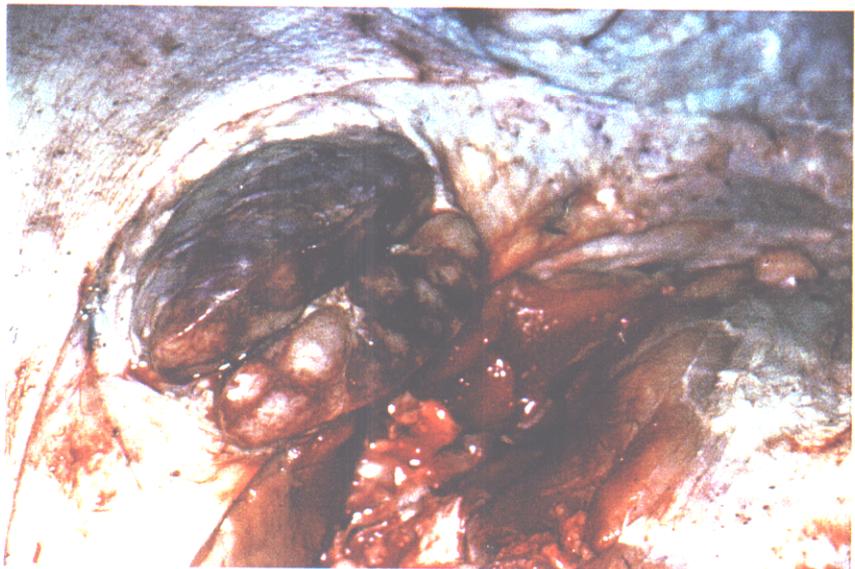
PDNS: subacute confluent cutaneous haemorrhages on the hindquarters and legs of a gilt



PDNS: enlarged kidney with multiple red foci of similar size and colour, which suggest the presence of congested haemorrhagic renal glomeruli

PDNS and both CSF and ASF, there is frequently a need to notify the local divisional veterinary manager (DVM) so that MAFF can establish whether swine fever is present or not. *Practitioners in any doubt whatsoever about possible swine fever should report suspect cases to the DVM.*

The occurrence of grossly haemorrhagic lymph nodes and of haemorrhagic lesions elsewhere in the carcass, means that it is not possible to differentiate cases of



PDNS: enlarged superficial inguinal lymph node with oedema and subcapsular and interfollicular haemorrhages

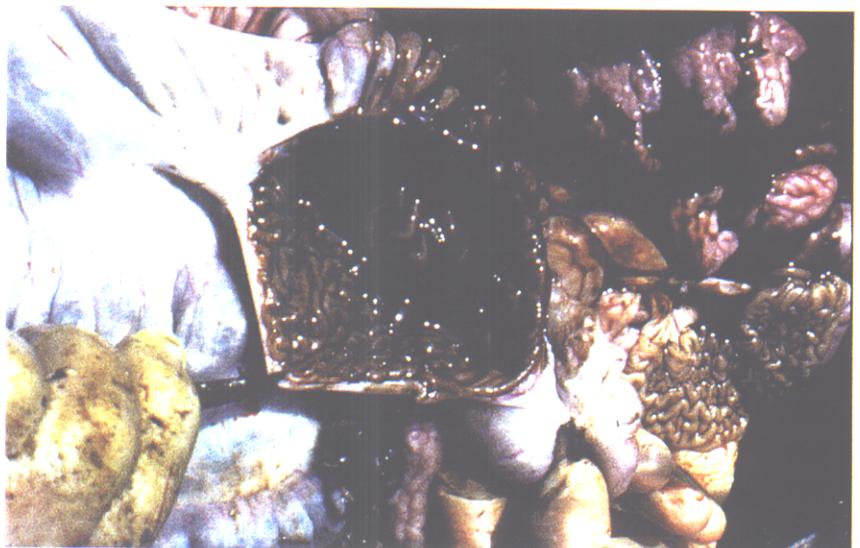
Pathology of acute epidemic PDNS cases seen in England since August 1999

Gross lesions

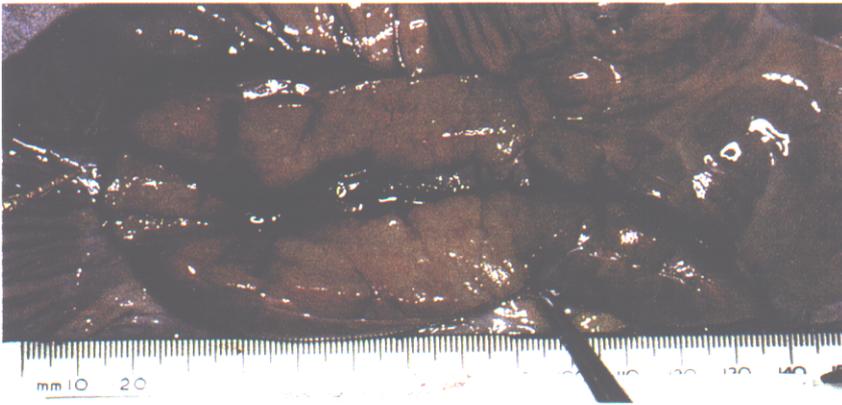
- Skin lesions (as described in the box on the left) may be severe and confluent
- Enlarged haemorrhagic lymph nodes (as seen in cases of CSF or ASF), which may be oedematous
- Enlarged kidneys with white foci and petechiation
- Pulmonary, perirenal and mesenteric oedema
- Serosal and mucosal haemorrhage of the small and large intestines
- Some pigs may have ulcers in the ileocaecocolic valve or pars oesophagea region of the stomach
- Some animals may have ulceration of the glandular area of the stomach

Histological lesions

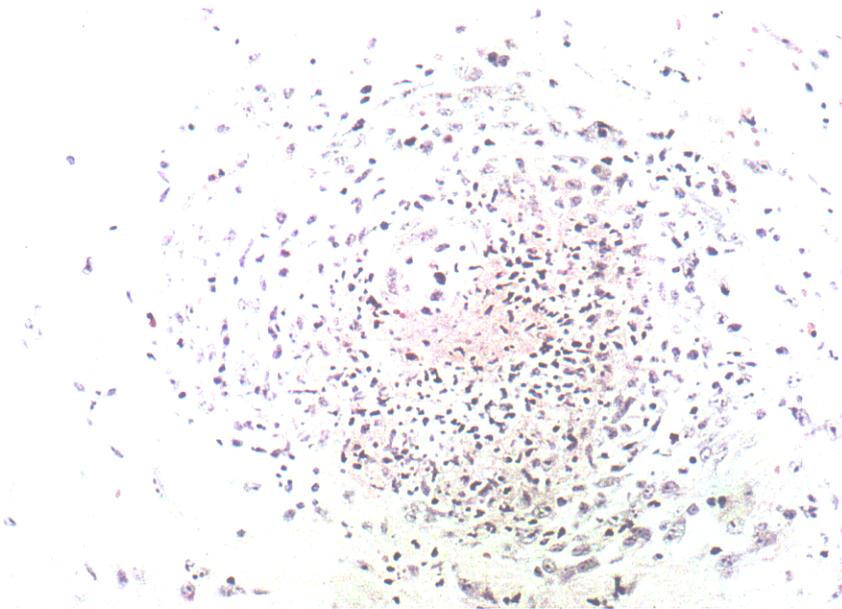
- Exudative and sometimes crescentic glomerulonephritis
- Interstitial nephritis
- Systemic necrotising vasculitis



PDNS: colon with haemorrhagic contents



PDNS: cross-section of enlarged oedematous mesenteric lymph nodes with mild haemorrhages



PDNS: severe acute vasculitis in a small arteriole in the skin

PDNS from either swine fever other than by specific laboratory investigations. These signs, and the associated pathology, are extensively reported by Done and others (2001). The signs of PDNS are the result of a necrotising vasculitis triggered by the deposition of antigen/antibody

complexes (immune complex vasculitis). The antigen or antigens involved in this mechanism are unknown but there are indications that a specific biotype of *Pasteurella multocida* may be involved.

Aside from the swine fevers, these lesions may be mistaken for other acute septicaemic or toxæmic diseases, such as *Actinobacillus* infection or swine erysipelas.

EPIDEMIOLOGICAL FACTORS

The epidemiology of PMWS and PDNS is not fully understood. However, as the epidemic of PMWS has spread across the south of England and East Anglia, a number of common factors have emerged. Points outlined in this section are the result of clinical observations only, and more detailed epidemiological studies are awaited.

The following factors seem to have been involved in the spread of PMWS and PDNS:

- The initial dissemination of PMWS since late 1999 has largely followed the movement of pigs from affected to unaffected pig farms. Large integrated pig-producing companies, which have merged pigs at weaning from multiple sources, have been at the forefront of the epidemic:

- More recently, lateral transmission of PMWS from affected sites into unaffected pig herds, without any pig movements between the two areas, has become more common. Many of these sites are either outdoor herds or straw barns, where there is no control over bird movements. Clinicians are now generally of the opinion that birds are likely to be a significant (probably mechanical) vector of PMWS:

- Epidemic PDNS appears to be a common sequela in herds affected by PMWS. However, not all PMWS-positive herds show PDNS. It seems possible that immune dysfunction caused by PMWS enables challenge with a further antigen(s) to precipitate the immune complex vasculitis that clinically presents as PDNS:

- Both PMWS and PDNS have been reported from all management systems, although those farms with multiple sourcing of piglets at weaning seem to be most at risk. Management factors which encourage mixing of young piglets appear to predispose to a higher level of disease associated with PMWS. If pigs are not mixed until they reach a bodyweight of 30 kg or more, the level

The role of porcine circovirus in the development of PMWS and PDNS

Although the role of porcine circovirus type 2 (PCV-2) infection and other agents in the development of PMWS and PDNS is not properly understood, it is now widely acknowledged that PCV-2 is intimately associated with the occurrence of both PMWS and PDNS. PCV-2 was demonstrated in the first case of PMWS in Canada (see Clark 1997, Harding 1997, Ellis and others 2000) and its antigen was first identified in lesions of affected pigs by Allan and others (1999) who also isolated the virus from pigs affected with both PMWS and PDNS from East Anglia. PCV-2 infection is thought to be widespread within the pig herd in Great Britain although not all infect-

ed herds show clinical manifestations of PMWS or PDNS. In a recent survey of herds in Scotland, for example, pigs showed virtually 100 per cent seropositivity to PCV-2, but no outbreaks of either PMWS or the epidemic form of PDNS have been reported in Scotland.

Retrospective analysis has shown that it is possible that disease, such as granulomatous enteritis in pigs, which was identified as long ago as 1986, was in fact associated with PCV-2 infection. Porcine circovirus type 1 (PCV-1) has been identified as a contaminant of pig tissue culture lines, but is thought to be of no clinical significance.

of disease seen is reduced compared to farms where significant mixing of pigs occurs before this stage. Even so, in some cases, transporting pigs of over 30 kg from affected units can result in dramatic further outbreaks:

■ It has been found possible to control PMWS and PDNS in continuous-flow finishing units. This is achieved by identifying the source of pigs that are introducing the problem and eliminating them from the site. This suggests that incoming weaned piglets introduce the disease into the herd. It is thought that persistently viraemic piglets that were infected in utero may underlie this problem:

■ The majority of outbreaks of PMWS and PDNS have occurred in East Anglia. The reason for this and the timing of the appearance of these diseases is unclear, but has been linked to the poor wheat harvest in this region in 1999. This may be related to mycotoxicosis and, in particular, ochratoxicosis, but at present there is insufficient information to support or refute this theory:

■ The appearance of PMWS and PDNS has also been linked to widescale use of vaccines in pigs, such as porcine parvovirus vaccine which has been used since the mid-1980s, vaccines for *Mycoplasma hyopneumoniae* infection which were introduced in 1998, and the widely reduced use of growth promoters in mid-1999. However, there is no evidence to support this hypothesis:

■ Many herds that have experienced problems with PMWS and PDNS have also been affected with porcine reproductive and respiratory syndrome (PRRS). This is not always the case and it would appear that PRRS virus infection is not a necessary component to these problems. However, PRRS is considered to aggravate the situation where other infectious diseases are present.

CONTROL MEASURES

In practice, it has been particularly difficult to manage PMWS on affected farms and mortality rates have remained very high despite various approaches to control and treatment. In all probability, this is due to the fact that piglets affected with PMWS are immunocompromised and are unable to cope with the normal disease challenges that might occur in rearing and finishing herds. A lack of appropriate diagnostic tests has also hampered the ability to control the problem. Furthermore it is not easy to identify affected weaner-breeder herds as they have no stock of an age that would demonstrate the clinical signs.

The following guidelines are generally used to limit losses in herds affected by PMWS:

■ Avoid taking pigs from affected sources. However, with this in mind, it is best to avoid changing the sources of breeding or growing stock. On rearing and finishing units, identification of pigs from affected sources can be difficult if piglets are moved from the breeding farm at weaning and mixed with piglets from other herds, unless the various sources identify their piglets by tattoos or tags:

■ Isolate replacement breeding stock for as long as practicable and check that there has been no change in the clinical situation at the supplying herd before moving the stock out of isolation:

■ Delay weaning and minimise mixing of piglets at weaning as far as possible. Most transmission is considered to occur shortly after weaning. Pigs mixed later seem less likely to develop PMWS. Mixing of pigs

should be reduced as much as possible until animals have reached a bodyweight of around 30 kg or until they are about 10 weeks of age:

■ Minimise stresses on pigs, as these often seem to trigger disease. Moving, mixing and inappropriate management or nutrition are all factors that may potentially be involved:

■ Treatment of sick pigs is generally unrewarding although there have been reports of better recovery rates following the use of steroidal or non-steroidal anti-inflammatory drugs in combination with broad-spectrum antibiotics. Many pigs will die whatever treatment is given and it is better to identify these promptly and euthanase them in order to limit the severe welfare problems associated with PMWS:

■ Identify sick pigs and move them to hospital accommodation or euthanase them, as appropriate. The more promptly affected pigs are moved to low density hospital pens the better the recovery rates:

■ Allowing for the points discussed above, identify the secondary pathogens that are active within the herd and use preventative management practices, antibacterial therapy and/or vaccination in order to minimise the risk of these diseases. Detailed laboratory investigations and sensitivity testing of relevant bacterial pathogens is invaluable:

■ Apply all-in-all-out management, either by site, building or pen:

■ Reduce stocking density and control ventilation to create optimal environmental conditions:

■ Clean and disinfect pens between batches (Virkon-S [Antec International] is the only disinfectant which, at the time of writing, claims to be active against PCV-2 specifically).

As discussed earlier, PDNS seems to be a common sequela in cases of PMWS. There has been some success on some farms in controlling this secondary manifestation by giving appropriate broad-spectrum antibiotic cover during the four-week period prior to the age when pigs develop signs of PDNS on any one farm. Presumably, this is as a result of controlling bacterial infections during the risk period and limiting the risk of antigen/antibody complexes developing.

SUMMARY

The age of weaning and the amount of mixing of piglets from different litters and sources are considered important factors in determining the level of disease associated with PMWS. At present, the reasons for this are not clearly understood. Other viruses may be involved, but it may simply be either that persistently viraemic pigs enter the weaner pool (as for bovine virus diarrhoea virus infection), or that circovirus may damage the immune system and as maternal antibody wanes in the period when a three-week-old pig is immunologically incompetent, the piglet is left with neither passive nor active immunity: the animal then becomes ill as a result of stress and bacterial challenge and overload.

In order to examine suspected predisposing factors and to identify areas for further research, a case-control epidemiological study of PMWS and PDNS is currently in progress in England and Wales. This investigation is funded by MAFF, organised by the VLA and is being carried out by veterinary practitioners.

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PDNS

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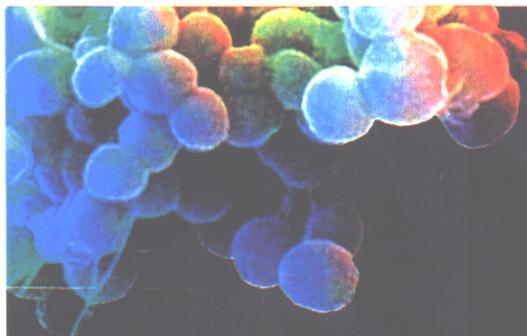
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