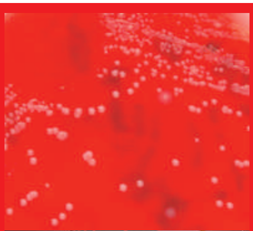
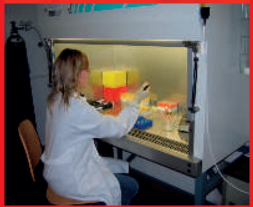
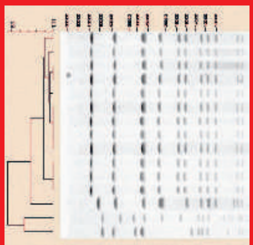


## RECENT ADVANCES IN RABBIT SCIENCES

Edited by L. Maertens and P. Coudert

This book is the result of the COST 848 cooperation Action between rabbit scientists of 14 different countries. The purpose to cover the latest advances in rabbit science has been achieved in this comprehensive work. The different reviews were written by experts in their field and are grouped in 5 chapters: reproduction, housing and welfare, pathology, nutrition and feeding strategies and finally meat quality and safety.

**An overview of nearly all relevant research related to rabbit production can now be found in one cover.**

Compared to other animal productions, rabbit research has received relatively little attention. Nevertheless the rabbit can be used as an economical and easy to manipulate model for other animal productions. Besides some species proper characteristics, the reproduction, pathology or digestive physiology research executed in rabbits could also be valuable for researchers working with other species.

Rabbits are important providers of meat in many EC countries. The species is known for its high reproduction capacity, rapid growth rate and the possibility of utilizing high fibre containing raw materials. Moreover, rabbit meat is appreciated for its healthy image e.g. low $\omega 6/\omega 3$ ratio. Rabbits are highly adaptable to be reared under different production systems and consequently also of considerable value both for small scale production and in developing countries.

An important chapter has also been devoted to the housing and welfare of rabbits. As a caged animal, pressure is executed to improve the housing conditions. The behaviour in different conditions is extensively reviewed and first attempts to enrich the environment of this social animal are given consideration.

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2006


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*Edited by*


**L. Maertens**

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*Animal Science Unit*

*Melle, Belgium*

and

**P. Coudert**

*INRA*

*UR86 BioAgresseurs, Santé, Environnement*

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**European cooperation in the field of Scientific and Technical Research**

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# 3.6. Viral enteritis of rabbits

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## 1. Introduction

In the group of diseases characterising the present situation of the rabbit industry, the so-called "multifactorial conditioned diseases" are really very important.

The "multifactorial enteropathy" is the most important of these technopaties, especially in relation to its productive and economic impacts. It is a pathologic complex of the growing rabbit, known also as "Enteric syndrome", characterized by a great number of stressors and pathogens acting in synergy with a different degree of virulence i.e. various aetiological agents (viruses, bacteria and protozoa) can act together to cause tissutal damage at the gut level, thus determining severe diarrhoea and malabsorption.

The seriousness of this bowel pathology is related to the losses it is able to cause, either direct due to the death of growing rabbits, or indirectly because of a reduced or absent growth and above all the high rate of discarded animals.

The unpredictable appearance and the clinical variability, as well as the variable pattern of pathologic lesions, make epidemiological, diagnostic and laboratory research very difficult. Post mortem lesions are not typical and many pathogenic agents are often involved at the same time, or they follow each other, and consequently their real pathogenic role is still uncertain. On the contrary, it is well known that many conditioning factors (wrong feed formulation, decreased food taking because of adverse seasonal conditions, managerial mistakes, excessive antibiotic administration, loss of passive immunity, cold, early weaning) are involved in inducing this syndrome by promoting the overgrowing of primary or potential pathogenic agents and/or increasing rabbit sensitivity (Lelkes et Ghang, 1987).

It is commonly accepted that rabbit enteric viruses can act as potential pathogens and therefore the presence of viruses in association with particular conditions can induce enteric problems.

## 2. Rotavirus

Among the viral agents identified in rabbits with enteric disease, Lapine Rotavirus (LRV) is certainly the more widespread agent even if it is considered only mildly pathogenic (Thouless *et al.*, 1988). It primarily causes enteric disease and is detected in post weaned rabbits but it could also be involved in the aetiology of more severe enteriris outbreaks in association with *E. coli*, clostridia and protozoa.

Rotavirosis in rabbits is usually caused by a Group "A" rotavirus (Figure 1). Several strains with different antigenic and genomic properties have been described (Martella *et al.*, 2004; Martella *et al.*, 2005). The LRV infection is characterized by a high rate of morbidity and clinical signs (i.e. diarrhea, anorexia, depression vomiting) and it mainly occurs in fattening rabbits, 4-8 weeks old but early infection in lactating rabbit of 8-21 days old as well as late reinfections in 10-12 weeks old rabbits are possible.

Rabbits can become infected by the oro-fecal route and the extension and the severity of the lesions are dose dependent i.e. the consequences of the infection (micro-villus degeneration, malabsorption and diarrhoea) are higher when the infectious dose is also high. Rotavirus was detected in 16.4% of post-weaned rabbits with enteric signs (Nieddu *et al.*, 2000) and, according to our data

**Table 1. Distribution of viral positivity for year and type of virus, detected by EM during the period 1997-2005 from rabbits with enteritis**

| Year | Total | Negative | | Rotavirus | | Parvovirus | | Coronavirus | | Enterovirus | | Adenovirus | | Calicivirus | | Reovirus | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | cases | n. | % | n. | % | n. | % | n. | % | n | % | n. | % | n. | % | n. | % |
| 1997 | 82 | 52 | 63.4 | 19 | 23.2 | 6 | 7.3 | 10 | 12.2 | 2 | 2.4 | 2 | 2.4 | 0 | 0.0 | 0 | 0.0 |
| 1998 | 98 | 63 | 64.3 | 20 | 20.4 | 8 | 8.2 | 10 | 10.2 | 3 | 3.1 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| 1999 | 59 | 37 | 62.7 | 12 | 20.3 | 2 | 3.4 | 8 | 13.6 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| 2000 | 49 | 38 | 77.5 | 5 | 10.2 | 6 | 12.2 | 6 | 12.2 | 1 | 1.2 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| 2001 | 73 | 48 | 65.7 | 9 | 12.3 | 20 | 27.4 | 12 | 13.7 | 1 | 1.4 | 1 | 1.4 | 0 | 0.0 | 0 | 0.0 |
| 2002 | 35 | 17 | 48.6 | 9 | 25.7 | 5 | 14.3 | 8 | 22.9 | 2 | 5.7 | 1 | 2.9 | 1 | 2.9 | 0 | 0.0 |
| 2003 | 34 | 18 | 52.9 | 8 | 23.5 | 4 | 11.8 | 8 | 23.5 | 3 | 8.8 | 0 | 0.0 | 1 | 2.9 | 0 | 0.0 |
| 2004 | 46 | 27 | 58.7 | 4 | 8.7 | 3 | 6.5 | 12 | 26.1 | 5 | 10.9 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| 2005* | 39 | 18 | 46.2 | 9 | 23.1 | 5 | 12.8 | 10 | 25.6 | 1 | 2.6 | 0 | 0.0 | 0 | 0.0 | 1 | 2.6 |
| Total | 515 | 318 | 60.0 | 95 | 18.6 | 59 | 11.5 | 84 | 18.1 | 18 | 4.1 | 4 | 0.7 | 2 | 0.6 | 1 | 0.3 |

* updated at 30 september 2005

such incidence has almost been the same (range 8.7-25.7) for many years (Table 1). However, seroepidemiological surveys have shown that most adult rabbits are seropositive for rotavirus, thus indicating that there is normally a constant circulation of low amounts of rotavirus in industrial rabbit farming (Peeters *et al.*, 1982: Peeters *et al.,* 1984; Di Giacomo *et* Thouless, 1986).

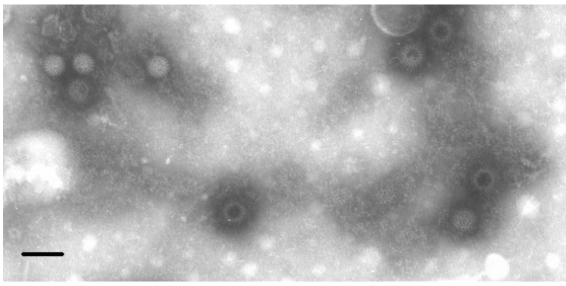

**Figure 1.** *Negative staining electron micrograph of rabbit rotavirus. Full and empty particles are visible. Bar=100nm*

Healthy rabbits became subclinically infected mostly at 4 weeks of age with viral particles excretion for only 3 days. Rabbit with clinical signs continue to eliminate virus for 6-8 days. The persistence of maternal antibodies until 30-45 days can reduce the symptoms of the disease. Diarrhoeic symptoms appear at the beginning of viral excretion and they are generally followed by stipsi. Lesions observed at necropsy are not constant: catharral, haemorragic or necrotic enterotyphlitis and caecal impaction.

Virological diagnosis can be achieved by testing faeces and intestinal contents by ELISA, electron microscopy (E.M.) and PCR.

The introduction of breeders of unknown origin, without the application of a quarantine period is an important risk factor. Thus, a reduction in biosecurity and hygienic activities (cleaning, disinfection, removal of litter, within others) can lead to a huge increase of the environmental contamination with rotavirus.

Even if rabbit rotavirus is considered only mildly pathogenic, meat rabbits suffering from enteritis can die due to dehydration and secondary bacterial infection. In those that recover, a decrease in productivity is commonly observed due to reduced absorption capacity (Thouless *et al.*, 1988; Thouless *et al.*, 1996; Schoeb *et al.*, 1986).

## 3. Coronavirus

Rabbit Coronavirus (RbCoV) is not yet definitively classified, and it is an unassigned member in the Coronavirus genus. Coronavirus particles are described as agent of two different pathologic forms in rabbit: a systemic disease (known as pleural effusion disease or cardiomyopaty of rabbit) and an enteric disease (Lapierre *et al.*, 1980; Osterhaus *et al.*,, 1982). The systemic disease is characterized by fever, anorexia, leucocytosis, lymphocytopenia, anaemia, hypergamma-globulinemia, iridocyclitis, which are often followed by death. The lesions are often localized to myocardial and pleuric level. The enteric disease shows the lesions and symptoms typical of enteritis caused by coronavirus in other species. The virus first observed at E.M. in faeces of rabbit with diarrhoea and its antigenic and structural properties were then determined (Descoteaux *et al.*, 1985). It replicates in small intestine with necrosis of apical villi followed by diarrhoea (Descoteaux *et* Lussier, 1990).

A high prevalence has been found in seroepidemiological surveys (Deeb *et al.*, 1993), indicating a wide diffusion of the RbCoV in rabbitries. Diagnosis of coronavirus could be done by using negative staining electron microscopy (Figure 2).

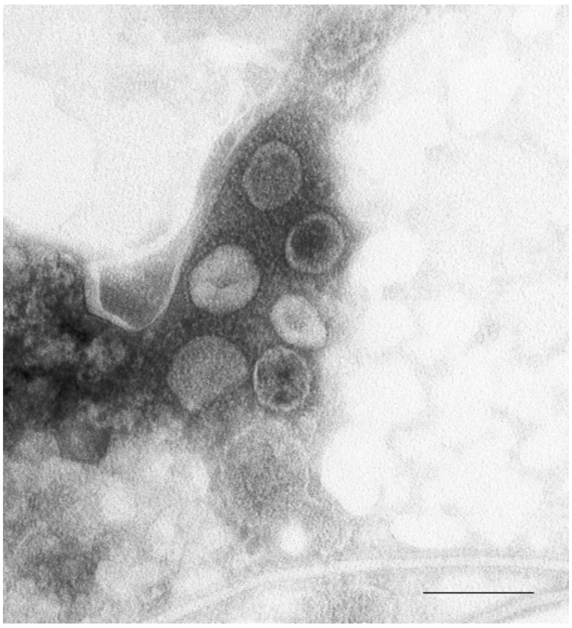

**Figure 2**. *Negative staining electron micrograph of rabbit coronavirus particles. Bar=200nm*

Just the important enhance of coronavirus-like positivity (Table 1) suggested improving the study on this agent, whose role as enteric and/or systemic pathogen is not yet completely cleared. A first serological surveys performed in three rabbitries, using an indirect ELISA based on the used of cross-reactive reagents for bovine coronavirus (BCV), indicated a widespread seroprevalence. However, by testing with a sandwich ELISA for BCV 16 samples resulted positive at EM for coronavirus-like particles, we only detected a faint positivity in 6 of them. We also tried to isolate *in vitro* the virus and to define its haemoagglutination properties: rabbit coronavirus, similar to bovine BCV seems to grow in HRT18 cell line and it haemogglutinates mouse red blood cells but not those of rabbit.

In our surveys coronavirus was frequently associated with other viruses, and mainly with rotavirus, accounting 80% of association during the period 2002-2004 (Table 2 and Figure 3), so it could be possible that it can bring together viral and bacterial agents to determine post-weaning enteritis. Therefore, the pathogenic role as the cause of primary enteric disease was not evident and clear but the spread of virus and its high seroprevalence (100% farms, 3-40% rabbits) suggest the possibility of subclinical infection and a probable role as opportunistic pathogen.

**Table 2. Type and number of viral associations detected by EM during the period 2002-2005 from rabbits with enteritis**

| Type of association | 2002 | 2003 | 2004 | 2005* | Total |
|---|---|---|---|---|---|
| Parvovirus + Enterovirus | 1 | 0 | 0 | 0 | 1 |
| Rotavirus + Enterovirus + Coronavirus | 0 | 0 | 1 | 0 | 1 |
| Rotavirus + Coronavirus | 3 | 3 | 0 | 3 | 9 |
| Enterovirus + Coronavirus | 0 | 1 | 1 | 0 | 2 |
| Parvovirus + Coronavirus | 1 | 2 | 1 | 0 | 4 |
| Rotavirus + Calicivirus | 0 | 1 | 0 | 0 | 1 |
| Rotavirus + Enterovirus | 1 | 0 | 0 | 1 | 2 |
| Rotavirus + Coronavirus + Calicivirus | 1 | 0 | 0 | 0 | 1 |
| Reovirus + Coronavirus | 0 | 0 | 0 | 1 | 1 |
| Rotavirus + Parvovirus | 0 | 0 | 1 | 0 | 1 |
| Total | 7 | 7 | 4 | 5 | 23 |

* updated at 30 september 2005

## 4. Other viruses

The rabbit parvovirus (Figure 4), first described by Matsunaga *et al.* (1977), has a very low pathogenicity and it is commonly isolated from the gut contents of healthy animals. It could cause very mild clinical signs (lethargy, disorexia and depression) in experimentally infected animals and a mild to moderate enteritis in the small intestine (Matsunaga et Chino 1981). Its primary pathogenic role is still unclear but considering its frequency of identification (Table 1), it could be important just in multiple infections together with other infectious agents (viruses, bacteria and parasites).

Some of the other viruses detected during diagnostic activity (Table 1) had only a sporadic occurrence so their pathogenic role is probably negligible. Adenovirus has been previously reported only once (Bodon et Prohaszka 1980). Reovirus and enterovirus have never been described before as enteric agents of rabbits. However we can not exclude that enterovirus-like particles correspond to the picobirnavirus (Gallimore *et al.,* 1993), stating the strict morphological similarities existing with this group of non cultivable RNA viruses, identified in several species (humans, pigs, chickens, guinea

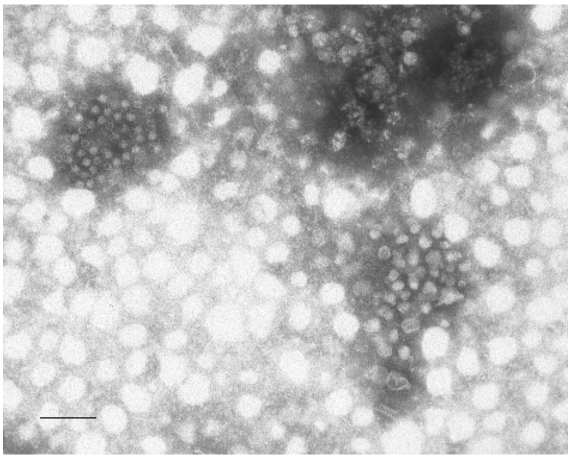

**Figure 3.** *Negative staining electron micrograph of rabbit parvovirus (group on the left) associated to coronavirus particles (group on the right). Bar = 200 nm*

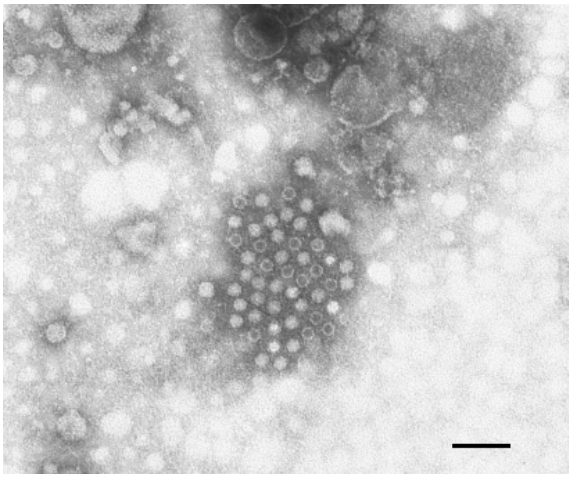

**Figure 4**. *Negative staining electron micrograph of rabbit parvovirus. Viral particles are clumped by using a specific hyperimmune. Bar=100nm*

pigs) including rabbits. Lusert *et al.* (1995) found that picobirnavirus were commonly excreted by 10% of rabbits without causing any symptom or lesions. A cultivable calicivirus, genus vesivirus, has been recently identified in juvenile growing rabbit showing symptoms of diarrhoea (Martin-Alonso *et al.*, 2005) and it was shown to be neither related to Rabbit Haemorrhagic Diseases virus (RHDV) nor to Rabbit Calicivirus (RCV).

## 5. Conclusions

Among the different pathogens that could be found in rabbits suffering from enteropathy, viruses seem to have and important but not definitive role. Viruses, and rotavirus particularly, are not able to induce primary episodes of high gravity but, acting as mild pathogens, they could have the capacity of becoming endemic.

The situation of intensive rabbit-breeding, is characterised by intense genetic selection, exasperated productive performances, sometimes overpopulation and consequently high environmental pollution of facultative pathogens. Therefore, these viruses and other low pathogenic agents (es. flagellata protozoa), can explicate a more important role for the occurrence of severe enteritis in rabbit, predisposing and aggravating secondary microbial infections.

One possibility, already proposed by others, is that they can primarily cause damage on the intestinal mucosa thus predisposing the attachment and replication of bacteria. In such case it does not exclude a dose dependant effect, nor a transient infection and a short period of excretion, thus making possible the detection of viruses in association with the presence of *E. coli*, *Clostridium* spp, Coccidia and other protozoa.

On the other hand we can't exclude that the changed physiological and metabolic conditions, induced to enteric level by various factors both alimentary or not, can enhance the replication of viruses normally present at a lower concentration, permitting them to explicate a pathogenic action.

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