THE PATHOLOGY OF SOME DISEASES OF YOUNG CALVES

by

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GENERAL INTRODUCTION

The diseases of calves constitute one of the most serious causes of loss to the agricultural community. The extent of this loss is difficult, if not impossible, to estimate, since it is not only the market value of each individual animal which dies that must be considered, but the potential value to the breeder if the latter is working with high grade stock. It is a generally accepted fact that calf mortality is often greatest on those farms in which the general standard of breeding is high, and in which the milk yields of the cows are greatest.

Another important factor is the high morbidity rate in young calves, since survivors from disease often take longer than normal to reach maturity and show a poor ratio food intake to weight gain. The present high cost of feeding stuffs makes this problem almost as important as mortality *per se*.

Several surveys have been made in an attempt to estimate the mortality rate of calves in Scotland. Jordan (1933) states that of 548 calves born on 26 farms in one year, 113 or 20% died. Lovell (1945), dealing with selected farms, found the mortality rate in Scotland to be 11.4%. He states that, if [redacted] figures for abortions and stillbirths are added, the calf mortality rate is approximately doubled. It is doubtful if this last

figure is now applicable since the majority of abortions were due to infection of cows with Brucella abortus; The Ministry of Agriculture calfhood vaccination scheme for Brucellosis has now greatly reduced the incidence of this disease.

Phillips (1950) reviewing the figures for calf disposal in England and Wales, where the calf mortality is about half that of Scotland, states that of 7,500,000 calves 5 to 10% succumbed to disease and 45% (i.e. most of the males born) were disposed of for slaughter. Bull calves are disposed of before the age at which calves normally succumb to disease. These figures indicate that the loss from calf diseases in Britain is at least £3,000,000 per year.

A moderate amount of research work has been done on calf diseases but almost none has been carried out from the pathological point of view. This has led to a great deal of confusion since accurate criteria for the differential diagnosis of diseases with similar clinical syndromes have not been established. The histo-pathology of calf disease is almost non-existent.

On account of this lack of accurate pathological data it was decided to take a series of consecutive calf necropsies and to investigate carefully the morbid anatomical and histological appearances of the calf diseases which occur in the West of

Scotland.

This work revealed that there are more specific diseases of calves than was formerly thought, and experimental and field investigations have been carried out on these conditions.

It was found that it is impossible to set an arbitrary age limit on "newborn" calves, as several disease complexes can affect them at any time in the first six months of life. This study is restricted to animals of this age group, except where lesions found in older animals throws some light on the problems of the diseases of the young calf.

This thesis is divided into two main parts:-

(1) Hydrops foetalis; a comparison of the human and bovine diseases, and

(2) A pathological and experimental study of the diseases of calves in the first six months of life.

Part 1

A study of Hydrops foetalis in the calf; and a comparison of this with the human disease.

INTRODUCTION

Hydrops foetalis in the bovine is a disease characterised by a generalised oedema of the subcutaneous tissues and serous cavities of the foetus.

Its occurrence has been recognised for many years but until now it has merited no more than an occasional mention in text-books of obstetrics as a sporadically occurring monstrosity (Craig 1941).

The condition is confined to pedigree Ayrshire cattle and it has, in the last decade, assumed serious proportions on certain farms dealing only in high grade animals. The incidence has apparently increased throughout the whole Ayrshire breed.

Recently Donald et al. (1952) have suggested that the disorder is hereditarily transmitted on Mendelian principles, the genes responsible being autosomal recessives. The increased frequency in the closely inbred Ayrshire strain would be readily understandable on these grounds.

Diagnosis of the disease is often possible at the fifth month of gestation by rectal examination of the dam. Although gross enlargement can be noticed at this early time, the foetus is usually carried to full term when dystocia almost always occurs. Due to the massive size of the foetus, embryotomy is usually necessary at parturition, and if any additional

impediment to delivery is present, e.g. twin pregnancy or malposition of the foetus, the dam, always a valuable animal, may die or have to be slaughtered.

Various degrees of severity of oedema are seen but the typical appearance is of gross enlargement of the head, legs and abdomen (Figs. 1 and 2). The face assumes a strongly convex profile, the loose subcutaneous tissues overlying the nasal bones being heavily infiltrated. The eyelids are swollen and closed; the upper end of the lachrymal canal is occluded resulting in tear scalding of the cheeks in surviving animals. The submandibular tissues are pendulous and hang several inches below the plane of the rami, while the ears show peculiar terminal bullae containing fluid. The legs are symmetrically swollen and pit on pressure. The degree of abdominal distension varies, the fluid content ranging from a few pints to several gallons.

Since there is no account in the literature of the morbid anatomical and histological features of the abnormality, it was thought desirable to describe the findings in a series of cases and to try to determine if the disease has an immunological and pathological basis similar to Hydrops foetalis in man, which is the most severe form of Haemolytic Disease of the Newborn.

The essential features of the pathogeneses of Hydrops foetalis in the human subject are:-

1. The existence of a blood group incompatibility between mother and father.
2. The inheriting by the foetus of some of the blood antigens possessed by the father but not by the mother.
3. Immunisation of the mother by one or more of these foetal antigens.
4. Sensitisation of the foetal erythrocytes by maternal antibodies.
5. The production of a haemolytic anaemia in the foetus by the antibodies derived from the mother. This severe anaemia is thought to be responsible for the severe oedema.

Accordingly, the investigation has been prosecuted in four ways, viz.:

(a) Serological tests have been applied to affected calves and to dams and sires responsible for producing hydropic calves.

(b) Haematological examinations of the blood of the affected calves have been carried out.

(c) The morbid anatomy of the foetuses has been studied and histological examination of the tissues of affected calves has been carried out.

(d) An attempt has been made to produce iso-immunisation of

cows experimentally, and to study the effects on the foetus on a subsequent pregnancy of which the donor bull was the father.

Haemolytic Disease of the Newborn occurs naturally in mules (Caroli and Bessis, 1947), horses (Coombs et al. 1948; Parry et al. 1949) and pigs (Buxton et al. 1953) and has been produced experimentally in dogs (Young, 1949). The serological basis of these conditions is essentially similar to that in the human subject, the foetus inheriting from the father one or more blood group antigens not possessed by the mother. The conditions differ from Haemolytic Disease in the human in that the maternal antibodies produced by iso-immunisation do not, in these animals, cross the placental barrier to produce Haemolytic Disease in utero. The maternal antibodies are passed to the newborn animal in the colostrum and after absorption into the bloodstream from the alimentary tract, give rise to haemolytic anaemia. Hydrops foetalis has not been observed in these animals. In the human subject Hydrops foetalis is always associated with ante-natal Haemolytic Disease.

Material Studied

Five carcases and one live calf were obtained from veterinary practitioners. Ten intact hearts, 40 umbilical arteries and a large number of blocks of normal tissue for histological purposes were obtained from calves, ranging in age from one to seven days, which were presented for slaughter at Glasgow corporation abattoir.

Serological Results

Of the six dropsical calves included in this series, a complete serological examination of calf, dam and sire was made in three cases; in one case the dam and sire only were examined; and in two cases no tests were possible.

An examination was made of a dam and sire four days after the birth of a calf which had been destroyed. Ten cows, each of which had given birth to a dropsical calf within the preceding year, were also studied.

A. Tests applied to the affected calves

(a) The Coombs' Test. The basis of this test is the observation that red cells to which an antibody is adsorbed may be agglutinated by serum prepared against the globulin of the

species providing the antibody. In this case the test was used to determine whether the erythrocytes of an affected calf had been sensitised by incomplete antibody derived from the serum of the dam.

Anti-ox-globulin sera were produced by immunising rabbits against ox globulin by Broom's method (1943). Three injections of alum-precipitated serum were injected at monthly intervals into the hind legs of each of three rabbits. A serum sample was taken from each rabbit immediately before injecting the alum-precipitated serum. Three further samples were taken from each at monthly intervals. The rabbits were numbered 1, 2 and 3 and the monthly serum samples a, b, c and d. The serum names 1a, 2a and 3a are used in the text to denote the pre-immunisation sera, and a corresponding nomenculature is used for the other sera, e.g. 2b is the serum of rabbit 2, one month after immunisation.

In order to test the efficiency of these sera, it was necessary to obtain red cells on to which ox globulin was adsorbed. To do this, a calf was immunised against pig erythrocytes and a calf anti-pig-erythrocyte serum obtained. After incubating pig red cells with this serum at 37° C, the cells were washed in saline and put up in an agglutination test with the rabbit anti-ox-globulin serum. The sensitised

pig erythrocytes were agglutinated. This proved the efficiency of the rabbit anti-ox-globulin sera.

Samples of washed erythrocytes from hydropic calves were set up in agglutination tests with the anti-ox-globulin sera, serum taken from the rabbits before immunisation being used as a control system. Doubling dilutions of serum were used from 1/2 to 1/64. The mixtures were incubated and inspected every few minutes until an hour had elapsed. The results were checked microscopically.

In no case was agglutination observed.

(b) The "Saline Agglutinin" Test

This test was employed to find if the sera of the dam contained any antibodies which would specifically clump the calves' erythrocytes when the latter were suspended in physiological saline.

A standard agglutination test was employed throughout this work. Seven 7 x 50 mm. round bottomed glass tubes were set up in a stand and numbered 1 to 6 with the last labelled control. 0.04 ml. of serum was then placed in tubes 1 and 2 and 0.04 ml. saline was added to tubes 2, 3, 4, 5 and 6. Tube 2 was shaken to ensure maximum mixing of serum and saline then 0.04 ml. was transferred to tube 3, mixed and so in series to tube 5 when 0.04 ml. which had been withdrawn was discarded. To each tube was then added 0.04 ml. of a 3% suspension of erythrocytes in physiological saline. The tubes were incubated at 37° C. for

60 minutes and the results read with a hand lens and then checked microscopically.

When these tests were employed using the erythrocytes of each calf against the serum of its dam, the results were consistently negative.

(c) The "Albumen" Agglutination Test

This was employed to find if the sera of the dams contained an "incomplete" antibody, which, while incapable of clumping calf erythrocytes suspended in physiological saline, could agglutinate them when suspended in 20% bovine albumen.

All of the tests were negative.

(d) The Haemolytic Test

This test was used in view of the fact that Coombs et al. (1951) showed that not all bovine erythrocytes are agglutinated by specific antisera, but that they can be haemolysed if complement is added. In carrying out the test, the following reagents were used:-

(1) A 3% saline suspension of calf erythrocytes.

(2) The serum under test for haemolytic antibodies to (1).

(3) Fresh guinea pig complement diluted 1 in 4.

(4) Washed sheep erythrocytes (sheep R.B.C.).

(5) Horse anti-sheep-erythrocyte serum (I.B.).

The M.H.D. of the complement was found by adding a range of volumes of it to mixtures of sheep R.B.C. and I.B. Four M.H.D.'s of complement were then added to tubes containing the suspension of calf erythrocytes and the serum under test. The tubes were incubated at 37° C. for 60 minutes and the results read.

In one case (CD/6) the erythrocytes of the affected calf were tested against the serum of its dam. No haemolytic antibodies were demonstrated.

B. In the 15 cases where the sera of the dams were examined for specific antibodies against the erythrocytes of the corresponding sires the following tests were employed:-

(a) The "Indirect" Coombs' Test

This test is designed to show if the sera of the dam contains a specific "incomplete" antibody for the erythrocytes of the sire.

The erythrocytes were washed and suspended in saline. They were then incubated with the serum of the corresponding dam in an attempt to sensitise the cells with incomplete antibody possibly present in the serum. After incubation, the cells were washed several times and resuspended in saline. They were then set up as described above in the "Coombs' test"

on the calf cells.

No agglutination occurred.

(b) The sera of the dams were examined for the presence of "saline" agglutinins active against the erythrocytes of the sire, as described above.

The results were negative.

(c) The "albumen agglutination" test, as described above, was used to find out if the sera of the dams contained "incomplete" antibodies to the erythrocytes of the corresponding sire. This test and the "indirect" Coombs' test do not necessarily give a positive "albumen"agglutination test.

No agglutination was observed.

Summary of results

1. In three cases, the erythrocytes of the affected calf were found not to have been sensitised in utero by "incomplete" antibody derived from the mother.

2. The sera of the mothers contained no antibodies either "complete" or "incomplete" capable of agglutinating, in vitro, the erythrocytes of their respective calves or sires; and such sera were incapable of sensitising the cells of the sires as adjudged by the "indirect" Coombs' test.

3. In one case, four days after the birth of a hydropic calf, the serum of the mother contained no antibodies, either of the "complete" or "incomplete" type, against the erythrocyte of the sire, and her serum was incapable of sensitising the erythrocytes of the sire.

4. In 10 cases where the dams had borne hydropic calves during the preceding year, the sera of the dams contained no antibodies to the erythrocytes of the corresponding sires.

Conclusion

In the cases studied, the results fail to show isoimmunisation of pregnancy to be responsible for the production of Hydrops in the calf.

Haematological Results

In the human subject all forms of Haemolytic Disease of the Newborn, of which Hydrops foetalis is one, have as their basis, haemolytic anaemia. In Hydrops this occurs in a severe form. The haemoglobin percentage, the red cell count and the packed cell volume are lowered; primitive nucleated red cells are present in the circulating blood; the reticulocyte count is raised and the erythrocyte fragility is increased. The bone marrow is hyperplastic and many organs show an increased

number of erythroblasts, i.e. there is a generalised erythroblastosis. The umbilical cord blood shows an increased bilirubin content, the indirect Van den Bergh reaction is positive and the surviving child becomes jaundiced.

These factors have been considered in the calf. In one case only the haemoglobin, erythrocyte, reticulocyte and P.C.V. estimations were made; and in another, a calf which lived for a few weeks, two complete blood examinations were made. Table 1 gives the results of these examinations together with the normal figures which represent the average values obtained from the blood of 36 calves of three to seven days old which were slaughtered in the abattoir.

The figures in Table 1 fall within the normal limits for the calf with the exception of the first bilirubin level and the plasma protein concentration.

The elevated bilirubin can be attributed to the transient "physiological jaundice" seen in the newborn of several mammals.

The normal plasma protein concentration is 7%, the figures in the table representing a relatively severe albumen deficiency.

In four cases bone marrow was taken at necropsy, both smears and sections being prepared. In one living calf two marrow biopsies were taken. The marrow from each of these

cases was normal in cytology, quantity and distribution.

Conclusion

The results show that these calves did not suffer from haemolytic anaemia, the condition of Hydrops foetalis thus differing fundamentally from the human condition, as outlined above.

Morbid Anatomy and Histological Findings

The external appearances of bovine and human hydrops are similar, there being marked oedema of the loose connective tissues and of the serous cavities. In the bovine, cases of varying severity are seen, some being born alive and living for a few weeks. One calf in this series was only moderately affected when born but the condition proved to be progressive. In the human, affected infants are either stillbirths or die almost immediately.

Kernicterus, or yellow staining of the grey matter of the brain, is a striking lesion commonly seen in human cases of erythroblastosis foetalis which die with icterus grevis about the third or fourth day of life. It occurs especially in the caudate and lenticular nuclei and occasionally also in the optic thalamus, the dentate nucleus and the nuclei of the

Table 1

The blood examination of two calves showing Hydrops foetalis

Case	Normal Mean	CD/2	CD/6 (1st week)	CD/6 (3rd week)
Haemoglobin	10 gm./ 100 ml.	9.4 gm./ 100 ml.	10.4 gm./ 100 ml.	9.3 gm./ 100 ml.
Erythrocyte count	7,000,000 / c. mm.	6,800,000 /c. mm.	6,400,000 /c. mm.	7,000,000 /c. mm.
White cell count	10,000 /c. mm.	-	13,350 /c. mm.	13,000 /c. mm.
Neutrophils	50%		50%	47%
Non lobulated	10%		10%	0
Eosinophils	0		0	0
Basophils	0		0	0
Monocytes	10%		15%	11%
Lymphocytes	40%		35%	42%
Cells counted	-		500	500
Reticulocytes	0-.1%	Absent	0.1%	Absent
Erythroblasts	Absent	-	Absent	Absent
P. C. V.	45	45	43	36
Erythrocyte fragility	0.4%		Commenced at 0.7%. Complete 0.4%	0.75% 0.45%
Total plasma protein	7%		4.5%	4.5%
Albumen	4		2.1	2.1
Globulin	3		2.4	2.4
Van den Bergh	-		Direct + Indirect +	Faint + Faint +
Serum bilirubin	1 mg.%		3.3 mg.%	0.3 mg.%

midbrain and medulla, or even extending down the spinal cord. A thorough search was made for this lesion in calves, without success. It is not surprising that kernicterus was absent since the calves were not jaundiced. No abnormality of any kind was found in the central nervous system.

The most outstanding feature observed was cardiac hypertrophy and dilatation. The organ was heavier than normal (v. Table 2) and instead of being conical had assumed a globular shape. The left ventricular wall was thickened; the right ventricular wall was thickened to a lesser degree but the right ventricle was dilated, this being mainly responsible for the abnormal shape of the heart. In Table 2 a comparison is made between the measurement and weight of normal hearts and those of the hydropic calves. The foramen ovale was normal in all cases and no obstruction was seen in the pulmonary artery or aorta.

Table 2

A comparison of the measurements and weights of normal hearts and hearts from hydropic calves.

Case	1	2	3	4	5	6	Normal
Circumference at transverse coronary groove	27 cm.		30 cm.	22 cm.	21 cm.	28 cm.	17 cm.
Aortic valve to apex of left ventricle	9.5 cm.		10 cm.	9 cm.	8 cm.	9.5 cm.	8.5 cm.
Thickness of left ventricular wall	3 cm.		3.5 cm.	2.5 cm.	2.5 cm.	3 cm.	2 cm.
Thickness of right ventricular wall	1.3 cm.		1 cm.	1 cm.	1.5 cm.	1 cm.	1 cm.
Weight	520 gm.	480 gm.	300 gm.	225 gm.	233 gm.	400 gm.	200 gm.

This cardiac hypertrophy and dilatation suggested that a state of systemic and pulmonary hypertension might have been present, therefore sections of all organs and the larger arteries were stained specifically for elastic tissue. There was no evidence of hypertension such as reduplication of the internal elastic lamina of any vessel. The arterioles in the kidney appeared healthy as did the media of vessels in every

organ.

In von Gierke's disease in the human child there is cardiac and hepatic enlargement and there is an increase in glycogen in the cells of the heart and liver. Since bovine Hydrops foetalis also shows heart and liver enlargement, sections of these organs from affected calves were stained for glycogen. No excess of glycogen was found.

Generalised jaundice and anaemia of the internal organs as found in human hydrops was absent in all cases.

The liver in human Hydrops foetalis due to iso-immunisation sometimes presents a fine cirrhosis partly inter-cellular and partly portal with some thickening of the reticulin framework of the organ. This is associated with slight centrilobular necrosis and sometimes also with the presence of bile thrombi. None of these lesions was found in the bovine cases, the only hepatic abnormality apart from some increase in weight being peculiar nodules of adenomatous structure, the individual cells resembling hepatic cells. These were studded all over the liver in one case and small subcapsular aggregates of similar tissue were seen in another. As stated above, the liver cells when stained specifically for glycogen, showed no stainable excess of that substance.

The severe haemolytic anaemia which is the probable basis

of human Hydrops foetalis leads to a deposition in the liver, spleen and often in the kidneys and suprerenals of an excess of stainable iron. Haemosiderosis could not be demonstrated in any of the calves. Also associated with the anaemia is the persistence of haemopoietic activity by the liver, spleen and kidneys. The spleen of a normal newborn calf contains a few foci of extra-medullary haemopoiesis and no increase was found in hydropic animals. In the liver, however, in two cases there were megakaryocytes present throughout the organ and a few small foci of round cells. This was considered to be the last trace of a normal foetal process since the foci were small and scattered and the bone marrow was not hyperplastic. No extra-medullary blood formation was seen in the kidneys. It has been claimed (Potter 1952) that in the lungs of hydropic foetuses, the blood in the vessels can be seen to contain large numbers of erythroblasts. This feature also was absent in the calves.

Two further lesions are said to be almost invariably present in the human condition. These are, increase in the number of islets of Langerhans in the pancreas, and lipoid infiltration of the adrenal cortex. The pancreases of the calves were normal. The adrenals were stained for fat both on frozen sections for soluble fat and on paraffin sections

for glycolipids. They were also examined under the polarising microscope to see if there was an abnormal amount of birefringent lipoid material. The fat content appeared normal in all cases.

It is much to be regretted that the placentas of the affected calves were not available for examination as it is conceivable that some abnormality of placental circulation would increase the work of the heart and thus lead to hypertrophy.

Conclusions

With the exception of cardiac enlargement, no lesions were found in affected calves of a similar nature to those seen in human Hydrops foetalis. There was no histological evidence for the presence of severe haemolytic anaemia, a process invariably present in hydrops caused by iso-immunisation of pregnancy.

The cause of the cardiac enlargement was not apparent but morbid anatomical evidence of hypertension is completely lacking. Excess glycogen storage was also eliminated as a cause of the enlargement. No other cause of increased work by the heart has been observed.

Experimental Results

The work of Ferguson (1941) and his colleagues (Ferguson et al. 1942) has shown that there are a large number of heritable antigens present in the blood of cattle, which occur in such varied combinations as to make individual bovine blood groups almost unique. His experiments were done with animals from various breeds of cattle which had not been extensively interbred.

The Ayrshire breed in the West of Scotland has been established by very intensive line breeding and interbreeding. A sire is mated to his daughter and grand-daughter, the progeny again often being mated to a close relative. It would be reasonable to expect that the very close family relationships in the Ayrshire breed would tend to give less variety to blood groups found. Ayrshire cattle were used in this experiment since it is only in this breed that hydrops has been reported.

The technique used by Ferguson was to inject a litre of blood intravenously into an animal, followed by several similar doses at weekly intervals. He then tested the recipient's serum for haemolytic antibodies to the erythrocytes of the donor. In the course of his work he caused several haemolytic transfusion reactions in some of the recipients. This

phenomenon was also noted by Little (1929), in the course of rinderpest immunisation experiments.

It was thought worth while in view of these reports to try to immunise cows against a bull's red cells and subsequently mate the recipients with the donor to find out if it was possible to produce a condition resembling iso-immunisation of pregnancy in the bovine. If this were possible, a comparison could then be made between experimentally produced Haemolytic Disease and naturally occurring Hydrops foetalis.

Unfortunately purely experimental animals were not available and it was necessary to use cows on a commercial farm. This was very kindly permitted by a farmer but the number available for use was limited.

A bull was chosen as donor which had not previously given rise to an oedematous calf. The three cows used had already borne normal healthy offspring.

The route of injection, the volume of blood administered and the times between transfusions are given in Table 3.

The transfusion technique was as follows. Standard human blood transfusion equipment was used with the exception of the intravenous needles which were three inches long and three millimetre bore. The anticoagulant was 3.8% sodium citrate solution.

Three main difficulties were encountered. (1) The donor bulls were fractious when handled or restrained so that venipuncture and blood withdrawal had to be done rapidly. (2) The constant movement of the animals tended to dislodge the needles and cause clotting in the bore. (3) The normal venous blood pressure was not sufficiently high to give a rapid enough flow to draw off several litres quickly and to prevent clotting in the needle.

It was originally intended to use all three available bulls, but, due to the intractability of two, it was possible to use only one for a full course of transfusions.

Clotting in the bore of the needles was effectively overcome by pre-treating them with silicone (Jarrett 1952). The needles were thoroughly cleaned and dried. Silicone (G. E. C. Dri-Film 9987; or I. C. I. silicone - M441) was drawn through them a few times followed by flushing with cold water. Residual traces of H Cl (the solvent for the silicone) were removed by a quick wash in weak ammonia solution and finally the needles were thoroughly washed in water and dried.

A rapid flow of blood was obtained by utilising the partial vacuum produced by autoclaving the transfusion bottles containing the anticoagulant mixture with the caps loose, and screwing the caps down firmly immediately after removal from

the autoclave while still hot.

The technique of blood withdrawal was as follows. A needle of the type described above was attached to one end of a six foot length of rubber pressure tubing and a record fitting adaptor inserted into the other. The bull was tied to a stall division by a neck chain and its neck extended by an assistant holding its nasal septum. A thin cord was passed round the base of the bull's neck and tightened until the external jugular vein was easily palpable. A needle was then thrust directly into the vein. When the blood flowed freely the needle was attached to the nozzle in the end of the pressure tubing. The needle at the other end was then pushed through the stopper of the partially evacuated transfusion bottle and a fast flow of blood resulted. When the bottle was full the needle was withdrawn and inserted into a second bottle. No difficulties were encountered using this method and several litres of blood could be rapidly withdrawn.

The standard human transfusion set was used to administer blood to the cow, free flow being maintained instead of the usual drip. The milk vein and the jugular vein were used for transfusion with equal ease and satisfaction. Intraperitoneal injections were made over the left flank. In the course of this experiment acute haemolytic transfusion reactions did not occur and the cows remained healthy.

Table 3

Details of the transfusions in the three experimental cows in which an attempt was made to produce iso-immunisation

Animal	First Transfusion	Route	Second Transfusion after 7 days	Route	Third Transfusion after 14 days	Route	Fourth Transfusion after 21 days	Route
Cow (1)	1,000 cc.	Intra-venous	1,000 cc.	Intra-venous	500 cc.	Intra-venous	200 cc.	Intra-venous
Cow (2)	1,000 cc.	Intra-venous	200 cc.	Intra-venous	200 cc.	Intra-venous	200 cc.	Intra-venous
Cow (3)	1,000	Intra-venous	100 cc.	Intra-peritoneal	100 cc.	Intra-peritoneal	100 cc.	Intra-peritoneal

Blood samples were taken from all of the animals before each transfusion and again after the course of transfusions had been completed. The pretransfusion tests were designed to show if any naturally occurring iso-antibodies were present in the cow sera, and the subsequent tests to show if any immune reactions had occurred. The tests were the same as those used in investigating the natural disease, viz.

(1) The "saline agglutination" test.

(2) The "albumen agglutination" test.

(3) The "indirect" Coombs' test.

After the course of transfusions, each serum was also examined for the presence of haemolytic antibodies.

The results were consistently negative.

During the experiment the cows were successfully mated to the bull and three apparently healthy calves were born. Two of these were bull calves and were disposed of before serological examination could be made. The blood of the female calf was obtained and was subjected to the "direct" Coombs' test. The erythrocytes showed no evidence of sensitisation. The Van der Bergh test was also negative. The mother's serum was re-examined against the calf's erythrocytes and contained neither "saline" or "albumen" agglutinins, or haemolytic antibodies to the calf cells.

Results

The experiment to produce immunisation of cows against their sires' or calves' erythrocytes failed. The probable cause of this is thought to lie in the small number of animals, the close family relationship of the animals employed or of a lesser variation in blood groups among the Ayrshire breed than occurs in other breeds or American strains of these breeds.

Discussion and Conclusions

In 15 cases no evidence was found that there was any blood group incompatability between the parents of oedematous calves. Five of these pairs were tested soon after parturition at a time when the mother's antibody titre would be expected to be at its maximum but neither agglutinins or haemolysins were detected.

In three cases the foetal cells could not be shown to be sensitised to maternal antibodies and the serum of the mother contained no antibodies to either the foetal or paternal erythrocytes.

In two cases studied, the blood picture was normal and the organs did not show the lesions associated with erythroblastosis. Various changes found in human cases, e.g. "Kernicterus" lipoid infiltration of the adrenal medulla and hepatic cirrhosis were also absent.

Since the criteria which must be present for the diagnosis of Erythroblastosis foetalis due to iso-immunisation of pregnancy are absent in all of the bovine cases examined, it is concluded that the pathogeneses of bovine and human Hydrops foetalis are fundamentally different.

Although there was no evidence in the vascular system to support it, the invariable presence of cardiac hypertrophy

suggested that the foetuses might have been hypertensive. No reason for such a state was found in the bodies of the animals though unfortunately no placentas were obtained. On theoretical grounds it was considered that either of two abnormalities could possibly have been responsible, (a) an anterio-venous "shunt" in the placenta or (b) some congenital obliterative or occlusive lesion in the placental vasculature, but no opportunity to investigate these possibilities was afforded.

In one case, CD/6, it was noticed that there was a fall in the plasma albumen concentration, and a possible explanation of the oedema may lie in some congenital disturbance of protein metabolism.

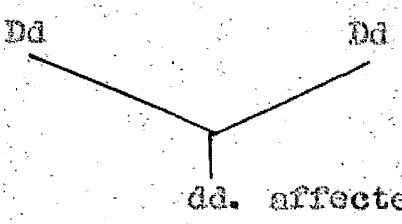
None of these three hypotheses has been substantiated.

No conclusions of any value were obtained from the experimental work since the attempt to immunise the only available cows failed. This could be due either to the close family relationship of the animals used or to the fact that the number of animals employed was too small.

The suggestion has now been advanced (Donald et al. 1952) that H.F.* in the bovine is determined by the double inheritance of a recessive factor. If this is the case, iso-immunisation of pregnancy could not be responsible for the production of the condition since the dam would possess a gene which the calf

* Hydrops foetalis.

also possessed, i.e. if the inheritance was represented thus:-



then the mother would not produce antibodies to the factor d, since she possessed it herself.

APPENDIX 1

The detailed post mortem, histological, haematological and serological examinations of each calf.

CASE CD/1

Calf. Brown and white Ayrshire male; born full term.

History. The dam showed unusual abdominal distension after five months gestation, when a diagnosis of Hydrops foetalis was made by rectal examination. Delivery, at full term, was affected by embryotomy of left forelimb and shoulder, incision of left thoracic wall followed by diaphragmatic puncture to release several gallons of ascitic fluid. The calf was alive until obstetrical interference was initiated.

Post Mortem Appearances

The external appearance was typical of the condition. The calf was completely covered with hair and all parts of the body showed oedema. The head resembled that of a seal; the facial profile was convex, the cheeks puffed out and the intermandibular tissue depressed about three inches below the plane of the rami. (This convexity of the face is accentuated by the fact that the skin of the forehead is very firmly attached to the underlying bone allowing of no hydropic distension, whereas the skin covering the nasal bones is very loosely attached.) The eyelids were swollen and the eyes closed. The sclera was white with no evidence of jaundice. Small oedematous bullae (1.5 cm. diameter) were present at

the ear tips. The normal number of teeth were present but not erupted. They were covered by soft pink mucous membrane. The tongue was enlarged and protruding. The legs were symmetrically thickened throughout their length.

Internal appearances. On section the facial and mandibular regions showed gelatinous infiltration of the connective tissue and muscles. They were pale, fluctuant and glistening having the appearance of cod flesh. The tongue showed a similar change. The mouth, pharynx and larynx showed no abnormality. The thyroid was normal in shape and size. The thymus appeared healthy. The trachea showed oedema of its adventitial coat but the mucosa was normal. The lungs were almost wholly destroyed at parturition; the remaining fragments were atelectatic but showed no abnormality. The pleurae were grossly traumatised at delivery. A gross excess of fluid was present in the thoracic cavity, the exact amount of which could not be determined due to embryotomy having been performed. The heart (520 gm.) was greatly enlarged and showed both hypertrophy and dilation. It was globular in shape, due in part to left ventricular hypertrophy and in part to right ventricular dilation. The foramen ovale was patent and the valve healthy. Small subendocardial haemorrhages were present in the left ventricle and were most pronounced on the mitral valve. The

valves and cusps were healthy. The structure and patency of the great vessels were normal. The abdominal cavity had been distended by several gallons of fluid, which escaped on embryotomy. The peritoneum was healthy, neither mesentery nor omentum being thickened or oedematous. The liver (760 gm.) was of pale brick red colour and unusually friable. It was negative to the "Prussian Blue" test for iron. The spleen (58 gm.) showed no abnormality. The "Prussian Blue" test was negative. The kidneys (80 gm. each). The capsule was slightly raised from the organ by fluid. The surface of the cortex appeared pitted and was very crumbly, while the lobulation was blurred by the oedematous state of the cortex. On section the medulla appeared normal. The adrenals appeared healthy. The alimentary tract showed no abnormality. The umbilical arteries were thick walled and tightly contracted; the lumina contained no blood. The calvarium and meninges were normal. The brain (845 gm.) showed no evidence of oedema or bile staining.

Microscopic Appearances

The dermis and subcutaneous fascia show marked oedema and separation of individual swollen fibres. The thyroid and thymus appear healthy. The heart shows muscular hypertrophy

but is otherwise normal. There is no glycogenous infiltration of the muscle cells. The lungs are atelectatic, the staining reactions for iron are negative and there is no evidence of erythroblastosis. The vascular walls appear normal. The liver shows no abnormality. There is no stainable iron and no extra-medullary haemopoeisis. The vessels appear healthy. There is no excess of glycogen present. The spleen shows some congestion but no evidence of excess blood destruction is noted. Extra-medullary haemopoeisis is minimal and within normal limits. The vasculature shows no abnormality. The adrenal glands are normal in architecture and fat content. The kidneys show some oedema of the outer cortex. Neither stainable iron nor erythroblastosis is present and hypertensive changes are not seen. The umbilical arteries are tightly contracted, but a lumen is still present and there seem to be no mural abnormalities. The C.N.S. shows no lesion of note. The pituitary gland is normal. The skeletal muscle shows only oedema of the fibrous supporting framework.

Haematological Examination

Owing to damage to the calf at parturition, it was impossible to obtain a blood sample suitable for detailed examination.

Serological Examination

While embryotomy was being performed the subclavian artery and great vessels were severed; hence the blood became mixed with the oedema fluid pouring from the thorax and abdomen. A sample of this mixed fluid was centrifuged and the red cells thus obtained were tested as follows:-

Direct Coombs' Tests	Results
R. B. C. CD/1 v Rabbit anti-ox-globulin (R. a. Ox. g.) 1a	Negative
R. B. C. CD/1 v R. a. Ox. g. 1b	"
R. B. C. CD/1 v R. a. Ox. g. 1c	"
R. B. C. CD/1 v R. a. Ox. g. 1d	"
R. B. C. CD/1 v R. a. Ox. g. 2a	"
R. B. C. CD/1 v R. a. Ox. g. 2b	"
R. B. C. CD/1 v R. a. Ox. g. 2c	"
R. B. C. CD/1 v R. a. Ox. g. 2d	"
R. B. C. CD/1 v R. a. Ox. g. 3a	"
R. B. C. CD/1 v R. a. Ox. g. 3b	"
R. B. C. CD/1 v R. a. Ox. g. 3c	"
R. B. C. CD/1 v R. a. Ox. g. 3d	"

"Saline Agglutination" Tests	Results
R. B. C. CD/1 v Serum of Dam	Negative
R. B. C. CD/1 v Serum of Normal Cow	Negative

"Albumen" Agglutination Tests	Results
R.B.C. CD/1 v Serum of Dam	Negative
R.B.C. CD/1 v Serum of Normal Cow	Negative

A blood sample was taken from the sire of the calf and the following tests were carried out.

	Results
R.B.C. Sire (saline suspension) v Serum of Dam	Negative
R.B.C. Sire (" ") v Serum of Normal Cow	Negative
R.B.C. Sire (albumen suspension) v Serum of Dam	Negative
R.B.C. Sire (" ") v Serum of Normal Cow	Negative

Indirect Coombs' Tests

The sire's red cells were washed three times in saline and resuspended in normal saline at 10%. They were then incubated with the serum of the dam diluted 1/4, at 37° C. for one hour. The cells were then washed three times and resuspended in normal saline at 5%. The following tests were carried out.

	Results
R.B.C. Sire v R.a.Ox.g.1a	Negative
R.B.C. " v " 1b	"
R.B.C. " v " 1c	"
R.B.C. " v " 1d	"

						Results
R.B.C.	Sire	v	R.a.Ox.g.	2a		Negative
R.B.C.	"	v	"	2b		"
R.B.C.	"	v	"	2c		"
R.B.C.	"	v	"	2d		"
R.B.C.	"	v	"	3a		"
R.B.C.	"	v	"	3b		"
R.B.C.	"	v	"	3c		"
R.B.C.	"	v	"	3d		"

CASE CD/2

Calf. Brown and white Ayrshire female; full term.

History. Parturition was normal and unassisted.

Post Mortem Appearances

The external appearances were those of a fully developed male calf. Abdominal and thoracic distension was absent, this probably explaining the unaided parturition. Oedema was prominent on the head and legs. The former was of the typical "seal head" type; the latter were symetrically thickened throughout their length. The ears did not show the usual terminal swelling. The scrotum was full of fluid giving a false

impression of containing testicles.

Internal appearances. The fascia over the nasal suture was 4 cm. thick; it had the appearance of cod-flesh and the consistence of a fine rubber sponge. The only remaining muscle was an interrupted line, 1 to 2 mm. broad, with most of the oedematous infiltration ventral to it. Free fluid could be expressed from this only if some force was used. Immediately under the muzzle was an accumulation of free gelatinous fluid. Teeth were present covered by reflexions of normal coloured buccal mucosa. The tongue itself was not enlarged, but the sublingual tissues showed a severe oedematous infiltration. The mouth and pharynx were healthy. The thyroid was healthy. The larynx, trachea and bronchi showed no abnormality. The pleurae were unthickened and the pleural cavity showed little or no fluid excess. The lungs (right lung 500 gm., left lung 700 gm.) were atelectatic. No excess fluid could be expressed. The pericardium was distended but unthickened; its sac contained 150 cc. of blood-tinged fluid. The heart (480 gm) was markedly enlarged and of a totally abnormal shape, being globular instead of the normal conical. The interventricular sulcus was deep and exaggerated. The auricles were not distended and the foramen ovale was normal, the fimbriae of the membranous part of the valve being almost

sealed. The left ventricular wall was very firm and grossly hypertrophic (4 cm. thick), but with little dilation. The right ventricle was dilated and its wall 8 mm. thick. This dilation was mainly responsible for the globular shape of the organ. The valvular apparatus was healthy. The pulmonary artery was slightly greater in diameter than the aorta but was otherwise normal and showed no stenosis. The ductus arteriosus was patent. The aorta was healthy. The abdominal cavity contained 2,000 cc. of golden yellow fluid. The omental sac was distended by this fluid but the serosae showed no intrinsic thickening. There was no abnormality in the alimentary tract. Meconium of normal colour and consistence was present. The spleen (75 gm.) was healthy. The liver (1,100 gm.). The organ was much enlarged and thickened antero-posteriorly, and the edges were rounded. The normal surface colour and marking were absent; the organ was smooth and of a mottled pink and yellow colour. Several small round circumscribed white areas were present below this capsule. The cut surface showed firm edges and mottled parenchyma. Scattered throughout the organ were many round discrete yellow nodules ranging in size from 5 to 8 mm. diameter. There was no apparent fibrous tissue excess. The gall bladder was normal and the bile ducts patent. The kidneys (120 gm. each).

There was excess fluid below the capsule allowing it to strip more readily than usual. The cut surface was normal. The urinary bladder and ureters showed no abnormality. The umbilical arteries were in the retracted position (ca. 10 cm. from the umbilicus). They were tightly contracted and difficult to cut; there was no blood clot in the lumen. The brain (250 gm.), calvarium and meninges appeared healthy. The femoral marrow was reddish-pink and extended the whole length of the bone.

Microscopical Appearances

The thyroid and thymus show no deviation from normal. The heart shows some hypertrophy of fibres. There is no excess of glycogen present. The lungs are atelectatic. There are no iron deposits or foci of extra-medullary haemopoiesis. The large vessels show no evidence of hypertensive change; the walls show a normal amount and distribution of elastic tissue. The liver. The Prussian Blue and Turnbull reactions for ferric and ferrous iron are negative, and apart from a few isolated megakaryocytes there is no evidence of extra-medullary haemopoiesis. Reticulin staining reveals no condensation of reticulin fibres; the fibrous stroma also is normal in amount. The hepatic cells show no excess of

glycogen. The vessel walls are normal; there is neither intimal hypertrophy nor increase in elastic fibres. Throughout the organ are scattered adenomatous areas of varying size. These are very discrete naked eye but are not so microscopically since they are unencapsulated and the cell cytoplasm has the same staining reactions as the normal hepatic cell. The adenoma cells do not contain fat. At the interface of normal and adenomatous tissue the transition in architecture is not abrupt. The cells are arranged in regular circular acini, are wedge shaped and have nuclei indistinguishable from those of hepatic cells. There are four or five cells per acinus in transverse section. There is no evidence of secretion into the acini, such as granular precipitate, globule formation or basal nucleolation. The reticulin framework is normal and the stromal tissue is quite abundant and very cellular. "Triads" are present but the "bile ducts" are small and not well developed. Although the stroma contains capillaries the whole structure is relatively bloodless compared to normal; this may account for the colour of the nodules. There are a few foci of round cells, resembling extra-medullary haemopoeisis. The spleen shows neither excess of stainable iron or extra-medullary haemopoeisis. There is no evidence of a haemolytic process. The vessels do not show hypertensive change. The adrenals appear normal in all respects.

The kidneys are normal. The glomerular loops are patent and unthickened; the afferent arterioles show no mural changes. The umbilical arteries are markedly contracted; their lumina contain no blood, but the structure of the wall seems unexceptional both in thickness and in the relative amounts of muscle and elastic fibres. The meninges and brain are healthy. A thorough and unsuccessful search was made for "kernicterus" lesions. The femoral and humeral marrows show haemopoeitic tissue normal both in cytology and quantity. The skeletal muscle shows some oedema of the supporting fibrous tissue but the fibres are normal.

Haematological Examination

An oxalated blood sample was obtained at parturition by the practitioner. Films for a differential leucocyte count were unsatisfactory.

The Red Cell and Haemoglobin estimations were:-

Haemoglobin	9.7 gm./100 ml.
Erythrocyte count	6,800,000
Reticulocyte count	No reticulocytes seen.
P. C. V.	45%

Marrow smears made at necropsy showed no detectable abnormality.

Serological Examination

Direct Coombs' Tests	Result
R.B.C. CD/2 v R.a.Ox.g. 1a	Negative
" " " 1b	"
" " " 1c	"
" " " 1d	"
" " " 2a	"
" " " 2b	"
" " " 2c	"
" " " 2d	"
" " " 3a	"
" " " 3b	"
" " " 3c	"
" " " 3d	"

"Saline" Agglutination Tests	Result
R.B.C. CD/2 v Serum of Dam	Negative
R.B.C. CD/2 v Serum of Normal Cow	"

Albumen Agglutination Tests	Result
R.B.C. CD/2 v Serum of Dam	Negative
R.B.C. CD/2 v Serum of Normal Cow	"

A blood sample was taken from the sire of the calf and the following tests were carried out.

		Result
R.B.C.	Sire (saline suspension) v Serum of Dam	Negative
"	" " " v " of Normal Cow	"
"	" (albumen suspension) v Serum of Dam	"
"	" " " v Serum of Normal Cow	"

Indirect Coombs' Tests

The sire's erythrocytes were washed three times in saline and a 10% suspension in normal saline was made. They were then incubated with a 1/4 dilution of the dam's serum for one hour at 37° C. The cells were then washed three times and resuspended in normal saline at 3%. The following tests were carried out.

					Result
R.B.C.	Sire	v	R.a.Ox.g.	1a	Negative
"	"	v	"	1b	"
"	"	v	"	1c	"
"	"	v	"	1d	"
"	"	v	"	2a	"
"	"	v	"	2b	"
"	"	v	"	2c	"
"	"	v	"	2d	"

					Result
R. B. C.	Sire	v	R. a. Ox. g.	3a	Negative
"	"	v	"	3b	"
"	"	v	"	3c	"
"	"	v	"	3d	"

CASE CD/3

Calf. Ayrshire female, born three to four weeks premature. Breech presentation.

Post Mortem Appearances

External appearance. The head was typical of the condition: it was almost globular in shape, the profile convex and the sublingual tissues markedly pendulous. The legs were symmetrically enlarged; on section the oedema was mainly confined to the fascia, and the muscles were pale and flabby. The degree of abdominal distension was not ascertainable as the abdomen had been incised and the alimentary tract removed to facilitate delivery.

Internal appearance. All organs showed advanced post mortem degeneration. The mouth, tongue, pharynx, larynx, trachea, thyroid and thymus were normal. The lungs (left 180 gm., right 400 gm.) were atelectatic. They were purple

in colour, had a smooth glistening surface, indistinct lobar divisions and were completely airless. The pericardium was opaque and contained only a few cc. of golden-coloured fluid. The heart (300 gm.) was globular in shape. The ventricular part of the organ measured 10 x 10 x 7 cm. The left ventricle showed great hypertrophy, the wall being uniformly 3.5 cm. thick. The right ventricle was dilated, the wall measuring 1 cm. in thickness. The foramen ovale was patent but the sealing apparatus was intact. The valvular apparatus and great vessels showed marked post mortem degeneration. The gall bladder was small and contained very viscid yellow bile. The bile duct was patent. The spleen (90 gm.) appeared normal. The kidneys (each 180 gm.) showed no abnormality. The umbilical arteries were very small with flabby vein-like walls in their proximal half; in the distal part the wall was thick and the lumen very narrow and empty of blood. The brain was degenerate but showed no obvious lesion. Red marrow was present in the metacarpals and metatarsals.

Microscopic Appearances

The tongue shows very little oedematous infiltration. The heart shows muscular hypertrophy. There is no excess of glycogen present. The vessels do not show hypertensive changes. The lungs are atelectatic. They contain large clumps of Gram

positive bacilli. There are no erythropoietic foci and no deposition of stainable iron. The vasculature does not show hypertensive change. The liver shows no abnormality. At one point just below the capsule is a small adenomatous area similar to those described in CD/2. There is no excess of glycogen or iron. The vessel walls appear healthy. The spleen is normal. There are no signs of a haemolytic process. The adrenals are very well preserved considering the post mortem changes in other organs. There is no fat streaking of the glands. The kidneys show no abnormality. The umbilical arteries are very small and the lumina a mere slit. The mural architecture appears normal. The femoral marrow has a large number of fat spaces and shows no appreciable sign of reaction. Cytological detail is poor due to post mortem disintegration. Fresh blood was not obtained from this calf.

Serological Examination

A blood sample could not be obtained from the calf due to the time which elapsed between death and necropsy. Blood samples were taken from the dam and the sire of the calf and the following tests were carried out.

"Saline" Agglutination Tests	Result
R.B.C. Sire v Serum of Dam	Negative
R.B.C. Sire v Serum of Normal Cow	Negative

"Albumen" Agglutination Tests	Result
R.B.C. Sire v Serum of Dam	Negative
R.B.C. Sire v Serum of Normal Cow	Negative

"Indirect" Coombs' Test

A 10% suspension of the sire's erythrocytes was incubated at 37° C. for one hour with a 1/4 dilution of the serum of the dam. The cells were then washed three times in normal saline and resuspended at 3%.

	Result
R.B.C. Sire v R.a.Ox.g. 1a	Negative
" " " 1b	"
" " " 1c	"
" " " 1d	"
" " " 2a	"
" " " 2b	"
" " " 2c	"
" " " 2d	"
" " " 3a	"
" " " 3b	"
" " " 3c	"
" " " 3d	"

CASES CD/4 & CD/5

These were twin Ayrshire female calves, obtained at Ayr slaughterhouse presumably from a cow slaughtered as a parturition casualty. No history was available. No serological examinations were made since the dam and sire were not available and the calves had lain two days before examination. Since the calves were identical in almost all respects, they will be described together.

Post Mortem Appearances

External appearance. The calves were rather small in size, but were typical specimens of the condition. The heads were grossly enlarged, the abdomen and legs moderately so.

Internal appearance. The subcutaneous tissue and fascia had the usual "cod flesh" appearance; the muscles were pale and flabby. The mouth, tongue, pharynx, larynx, trachea, thymus and thyroid presented no abnormality. The pleurae were unthickened. The thoracic cavity contained several litres of transudate which appeared to have prevented the lungs from forming normally. The latter were foetal in type and the lobes were almost wholly discrete. The pericardium was thickened and contained about 100 cc. of straw coloured fluid. There was subepicardial gelatinous infiltration in

the transverse coronary grooves. The hearts presented the usual globular shape with left ventricular hypertrophy and right ventricular dilatation. They showed no other abnormal feature. The abdominal cavity contained three litres of straw coloured fluid. The liver (CD/4-600 gm.: CD/5-630 gm.). The organs appeared normal. The spleens (CD/4-45 gm.: CD/5-40 gm.) showed no microscopic lesions. The kidneys (CD/4-75 gm.: CD/5-90 gm.) showed no abnormality. The adrenal glands showed marked degenerative changes and were unsuitable for histological study. The umbilical arteries:- CD/4. The arteries were thick walled and large. They were contracted and contained no blood. CD/5. One artery was normal; the other was very small. The brain, meninges and calvarium appeared normal. Red marrow was present at the distal ends of all limbs. Owing to post mortem changes it was unsuitable for histological study.

Microscopic Appearances

The thyroid shows no abnormality. The cardiac muscle shows no excess glycogen deposit. The cardiac vasculature appears normal. The lungs are completely atelectatic. No extra-medullary haemopoiesis is seen. The liver in both cases shows many megakaryocytes scattered throughout the organ.

There are also small round-cell foci the nature of which is impossible to ascertain due to post mortem degeneration. The appearances are compatible with a slight degree of extra-medullary haemopoiesis. There is no excess of stainable iron or of glycogen. The spleen shows a profusion of megakaryocytes, often four or five to a high power field. Tests for stainable iron were negative. The kidneys show advanced post mortem tubular disintegration. In CD/4 there are a few small inter-tubular round cell foci. No iron can be demonstrated. The vasculature appears normal. The brain shows no abnormality

CASE CD/6

Calf. Brown and white Ayrshire bull.

History and clinical examination. The calf was born at full term; the delivery was unaided. It was able to stand and eat but movement was uncertain due to weakness of the hind limbs.

In appearance, although unmistakably an oedematous calf, it did not show the extreme features of the condition which have come to be regarded as characteristic (v. Case CD/1, Appendix). The face presented lateral swellings; the profile was not markedly convex and the intermandibular region was only

moderately affected. The eyelids were swollen, occluding the tear ducts, and causing constant lachrymation and scalding of the face. The abdomen was not grossly ascitic; this probably accounted for the unaided delivery.

The animal was housed in a large, well-bedded loose-box and given one gallon of milk daily. During the first week it appeared to thrive well, becoming very agile and showing avidity for food. The pulse rate was 100 per minute and the quality of the pulse was normal. Respiration was normal, but when the calf was made to run, breathlessness occurred after a short time.

In the second week the calf became less active and the oedema more marked. The hocks thickened, the prepuce became pendulous and the sublingual tissue dependent. The face became convex and the ears and lips developed swellings. In the third week, owing to rapid deterioration in the condition of the calf, an attempt was made to obtain more accurate clinical data. Due to intractability the calf had to be anaesthetised.

The procedures envisaged were (1) electrocardiography, (2) retinal examination for evidence of hypertension, (3) recordings of blood pressure. The last was not accomplished as the animal died under the anaesthetic.

Both corneal reflexes were normal, as was pupillary response to light. Ophthalmoscopic examination revealed no abnormality.

Other observations are shown in Table 4 and the electrocardio"Saline" Agglutination Tests

R.B.C. CD/6 v Serum Dam

The electrocardiogram suggests a left-axis deviation. An examination of the urine revealed Albumen .5 Esbach units but no other abnormality.

Blood examination. Two examinations were made in the first and third week. These are shown in Table 1.

Serological Examinations

Two serological examinations were carried out in the

Two serological examinations were carried out in the

first and third weeks respectively.

Blood samples were taken from the calf and from its sire

"Saline" Agglutination Tests	Result
R.B.C. CD/6 v Serum Dam	Negative
" " Serum of Normal Cow	"
R.B.C. Sire v Serum of Dam	"
" " Serum of Normal Cow	"

Table 4

Details of reaction of calf to anaesthetisation

Time p.m.	Heart rate	Anaesthesia	Position of apex beat	Jugular pulse
12.7	142	-	7th I.C. space	Present at inspiration
12.15	142	12 grams Pentothal intravenously	"	"
12.18	188	No pain, corneal or anal reflexes	"	More marked
1.30	160	19 grams Pentothal intravenously	"	"
1.45	Death			

"Albumen" Agglutination Tests (R.B.C.'s at 3% in 20% bovine albumen)	Result
R.B.C. CD/6 v Serum Dam	Negative
" " v Serum of Normal Cow	"
R.B.C. Sire v Serum Dam	"
" " v Serum of Normal Cow	"

Direct Coombs' Tests (R.B.C.'s at 3% in normal saline)	Result
R.B.C. CD/6 v R.a.Ox.g. 1a	Negative
" " v " 1b	"
" " v " 1c	"
" " v " 1d	"
" " v " 2a	"
" " v " 2b	"
" " v " 2c	"
" " v " 2d	"
" " v " 3a	"
" " v " 3b	"
" " v " 3c	"
" " v " 3d	"

Post Mortem Appearances

Weight - 96 lbs.

Internal appearances. The mouth, pharynx, larynx, thyroid,

trachea, thymus and bronchi were normal. The lungs (right 550 gm., left 350 gm.) were in the healthy fully expanded state. They were light pink with a few discrete atelectatic lobules. The pleurae were healthy and the pleural cavities did not contain excess fluid. The heart (400 gm.) was enlarged and globular. There was marked subepicardial gelatinous oedema in the transverse coronary grooves. The right ventricle was dilated and the wall uniformly 1 cm. thick. The left ventricular wall was uniformly 3 cm. thick. The foramen ovale was almost sealed; the valvular apparatus and great vessels were normal. The pericardium was healthy and the sac contained minimal fluid. The umbilicus was infiltrated with oedema which had masked, clinically, a sclerosing lesion of the umbilical ring. At this point, the umbilical vein was dilated, endophlebitic and packed with green gritty granules of inspissated pus. The abscess was walled off and apparently static, the proximal 4/5 of the vein being healthy. Adhesions were present between rumen and umbilicus. The alimentary tract was normal. The liver (1380 gm.) showed no abnormality. The spleen (160 gm.) was large and pale. It appeared healthy on cut surface. The kidneys (175 gm. each). There was no infiltration of the capsule. Both cortex and medulla had normal architecture. The peritoneal

cavity contained a minimal quantity of fluid. The brain (250 gm.) showed no deviation from the normal. There was pink marrow in the distal parts of radius and tibia.

Microscopic Appearances

The thyroid and thymus are normal in structure. The lungs - most bronchi contain casts of erythrocytes. The epithelium is intact. The mural capillaries are congested and tortuous and at many places there is frank intra-alveolar haemorrhage. This haemorrhagic consolidation in places affects whole lobules. There is no evidence of inflammatory change. The cardiac muscle shows hypertrophy; the muscle bundles are widely separated by spaces which probably contained fluid. The loose tissue in the transverse coronary grooves shows marked oedema; glycogen is not present in excess in the muscle cells. The vasculature is normal. The liver shows no abnormality. Iron and glycogen staining are negative. There is no erythroblastic reaction and no hypertensive change in the blood vessels. The spleen appears normal. No trace of iron deposition or erythrophagocytosis is seen. The adrenals are healthy. There is no fat streaking. The kidneys show separation of the tubules by oedema fluid. Signs of hypertension in glomeruli and afferent arterioles are

absent. The brain is normal in appearance. The marrow shows no hyperplasia. The walls of the umbilical arteries are becoming fibrosed. The lumen contains organising thrombus.

CASE 7

In this case a live dropsical calf was born but was shot and disposed of. Blood samples were taken from the sire and dam of the calf. The following tests were carried out.

"Saline" Agglutination Tests	Result
R.B.C. Sire and Serum of Dam	Negative
" " " " " Normal Cow	"

"Albumen" Agglutination Tests	Result
R.B.C. Sire and Serum of Dam	Negative
" " " " " Normal Cow	"

"Indirect" Coombs' Test

A 10% suspension of the sire's erythrocytes was incubated at 37° C. for one hour with ½ dilution of the serum of the dam. The cells were then washed three times in normal saline and resuspended at a concentration of 3% in normal saline.

					Result
R. B. C.	Sire	and	R. a. Ox. g.	1a	Negative
"	"	"	"	1b	"
"	"	"	"	1c	"
"	"	"	"	1d	"
"	"	"	"	2a	"
"	"	"	"	2b	"
"	"	"	"	2c	"
"	"	"	"	2d	"
"	"	"	"	3a	"
"	"	"	"	3b	"
"	"	"	"	3c	"
"	"	"	"	3d	"

APPENDIX 2

Details of the serological examinations made in an attempt to produce iso-immunisation of pregnancy experimentally.

COW 1

This animal received a course of four transfusions of blood from the donor bull. These were given at weekly intervals and were all by the intravenous route.

First week

A blood sample was taken before the first transfusion and the following tests were carried out:-

"Saline" Agglutination Test	Result
R.B.C. bull v. serum of cow	Negative

"Albumen" Agglutination Test	Result
R.B.C. bull v. serum of cow	Negative

"Indirect" Coombs' Test

A 10% saline suspension of bull's erythrocytes was incubated at 37° C. for one hour, with a one in four dilution of the serum of the dam. The cells were then washed three times in normal saline and re-suspended at 3% in normal saline.

	Result
R.B.C. bull v R.A.Cx.g. 1a	Negative
" " " 1b	"
" " " 1c	"
" " " 1d	"
" " " 2a	"

	Result
R.B.C. bull v R.A.Ox.g. 2b	Negative
" " " 2c	"
" " " 2d	"
" " " 3a	"
" " " 3b	"
" " " 3c	"
" " " 3d	"

Cow (1) then received 1,000 c.c. of bull's blood via the external abdominal vein.

Second week

Before the second transfusion the following tests were carried out:-

"Saline" Agglutination Test	Result
R.B.C. bull v serum of cow	Negative
"Albumen" Agglutination Test	Result
R.B.C. bull v serum of cow	Negative

"Indirect" Coombs' Test

This test was carried out as before. The results were negative. Cow (1) then received 1,000 c.c. of bull's blood via the external abdominal vein.

Third week

Before the third transfusion the following tests were carried out:-

"Saline" Agglutination Test	Result
R.B.C. bull v serum of cow	Negative
"Albumen" Agglutination Test	Result
R.B.C. bull v serum of cow	Negative

"Indirect" Coombs' Test

This test was carried out as before; the results were negative.

Cow (1) then received 200 c.c. via the external abdominal vein.

After a further two weeks the serum of the cow was again examined as follows:-

"Saline" Agglutination Test	Result
R.B.C. bull v serum of cow	Negative
"Albumen" Agglutination Test	Result
R.B.C. bull v serum of cow	Negative

"Indirect" Coombs' Test

This test was carried out as before; the results were negative.

At this time the serum of the cow was also tested for haemolysins against the bull R.B.C.'s. The results were negative.

During the experiment Cow (1) was mated to the bull. This service produced an apparently healthy bull calf which was disposed of by the farmer before a serological examination could be made.

COW 2

This animal received a course of four transfusions of blood from the donor bull. These were given at weekly intervals and were all by the intravenous route.

First week

A blood sample was taken before the first transfusion and the following tests were carried out:-

"Saline" Agglutination Test	Result
R.B.C. bull v serum of cow	Negative
"Albumen" Agglutination Test	Result
R.B.C. bull v serum of cow	Negative

"Indirect" Coombs' Test

This test was carried out as on Cow (1); the results were negative.

Cow (2) then received 1,000 c.c. of bull's blood via the external abdominal vein.

Second week

Before the second transfusion the following tests were carried out:-

"Saline" Agglutination Test	Result
R.B.C. bull v serum of cow	Negative
"Albumen" Agglutination Test	Result
R.B.C. bull v serum of cow	Negative

"Indirect" Coombs' Test

This test was carried out as before; the results were negative.

Cow (2) then received 200 c.c. of bull's blood via the external abdominal vein.

Third week

Before the third transfusion the following tests were carried out:-

"Saline" Agglutination Test	Result
R.B.C. bull v serum of cow	Negative
"Albumen" Agglutination Test	Result
R.B.C. bull v serum of cow	Negative

"Indirect" Coombs' Test

This test was carried out as before; the results were negative.

Cow (2) then received 200 c.c. of bull's blood via the

external abdominal vein.

Fourth week

Before the fourth transfusion the following tests were carried out:-

"Saline" Agglutination Test	Result
R.B.C. bull v serum of cow	Negative
"Albumen" Agglutination Test	Result
R.B.C. bull v serum of cow	Negative

"Indirect" Coombs' Test

This test was carried out as before; the results were negative.

Cow (2) then received 200 c.c. of bull's blood via the external abdominal vein.

After a further two weeks the serum of the cow was again examined as follows:-

"Saline" Agglutination Test	Result
R.B.C. bull v serum of cow	Negative
"Albumen" Agglutination Test	Result
R.B.C. bull v serum of cow	Negative

"Indirect" Coombs' Test

This test was carried out as before; the results were negative.

At this time the serum was also tested for haemolysins.

The results were negative.

During the experiment Cow (2) was mated to the bull. This service produced an apparently normal heifer calf. At three days of age the following tests were carried out on the calf's erythrocytes.

"Saline" Agglutination Test	Result
R.B.C. calf v serum of dam	Negative
"Albumen" Agglutination Test	**Result**
R.B.C. calf v serum of dam	Negative
"Direct" Coombs' Test	**Result**
R.B.C. calf v R.a.Ox.g. 1a	Negative
" " " 1b	"
" " " 1c	"
" " " 1d	"
" " " 2a	"
" " " 2b	"
" " " 2c	"
" " " 2d	"
" " " 3a	"
" " " 3b	"
" " " 3c	"
" " " 3d	"

COW 3

This animal received a course of four transfusions of blood from the donor bull. These were given at weekly intervals, one being given intravenously and the others intraperitoneally.

First week

A blood sample was taken before the first transfusion and the following tests were carried out:-

"Saline" Agglutination Test	Result
R.B.C. bull v serum of cow	Negative

"Albumen" Agglutination Test	Result
R.B.C. bull v serum of cow	Negative

"Indirect" Coombs' Test

This was carried out as before; the results were negative.

Cow (3) then received 1,000 c.c. of bull's blood via the external abdominal vein.

Second week

Before the second transfusion the following tests were carried out:-

"Saline" Agglutination Test	Result
R.B.C. bull v serum of cow	Negative

"Albumen" Agglutination Test	Result
R.B.C. bull v serum of cow	Negative

"Indirect" Coombs' Test

This was carried out as before; the results were negative.

Cow (3) then received 100 c.c. of bull's blood by the intraperitoneal route.

Third week

Before the third transfusion the following tests were carried out:-

"Saline" Agglutination Test	Result
R.B.C. bull v serum of cow	Negative

"Albumen" Agglutination Test	Result
R.B.C. bull v serum of cow	Negative

"Indirect" Coombs' Test

This was carried out as before; the results were negative.

Cow (3) then received 100 c.c. of bull's blood by the intraperitoneal route.

Fourth week

Before the fourth transfusion the following tests were carried out:-

"Saline" Agglutination Test	Result
R.B.C. bull v serum of cow	Negative
"Albumen" Agglutination Test	Result
R.B.C. bull v serum of cow	Negative

"Indirect" Coombs' Test

This was carried out as before; the results were negative.

Cow (3) then received 100 c.c. of bull's blood by the intraperitoneal route.

After a further two weeks the serum of the cow was again examined as follows:-

"Saline" Agglutination Test	Result
R.B.C. bull v serum of cow	Negative
"Albumen" Agglutination Test	Result
R.B.C. bull v serum of cow	Negative

"Indirect" Coombs' Test

This was carried out as before; the results were negative.

At this time the serum was also tested for haemolysins. The results were negative.

During the experiment Cow (3) was mated to the bull. This service produced an apparently healthy bull calf which was disposed of by the farmer before a serological examination could be made.

Part 2

A pathological and experimental study of the diseases of calves in the first six months of life.

INTRODUCTION

Sporadic cases of conditions affecting every system of the body have been reported in the literature of calf diseases, but the majority of papers are concerned with a few conditions of widespread occurrence which outweigh all others in incidence and economic importance.

These conditions and their relations to each other have not been accurately defined, but in general they fall into three main groups, which are (1) the disease complex known as "white scour" and calfhood septicaemia; (2) pneumonia; and (3) omphalophlebitis or "navel ill".

In a series such as the present one, the relative incidence of a given disease cannot be accurately calculated for several reasons. First, the most important diseases occur as enzootics and only a representative case, or a few cases, is submitted for laboratory diagnosis. Secondly, these important diseases, on account of the relative failure of therapeutics, have come to be regarded almost fatalistically by many farmers as inescapable in cattle breeding and not justifying the expense of veterinary consultation. Thirdly, veterinary surgeons tend to submit to the laboratory, unusual cases for their "interest" or "rarity" value.

In this study, the detailed results of 100 consecutive

necropsies are presented. These have been subdivided into groups on a pathological basis. Table 5 shows the different groups, and the number of cases in each. Experimental work is described under the appropriate groups.

Table 5

The numerical distribution of diseases in the 100 cases

Disease	No. of cases
Septicaemia and white scour	36
Pneumonia	52
"Navel ill"	9
Lead poisoning	2
Tuberculosis	2
Sulphonamide poisoning	1
Cystic kidneys	1
Peptic ulceration	4
Calf diphtheria	2
Interventricular septal defect	1
Hydrocephalus	1
Total	111

(Note: 11 cases show more than one lesion: a further 15 cases of the "white scour" group also show a varying degree of

pneumonia; for convenience of classification these have not been put in the primary pneumonia group.)

"WHITE SCOUR" AND "CALFHOOD SEPTICAEMIA"

INTRODUCTION

Under modern agricultural conditions the system of calf rearing is highly artificial. Detailed practice varies in different herds, but usually a calf is suckled on its dam for two days, and is then removed to a calf house where it is pail fed with the pooled milk of the herd. This system is used for two main reasons. First, the dam produces milk greatly in excess of the requirements of the calf and secondly, cows are fed according to their milk yield and artificial milking is necessary in order to determine the milk yield accurately. Calf rearing, therefore, must take second place to milk production for human consumption.

Under these conditions it is very common to find outbreaks of the disease known generally as white scour. It occurs in enzootic form and the clinical picture varies, but generally three main clinical types can be seen occurring in the same outbreak. These are (1) the calf is born suffering from diarrhoea; watery faeces may contaminate the foetal membranes at parturition. Death occurs within a few hours of birth. (2) The calf may be normal at one feeding time and dead at the next, without symptoms being noticed. Death usually occurs

from the second to the fifth day of life in this type.

(3) The affected animal suffers from typical "white scour". Different degrees of severity occur, but the faeces are usually greyish-white or canary yellow, are of watery consistence and have a foetid odour. Defecation appears to be involuntary. Apathy and dejection are common and the animal may become recumbent. Appetite is variable; sometimes there is complete anorexia but some cases will drink milk, even when recumbent, if they are supported over a pail. Febrile response varies, but unless there are secondary complications, the body temperature is not usually grossly elevated. This type of illness generally affects calves up to four or five weeks of age, but it may occur in older animals. In general it is confined to unweaned animals. Udall (1946) states that the older the calf, the less severe the diarrhoea; but such a generalisation cannot be applied to animals in the first five weeks of life.

Pneumonia is a recognised complication of scours, but due to the confusion which exists through the almost universal conception that calf pneumonia is a single entity, it is difficult to decide in many reports if the outbreak consists of pneumonia which is secondary to white scour, or diarrhoea which is secondary to pneumonia.

THE HISTORY OF THE DISEASE

This disease has been recognised by farmers for many years. Several old farmers state that they remember it from childhood when it was their duty to feed the calves. The first scientific investigation was made by Smith and his co-workers (Smith and Little 1922a; Smith and Little 1922b; Orcutt and Howe 1922). They regarded the disease as a B. coli septicaemia which occurred when the calf did not possess a passive immunity to the indigenous strains of this organism. They showed that a degree of passive immunity was conferred on the calf by antibodies contained in the colostrum of the dam; these antibodies are assimilated in the first 36 hours of life. They also demonstrated that the incidence of the disease was increased when colostrum was withheld from the calf during this critical period. They claimed that the feeding of colostrum or serum from the dam to a large measure prevented the disease. This latter claim has been proved incorrect in practice since, in the West of Scotland at least, where white scour is very prevalent, it is an almost universal practice to feed colostrum to the calf, one reason being that it is useless for anything else.

The hypothesis of Smith et al. that infection by B. coli is responsible for the disease has been widely accepted.

(Hutyra and Marek 1938; Cohrs 1942; Thorp et al. 1942; Lovell 1945; Udall 1946.)

Other workers attempted to show that the condition was primarily a Vitamin A deficiency. Thorp et al. (1942) described the findings in 25 necropsies on calves which were fed diets deficient in Vitamin A. The lower the Vitamin A levels in these calves, the severer was the diarrhoea. At post mortem they showed a relatively severe gastro-enteritis. They also described focal hepatitis and interstitial nephritis. Moore and Berry (1944) showed that the serum Vitamin A level of the calf rises when colostrum is fed but remains at the low level normally seen at birth if colostrum is withheld. Udall (1946) in one year conducted a large scale field trial on several thousand animals, using Vitamin A as a prophylactic and the incidence of white scour was not significantly lower than in other years. This vitamin has been widely used in Britain for prophylaxis and treatment without success.

Baker (1942) isolated a virus from an outbreak of scour which, when inoculated into healthy calves, caused mild diarrhoea. He was unable to reproduce the more severe and typical form of the disease.

Inglis (1953 and personal communication) stated that the diet of the dam may play a part in the pathogenesis of the

disease in calves. He has reported three main findings. (1) In the outbreaks investigated by him, the cows were being fed high protein diets in order to boost milk production. (2) On some farms he adjusted the relative proportions of the various high protein components of the diets. He found that when bean meal and coarse fish meal were fed in relatively large amounts to the dams, scouring was present in the calves. When these components were removed from the diet the scour enzootic cleared up. (3) In a series of small pilot experiments he has reproduced the disease by manipulating the diet components of the dam. The present author carried out the necropsies in the experimental calves used by Inglis. These corresponded exactly to natural cases.

There are few accurate descriptions of the morbid anatomical changes and there is no accurate account of the histological lesions present in this disease. The aim of the present work was to study the pathology of the disease as it occurs in the West of Scotland, and to see if the morphological changes indicated in any way the aetiological factors concerned.

An attempt was made to get as much information as possible about each calf from the veterinary surgeon and from the farmer. In many cases no information at all was obtained as the veterinary surgeon concerned had made no detailed clinical examination

or attempt to obtain accurate information on the epidemic.

A questionnaire was prepared which covered the following points:-

1. The age of the calf.
2. The date and time of death.
3. The duration of illness.
4. The rectal temperature.
5. The appetite.
6. The state of the faeces.
7. The presence or absence of pneumonic symptoms.
8. Other symptoms.
9. Whether or not colostrum was fed.
10. Whether other calves were ill.
11. The general standard of hygiene and state of the environment.

RESULTS

Of the 36 cases in this series, 32 came from outbreaks in which more than one animal was affected; the four remaining cases came from farms with a history of recurrent scour enzootics.

The relation of white scour to calfhood septicaemia

24 cases had illnesses lasting longer than one day, with scour as a symptom; 12 died without any symptoms being noticed in the interval between two feeds.

In all of the outbreaks in which calves died suddenly, there were also calves suffering from white scour or general malaise.

Table 6 shows the age incidence in the 24 cases in which the age at death is known. The seven cases of sudden death all occurred in the first week of life, while scour was observed in animals dying from the third day to the second week of life.

In 10 of the cases showing diarrhoea, the accurate duration of the illness was obtained. This is shown in Table 7.

Colostrum

In every case in which any information could be obtained, it was found that the calf had been given at least one, and usually more, feed of colostrum.

Table 6

The Age Incidence in 24 Cases

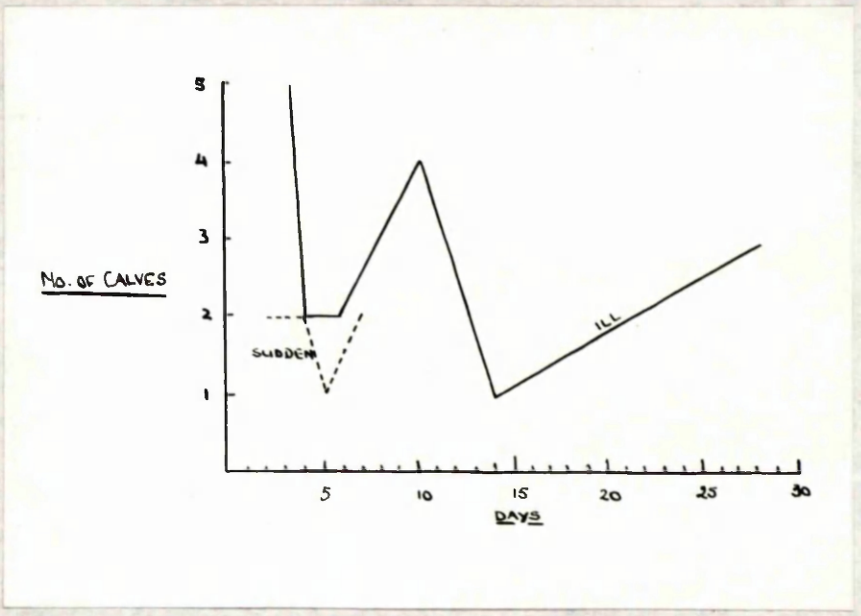
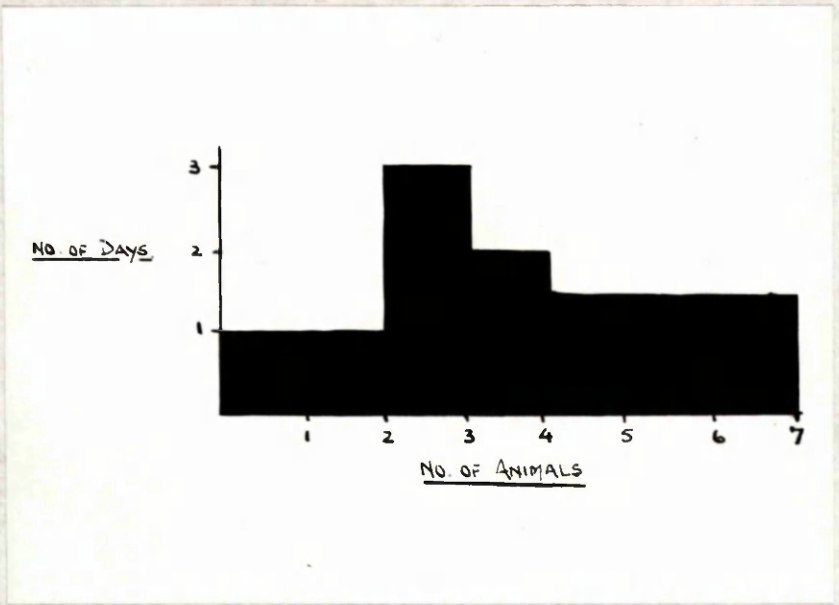


Table 7

The Duration of Illness in 10 Cases



THE PATHOLOGY OF THE DISEASE

The numerical distribution of lesions among the various organs is shown in Table 8.

Table 8

The numerical distribution of lesions among the various organs

No. of cases	36
Brain	11
Heart	10
Lungs	15
Liver	2
Spleen	18
Kidneys	3
Alimentary	-
Lymph nodes	2
Serosae	-
Umbilicus	1
No lesions	5

There were no frequent associations of groups of lesions to form pathological types of the disease. In five cases there were neither macroscopic nor microscopical lesions found. In two of these, clinical histories were furnished; one was ten days old and had been ill for three days showing scour; the other was 28 days old and had been ill for seven days without having scour. Both cases came from farms on which there was an enzootic of the disease.

The Central Nervous System

Of the 36 cases 11, or 30.4%, showed lesions of the brain. These were of two types, meningitis and subarachnoid haemorrhage, and they occurred both singly and in combination. Five showed meningitis alone, four showed subarachnoid haemorrhage alone, and two had a combination of the changes.

Subarachnoid haemorrhage

A clinical history was available in five of the six cases. Their ages were three, five, six, 14 and 28 days. Four died suddenly without symptoms; one was ill for a few days with scour before dying suddenly, and this calf also had meningitis.

The lesions were found on the occipital poles of both cerebral hemispheres, and over the dorsal aspect of the cerebellum.

The meninges were slightly raised and the sulci widened as the haemorrhages extended into the convolutions. Section of the areas involved showed that in two cases the haemorrhages extended deeply into the cortical substance.

Histologically, the subarachnoid space is filled with blood, and the arachnoid structure and vasculature obscured (Fig. 3). Even in those cases where deep penetration of the brain substance has occurred, there are no cellular or other reactive changes and the haemorrhage seems to have been a terminal event.

Meningitis

Seven cases showed meningitis; the available data and the degree of development of the lesions are summarised in Table 9.

At autopsy, the mild cases showed only a slight thickening and oedema of the arachnoid; this naked eye appearance was also present in cases which histologically showed no meningitis, and therefore it cannot be regarded as characteristic. Vascular congestion was present, but this also is seen in the absence of meningitis. In the severe cases the meninges were congested and grey in colour, but were completely opaque in only a few localised areas. The changes were most marked on the postero-lateral aspects of the cerebral hemispheres and

Table 9

A summary of the cases showing meningitis

Case	Age Days	Duration of illness	Torticollis	Degree of development of lesions
1	3	3 days	+	Moderate
2	10	5 days	+	Mild
3	3	Few hours	?	Mild
4	10	?	?	Mild
5	10	5 hours	+	Severe
6	10	?	+	Severe
7	2	Sudden death	-	Mild

over the cerebellum.

Histologically the earliest lesions seen are congestion of the arachnoid vessels, separation of connective tissue fibres by serous fluid and the presence of small numbers of polymorphs and macrophages in this fluid. This cellular reaction intensifies and in some areas the meningeal structure is largely replaced by a band of closely packed cells, the majority being polymorphs, although macrophages are abundant. Necrosis and fibrin deposition are not features. The exudate extends into the sulci. In the severe cases there is a marginal

encephalitis (Fig. 4). The inflammatory cells are present diffusely in the grey matter immediately subjacent to the meninges, and as perivascular cuffs extending quite deeply into the brain substance. In no case has the process become frankly suppurative.

Both of the cases which are associated with subarachnoid haemorrhages show a well developed meningitis.

Four of the cases showed torticollis in life but this symptom has also been seen in recumbent calves which suffered from white scour, but did not show meningitis.

In four of the cases only B. coli was isolated from the heart's blood.

Heart

Ten cases showed heart lesions. Seven of these showed subepicardial and subendocardial petechial haemorrhages in the region of the mitral and tricuspid valves. This is of no pathological significance, and is often seen in normal calves. Five cases showed replacement of the normal firm fat of the transverse coronary groove with gelatinous fat. This lesion is not specific, and is often seen in calves which have been ill for a day or two.

The lungs

15 of the 36 cases (41.3%) showed pulmonary lesions. The latter ranged from focal changes, seen only on microscopical examination, to pneumonias of lobar dimensions. Occasionally it is difficult to decide if an outbreak of disease in calves is primarily pneumonia or septicaemia, since diarrhoea occurs frequently in endemics of pneumonia and vice versa. All of the cases recorded here came from outbreaks which were obviously septicaemic in nature.

The age of the calf and the duration of illness was known in six cases. These data are summarised in Table 10.

Four main types of lung lesion were found; focal lesions (six cases); diffuse interstitial cellular increase (three cases); early diffuse pneumonia (four cases); fully developed diffuse pneumonia (two cases).

Focal lesions. These lesions are found both alone and in conjunction with the two other types of lung lesion. They appear to be among the most constant lesions found in calfhood septicaemia. They consist of a small area of necrosis in the wall of an alveolus and associated with the necrosis is a focal increase in polymorphs and septal cells.

The alveolar wall is usually thickened at this point. Bacteria can sometimes be demonstrated in the lesions and this

Table 10

The ages of, duration of illness in, and type of pulmonary lesion found in, six calves which died of calfhood septicaemia.

Case	Age Days	Duration of illness	Type of lesion
1	6	4 days	Focal
2	2	Sudden death	Focal
3	?	?	Early diffuse
4	7	Sudden death	Focal
5	14	?	Diffuse
6	10	4 days	Early diffuse

suggests the start of pulmonary localisation of the infective agent from the bloodstream. The lesions vary widely in number, from case to case, but they can be found in cases which show no other lesion in the body (Fig. 5).

The lung in these cases usually shows marked capillary engorgement, and often has areas of partial or complete collapse (Fig. 5). The bronchi and bronchioles are unaffected.

Diffuse interstitial infiltration. The salient feature of

this type is a diffuse increase in cellularity of the alveolar interstitium (Fig. 6). The cells are mainly neutrophil polymorphs but there appears to be also an increase in the numbers of septal cells. The alveolar walls are thickened both by cells and by capillary congestion, but inflammatory cells are absent from the lumina of both the alveoli and bronchioles. Again, no macroscopic evidence of this change was found.

Early pneumonia. In the four cases showing this lesion there is a diffuse polymorph increase in the alveolar walls, together with many areas showing polymorphs present in varying numbers in the alveoli (Fig. 7). There are no areas of necrosis. The polymorphs appear healthy as judged by the clarity of nuclear detail, and the infiltration is more pronounced in the alveoli than in the bronchial tree. Macrophages are few in number and there is no fibrin deposition.

Frank pneumonia. At autopsy the two cases of this type showed a diffuse pneumonia involving most of the lung. The volume of each lobe was increased, and the tissue was congested and friable. There did not appear to be peribronchial localisation of the inflammatory changes and when pressure was applied to the cut surface of the lobes, there was a diffuse exudation of dark pink fluid. The main bronchi contained frothy white

fluid, but no mucoid pus. The broncho-mediastinal nodes were congested and slightly enlarged.

Microscopically, the pulmonary capillaries are very congested and this accounts for the thickened alveolar walls; there is no marked cellular infiltrate into the walls. The alveoli are filled with polymorphs but there is neither fibrin deposition nor obvious necrosis. This change is quite diffuse throughout the individual lobules. The changes found in the specific pneumonias described later are absent; there is no epithelialisation, giant-cell formation or septal lymphatic dilatation. The bronchiolar lumina contain polymorphs and here again there is no necrotic debris. The bronchial epithelium is intact and there are no inflammatory changes in the walls.

The liver

Structural changes in the liver ~~was~~ were found in only two cases. They were not visible to the naked eye. Microscopically these are multiple small foci of necrosis scattered throughout the organ with no specific anatomical localisation. They are sublobular in size and consist of small areas of liquefactive necrosis of both hepatic cells and sinusoids.

The spleen

18 of the 36 cases showed splenic lesions. This was the commonest lesion found, and was often the only one. The organ was enlarged and thickened, especially in its dorsal part. On section, the pulp was deeply congested and almost fluid. Histologically a few cases show focal necrosis and aggregates of neutrophil leucocytes; the increased size of the organ is related only to the severe congestion.

The kidneys

Renal lesions, apart from congestion, were found in only three cases. These changes are microscopical and consist of eosinophilic casts in the renal tubules, the presence in some of these casts of clumps of pyknotic nuclei, and severe cloudy swelling of the tubular epithelium.

The alimentary system

No lesions of the stomach or intestines were found.

The mesenteric lymph nodes

Congestion of the mesenteric nodes was seen in two cases. There were no inflammatory changes present.

The umbilicus

A small abscess of the external umbilical ring was found

in one case. The gritty inspissated pus was surrounded by a thick fibrous wall. The process did not extend to the umbilical vein which was fibrosed in the normal way.

DISCUSSION

The purpose of this work was to describe the pathology of "white scour" and to see if this indicated in any way the cause of the disease. It has shown some of the ways in which the animals die, and has suggested the pathogenesis of the pneumonia which frequently is a sequel to the diarrhoea. It has not shed light in any way on the primary etiological factors.

The information obtained about the age groups affected, duration of illness, etc., was not a primary consideration in this work, but several interesting facts emerged. In every case in which calves died after a very short or unobserved illness, i.e. so-called "calf septicaemia", there were other calves on the same farm suffering from "white scour". This, together with the fact that the lesions were indistinguishable from the "white scour" cases, lends support to the view that "calf septicaemia" is one form, and "white scour" another of a single entity. 80% of the cases in which the age at death was known, died in the first 10 days of life. It was evident throughout

this investigation that the feeding of colostrum was having no absolute effect in preventing scour. It is possible that the number of outbreaks and the death rate would be increased if colostrum was not given, but no evidence to support this was obtained since all of the farmers were feeding it to the newborn calves.

In this series, meningitis was found in seven cases out of 36 (19%) and was the third most common lesion. Udall (1935) has recorded a case of purulent meningitis in a calf but this was associated with extension of a septic phlebitis into the parieto-temporal canal and is of a different nature from my cases, the latter having no obvious primary suppurative lesion. Johanssen (1943) in a review of 98 cases of meningitis found 82 of these to be associated with pyaemia and 16 with septicaemia. His 98 cases represented 17% of a series of calf autopsies, but he does not give the relative percentages in his series of septicaemia and pyaemia cases and these two conditions differ fundamentally from each other.

Neither of these authors mentions subarachnoid haemorrhage. This occurred in 16.6% of my septicaemia cases and it appears to be an important cause of sudden death in the calf.

10 of my cases showed subepicardial petechial haemorrhages. This lesion was present in many of the normal hearts examined

in an abattoir, and is of no significance.

Lung lesions were present in 41.8% of the calves autopsied. These ranged from focal necroses with slight cellular reaction to diffuse pneumonias. Some showed a diffuse polymorph infiltration of the alveolar walls and others mild diffuse pneumonia. It is possible that the pneumonia often associated with scour is an integral part of the disease and not merely a secondary pneumonia in a debilitated animal. The focal necroses may be a development of a septicaemia, the lesion then progressing through diffuse infiltration of the alveolar walls to invasion of the alveoli by leukocytes. It is interesting to note that none of the "atypical" or "specific" types of pneumonia which are described later, were found in relation to white scour outbreaks.

A "septicaemic" spleen was found in 50% of the cases. The organ was enlarged, and the cut surface was bulging and pulpy. No specific lesions were found.

There was no evidence of gastro-enteritis in any of the cases, and in only two was there congestion of the mesenteric lymph nodes. This does not conform to the usual account given of this condition, but it is thought that the post mortem discolouration which is so rapid in onset in the gut of calves, is frequently mistaken for inflammation. The same applies to

the so-called lymphadenitis.

There was no relationship between "white scour" and "navel ill", or suppurative omphalophlebitis. The latter condition only occurs sporadically in the South West of Scotland, due to the good hygienic conditions now almost universal in cow byres. Hutyra et al. (1938) drew no sharp line of division and indicated that under certain conditions "navel ill" might be responsible for septicaemia. This factor does not operate in this area.

A careful histological search was made in many cases for inclusion bodies which might indicate a viral etiology. None was found.

A consideration of these lesions shows that there are no absolute pathological diagnostic criteria for "white scour".

In many cases it must be impossible to differentiate on lesions alone between calf septicaemia and such conditions as acute lead poisoning and hypomagnesaemia. These latter conditions show no lesions at autopsy.

CALF PNEUMONIA AND RELATED PULMONARY DISEASE

INTRODUCTION

Calf pneumonia is one of the most important diseases of cattle in Britain. It is impossible to make an accurate assessment of the loss to the agricultural industry but it is certainly in excess of £1,000,000 per year. The main difficulty in arriving at an accurate estimate is the high degree of morbidity as distinct from mortality, with the concomitant loss of condition of affected calves, the impairment of food utilisation, the delaying of maturity and the residue of badly thriving animals. Mortality is also high, but this appears to vary markedly from year to year and from farm to farm. It is not uncommon to find a farmer losing 50% of his calves from a severe outbreak of pneumonia and mortality rates of 100% have been seen on more than one occasion. It is not proposed to deal with all types of pneumonia in this work. A large part of the morbidity and mortality of calf pneumonia is associated with the lung changes which accompany or are a sequel of, infestation with the nematode lungworm Dictyocaulus viviparus. The larvae of this worm are ingested from pasture and therefore calves do not suffer from parasitic bronchitis until they start to graze; accordingly they are not included here.

Pneumonias contracted while the calves are housed are, however, a serious problem, and probably account for approximately 40% of calf morbidity.

THE HISTORY OF THE DISEASE

The detailed study of calf pneumonia began with the studies by Smith (1921) and by Carpenter and Gillman (1921). Both of these contributions are concerned with bronchopneumonia, it being assumed that this is the main type of lesion found. Smith (1921) considered that the micro-organism primarily responsible was Actinobacillus actinoides. He isolated this bacillus in pure culture from several field cases of pneumonia and by injecting these cultures into five calves by the intratracheal route, he produced, in three cases small circumscribed areas of necrosis in the lungs. He was unable to produce, by this method, a confluent bronchopneumonia similar to the natural cases. From a study of a small number of field cases and from the small amount of experimental work described above, he considered that the pathogenesis of calf pneumonia is as follows. A primary necrotic focus is established in the lung parenchyma by A. actinoides. This becomes invaded by mononuclear cells and at the same time the inflammatory process spreads to involve the bronchi and bronchioles. Later there is an invasion of the

consolidated areas by polymorphonuclear leukocytes and an infiltration of plasma cells into the mucosa of the bronchi. He thought that all of his cases were manifestations of a single disease process, the series of changes being sequels of infection by A. actinoides.

Carpenter and Gillman (1921) reviewed the previous observations on the etiology of calf pneumonia. They stated that the following organisms had been incriminated. Corynebacterium pyogenes, Bacterium coli, Streptococcus pyogenes, Pseudomonas pyocyaneus, Brucella abortus, Staphylococci and various types of Pasteurellae.

They divided calf pneumonia into two groups on a rough clinical and pathological basis. (1) The animals are born weak, soon become febrile and die after a period ranging from a few hours to a few days. The lungs show congestion, mild oedema, and bronchiolitis. (2) The disease runs a more chronic course with a mucopurulent nasal discharge, decreased appetite, emaciation and a normal rectal temperature. Respiratory disturbance is not evident until the terminal phases. The lesion consists of infiltration of bronchi and alveoli with fibrin, polymorphs and desquamated cells. Some cases show abscess formation with or without pleurisy. No detailed pathological descriptions were given by these workers.

They attempted to transmit the disease by intra-nasal and intra-tracheal injections of tracheal pus, saline suspensions of pneumonic lung tissue and by cultures of bacteria isolated from field cases. In 22 experimental calves, they produced two cases of definite pneumonia and four doubtful cases. Three of their six controls also contracted pneumonia. Their positive transmissions were obtained by each of the three methods outlined above.

Scholl (1935) thought that maternal infection with Brucella abortus was responsible for some calf pneumonia. He recovered this organism from 25 of 69 cases; 32 of the latter came from cows which showed positive agglutination tests to Br. abortus.

Lamont and Kerr (1939) transmitted a pneumonia serially for three passages with a cell-free filtrate. This material was obtained from field cases from which they also cultured Coryne. pyogenes and an organism similar to Haemophilus influenzae. They did not describe the pathology of the lesions.

Sanders (1940), in a large-scale experiment, was unable to transmit "enzootic calf pneumonia" with bacterial cultures or lung suspensions from field cases.

A group of American workers (Thorp and Hallman 1939;

Thorp, Shigley and Farrel 1942; Langham, Thorp, Ingle and Scholl, 1942; Shigley and Thorp, 1943) described an acute bronchopneumonia which was associated with two types of organisms (1) Gram negative non-motile rods, and (2) an organism related to Haemophilus influenzae. Thorp et al. (1942) attempted to transmit the pneumonia with pure cultures of these bacteria but stated that their results were inconclusive and suggested that a virus might be the primary agent.

Tutt (1941) reported the isolation of Staph. aureus in pure culture from one outbreak of calf pneumonia.

Baker (1942) isolated a virus from calves which produced on inoculation into calves, an enteritis followed by a relatively mild bronchopneumonia. The condition was acute and afebrile and had a constant syndrome on passage. The virus passed a Berkefeld "N" filter, it could infect mice and it stimulated the production of a neutralising antibody. This condition is known as pneumoenteritis in America. Baker did not give a description of the pathology of the lesion.

Blakemore (1945), Gunning (1946) and Levi and Cotchin (1950) recorded the isolation of A. actinoides from field cases in Britain. Levi and Cotchin were uncertain if this organism was primarily responsible and suggested a virus causation. They gave a short description of the pathology of their cases

but did not attempt to classify them into pneumonic types.

Gallo and Calderan (1951) described a virus isolated from calves capable of being transmitted to calves and mice but not to chick embryos. The field cases from which the virus was recovered were said to be "pneumo-enteritis". No pathological details were given.

Jennings and Glover (1952) reported the passage of a pneumonia to 18 out of 21 calves. In two cases the pneumonia was produced by combined intranasal, intravenous and intraturbinate inoculation of cell free filtrates of pneumonic calf lung. In one case the filtrate was inoculated by the intravenous route only. In two cases inoculated with sterile suspensions of lung tissue, they recovered Coryne. pyogenes. They did not recover A. actinoides from any of their cases. They were unable to infect mice or chick embryos with their material.

Clinically the disease was a febrile pneumo-enteritis. The lesions varied from areas of lobular collapse to extensive suppuration and consolidation. The series of changes seen in the lungs was as follows. (a) Congestion of the alveolar capillaries, oedema of the interlobular septa and lobular collapse. (b) Thickening of the alveolar walls by macrophages and polymorphs. (c) Invasion of the alveolar spaces by macrophages and an exudate relatively free of fibrin. (d) Suppuration of

the affected areas. There was also a marked congestion of the turbinate bones. The pneumonia was usually of a low grade type and was accompanied by enteritis.

Watt (1952) isolated an organism of the Haemophilus group from field cases of calf pneumonia. He induced pneumonia in a calf by nasal instillation of this organism in combination with a filterable agent from pneumonic calf lung which had been passaged serially through mice.

Several conclusions can be drawn from this body of work.
(a) No large scale experiment has been undertaken to prove conclusively that any one organism is primarily responsible for any one type of calf pneumonia.
(b) There is an increasing amount of evidence that viruses, probably several in number, are concerned in the production of some types of calf pneumonia.
(c) No sound criteria have been established for the recognition of different types of calf pneumonia from either the etiological or morphological point of view. It is felt that much of the confusion which exists in this field results from considering calf pneumonia as a single entity, which it certainly is not.

The major purpose of this work is to suggest a clarification of some of these pneumonias based on a histo-pathological basis. It is fully realised that these types may not

be completely distinct and that different agents may produce similar changes; however the structural changes described below show so many striking differences from case to case, that any classification must of necessity take account of them.

It is also felt that some emphasis must be placed on certain sequels of the acute pneumonias, e.g. bronchiectasis and pulmonary abscesses since these are often presented to the practising veterinary surgeon as individual clinical cases divorced from outbreaks of pneumonia. A fairly extensive experience of necropsies of adult bovines has convinced the present author that these residual lesions are one of the main causes of that "enigma" of veterinary practice, the "wasting bovine".

RESULTS

52 cases were studied in which the major factor concerned in the illness was pneumonia. As has already been stated, 15 cases included in the "white scour" group also showed pulmonary lesions.

The various types of pneumonia are dealt with individually on the following pages.

Table 11

A summary of the pulmonary changes observed

Type of lesion	No. of cases
Bronchopneumonia	
(a) simple	10
(b) acute necrotising	7
Interstitial pneumonia	6
Inclusion body pneumonia	3
Other epithelialising pneumonias	5
Aspergillosis	2
Cuffing pneumonia	13
Pulmonary abscesses	3
Bronchiectasis	3
Total	52

PNEUMONIA ASSOCIATED WITH "WHITE SCOUR"

This has been dealt with in detail in the section on white scour. While the lesions seen in my cases suggest that one type of pneumonia may be an integral part of the septicaemia syndrome, it is almost certain that other types may complicate the disease especially if there is a concurrent pneumonia outbreak on the farm.

BRONCHOPNEUMONIA

This term is applied here to all pneumonias which appear to originate in a bronchitis or bronchiolitis with subsequent spread to surrounding alveoli via the air passages. Only "typical" cases are included, i.e. those showing acute inflammatory changes of the usual pattern; those associated with proliferative changes such as peribronchial lymphoid hyperplasia or epithelialisation of alveoli, although appearing to start in bronchi or bronchioles, are described under separate headings.

(a) Acute purulent bronchopneumonia

10 out of 54 cases showed this lesion. The individual variation in morphology found in this group possibly indicates that more than one type exists; and it is also possible that there is no sharp line of division between some of the cases in this group and those of the next, acute necrotising bronchopneumonia.

In general the factors which the cases in this group have in common are: obvious initial localisation of the acute inflammatory process to the bronchi and peribronchial area; no widespread necrosis of the bronchial structures; little evidence of origin in the vascular channels (c.f. interstitial

pneumonia); the inflammatory changes are of the normal exudative type.

The cases may be subdivided into three types.

Type 1. (Three cases; only one will be described.)

Subject. Ayrshire heifer calf aged eight weeks.

History. No clinical history was available. The farmer noticed diarrhoea only a few hours before death occurred.

Post mortem findings. The lesions were confined to the lungs. The greater part of both lungs was congested. The left lung showed consolidation of the posterior border of the apical lobe and complete consolidation of the cardiac and diaphragmatic lobes. The hepatised tissue was slightly increased in volume, dark brown, of friable consistency and selected portions sank in water. The major bronchi in this part did not contain pus but only white frothy fluid. Pus could be expressed from the bronchioles. The right lung showed only scattered consolidation of lobules; most of the parenchyma was crepitant and air-containing. The broncho-mediastinal lymph nodes were congested but were not appreciably enlarged; the normal pattern of cortex and medulla could be seen.

Microscopic appearances. 1. Left lung - apical lobe. The bronchi are normal and most of the bronchioles are free of exudate. The alveolar capillaries are very congested and

several small intra-alveolar haemorrhages are present. A few polymorphs are present in most of the alveoli but fibrin deposition is absent. Several foci of consolidation are scattered throughout the lobe; in these areas both the bronchioles and surrounding alveoli are filled with polymorphs. Necrosis is not a feature.

2. Left lung - cardiac lobe. The larger bronchi occasionally have clumps of polymorphs pressed against their lining epithelium, but the latter is intact, normal in type and shows no infiltration. The rest of the bronchial wall is normal. The smaller bronchi and respiratory bronchioles are completely plugged by inflammatory cells (Fig. 8).

The latter are mainly polymorphs with occasional mononuclear macrophages. The cell morphology is clear and fibrin and necrotic debris are absent. The epithelium is intact and the wall itself is not invaded by inflammatory cells. Inclusion bodies cannot be seen in the bronchial epithelium.

The alveolar capillaries are congested and there are many small areas of haemorrhage involving from 10 to 30 alveoli. Congestive collapse is not a feature. Although almost every lobule shows inflammatory change, the degree of the latter varies from lobule to lobule. In some, every alveolus is packed with polymorphs; in others, only the bronchioles and

peribronchial alveoli are heavily infiltrated, there being a much lighter cellular concentration in the peripheral areas. In some lobules, alveolar oedema is well marked, and the polymorphs appear to be spreading via this fluid. Only occasional macrophages are present. These have, in H. & E. staining, a pale pink homogeneous cytoplasm and a large oval coarsely reticulated nucleus. In a few places there are alveoli filled with large foamy macrophages. At no place in the lobe is there necrosis or suppurative softening. A search was made for both eosinophilic and basophilic intra-cytoplasmic and intra-nuclear inclusion bodies without success.

Right lung - diaphragmatic lobe. There is no inflammatory change present in either bronchi or alveoli. A few lobules show congestion and collapse of alveoli with a few macrophages in the collapsed lumina.

The broncho-mediastinal nodes show only congestion and some sinus catarrh.

In the other two cases showing this type, consolidation involved in one, the right apical and both cardiac lobes, and in the other, all of the anterior lobes.

Type 2. (Four cases)

Subjects. Ayrshire calves, females, of unknown age but they appeared to be unweaned (judged by size and relative degree of

development of the rumen and the abomasum.)

These cases all came from the same herd and showed the same clinical syndrome. The latter, and the pathological picture, was similar to that described by Jennings and Glover (1952). The calves had been febrile and had a marked catarrhal nasal discharge and some diarrhoea. The disease ran a relatively short course and spread fairly rapidly through the calf herd only the weakest animals succumbing. In two cases the carcase was obtained and in the other two only the thorax was submitted.

Post mortem findings. In the two cases in which they were present, the turbinate bones were congested. The lungs were normal in volume and consistency, apart from some mottling due to patchy congestion and collapse. On the cut surface, a few of the bronchi exuded pus. The lungs were mildly oedematous. It was impossible to make a diagnosis of pneumonia at autopsy due to the absence of macroscopic consolidation.

Microscopic appearances. The pneumonia in these cases appears histologically to be a mild lesion and it is difficult to reconcile the death of the calves with the degree of obliteration of air space and the damage to the lung parenchyma.

There is inflammatory exudate present in many of the bronchi and bronchioles but few of these are plugged by it. The

exudate is composed of roughly equal proportions of polymorphs and mononuclear phagocytes. There is little necrotic debris or fibrin present. The alveoli show some mural congestion but there are usually only a few inflammatory cells in each alveolus; many alveoli show none. There is no evidence of any hyperplastic change. Scattered lobules show complete or partial collapse. In these areas the capillaries are congested but there is no inflammatory reaction; there does not appear to be bronchial obstruction or any other change causing the collapse. Such areas are quite common in the lungs of calves dying from all causes but appear to be more numerous in this type of pneumonia.

Lesions which might have caused death were not found in any other organ.

Type 3. (Three cases, one only described)

Subject. Ayrshire calf, female, aged four weeks.

History. Little clinical history was available. Most of the calves on the farm were affected and several had died in the preceeding fortnight. Some of the calves were febrile, others not. Some had a muco-purulent nasal discharge. The appetite was capricious, and there was marked loss of condition. The duration of illness in this particular case was unknown.

Post mortem findings. Lesions were confined to the respiratory tract. The apical and cardiac lobes of both sides were

consolidated as was a strip two inches wide on the anterior border of both diaphragmatic lobes. The intermediate lobe showed consolidation of its anterior half. There was a sharp line of demarcation, corresponding to the borders of several lobules, between apparently healthy and diseased tissue. The consolidated tissue was deep red and was of considerably greater volume than normal. The lobe edges were tense and rounded. The tissue was very friable and crumbled readily between the fingers. Lobular delineation could be seen clearly, but there was no obvious necrosis of the septal tissues. On section, the parenchymal tissue bulged from the cut surface. When pressure was applied plugs of viscid muco-pus projected from bronchi and bronchioles, and oedema fluid flowed freely from the alveoli. Muco-pus was present in all of the anterior lobe bronchi, in the trachea and in the nasal passages; it was irregular in distribution. The turbinates appeared to be normal. The hilar lymph nodes were mildly congested and only slightly enlarged.

Microscopic appearances. The lesions are mainly confined to the areas which appeared affected at autopsy. Two main types of lesion are present and these are of well marked lobular distribution.

(a) The bronchioles are almost or completely unaffected. The alveolar walls are thickened by tortuous congested capillaries.

The alveolar lumina are filled by homogenous palely eosinophilic precipitated oedema fluid. Fibrin deposition is scanty although a few strands occur occasionally in the oedema fluid. The only cellular reaction is the occasional presence of a few macrophages in the alveoli. These cells have a large round or oval coarsely reticulated nucleus which is usually excentrically placed. The cytoplasm is eosinophilic and usually homogeneous, fatty vacuolation or phagocytosed debris being unusual.

(b) These lobules are in the majority and show the lesions characteristic of this type of pneumonia. The individual lobule shows several distinct zones and there is no doubt that the primary and major seat of change is in the bronchiolar area. The bronchiole is plugged with an exudate mainly cellular in character. The cells are largely polymorphs but many macrophages are also present. Nuclear outline and cytoplasmic detail are usually clearly preserved, and necrotic debris and fibrin minimal in amount. The bronchiolar epithelial lining is intact, and the cellular morphology normal. In many places the cilia can be clearly seen. The bronchiolar walls show a varying degree of congestion but cellular inflammatory phenomena are absent.

In the immediate peribronchial area the alveoli are packed with an exudate similar to that in the bronchi. Necrosis is

generally absent, but in some places there is fairly heavy fibrin deposition. The mural capillaries are tortuous and congested. In the middle and peripheral "zones" of the lobule, the cellular reaction is much less intense and is largely mononuclear in character. These macrophages are similar to those described above, their main characteristic being the homogeneous nature of the cytoplasm. Binucleate and large multinucleated types are common (Figs. 9 and 10). (These figures are taken from another case showing some of the same lesions: vide page 135 Case 1.) In this area there is often precipitated oedema fluid with deposition of fine fibrin strands. The capillaries here too, are intensely congested.

The inter-lobular septa are usually normal but in some places there is dilation of the septal lymphatics and oedema of the stroma. In a few areas, this process has advanced to the stage of acute interstitial pneumonia. This lesion is described fully in the section on interstitial pneumonia; in this context it is interpretated as indicating that intra-pulmonary vascular spread is commencing from a lesion primarily situated in the bronchi.

Sections stained by eosin-phloxine-tartrazine, Giemsa and Machiavello's and Castaneda's methods, failed to reveal the presence of either eosinophilic or basophilic intra-cytoplasmic

or intra-nuclear inclusion bodies.

Sections of the hilar lymph nodes show acute reactive changes in the cortex and the presence of many macrophages, similar to those found in the alveoli, in the medullary sinuses. There is no acute inflammatory reaction.

(b) Acute necrotising purulent bronchopneumonia

Seven of the 52 cases showed this lesion. The lesion which they have in common is an acute bronchopneumonia in which most of the bronchi show severe damage to their walls. This is in marked contrast to the types described above where the bronchial walls were in a remarkably good state of preservation. Another common accompaniment was the extension of the inflammatory process to involve the pleura overlying the affected lung. One case has been selected for detailed description.

Case 1

Subject. Ayrshire calf, male, aged 14 days.

History. The exact duration of illness was not known, but was thought to have been about a week. When the calf was seen by the veterinary surgeon the rectal temperature was 105.5°, there was complete anorexia and copious yellow mucoid faeces were passed. There was a purulent nasal discharge, the animal was dyspnoeic, coughed frequently and showed pain when pressure was

applied to the wall of the thorax. The calf was given sulphonamide drugs but died the next day.

Post mortem findings. The nose, pharynx and trachea were normal, and did not contain pus. There was bilateral empyema and many fibrinous adhesions were present between the visceral and parietal pleurae. The pericardial sac contained 60 ml. of sero-haemorrhagic fluids; there was no fibrinous pericarditis.

The left lung. A sharp vertical line divided the anterior and posterior parts of the apical lobe. The anterior part was relatively normal, contained air and was crepitant to feel. The posterior part was completely consolidated but showed no evidence of abscess formation. The bronchi exuded frothy white fluid. The cardiac lobe was completely consolidated and appeared superficially to be studded with small abscesses. On section however, these were seen to be bronchi, some of which were yellow, necrotic and crumbly while others were filled with pus. Some of these had ruptured on to the pleura between the cardiac and diaphragmatic lobes, and had caused complete fibrinous adhesions between the lobes. The diaphragmatic lobe showed a strip of air-containing tissue about one inch wide along its dorsal border. The remainder of the lobe resembled the cardiac lobe.

The right lung. This was completely consolidated and was

similar in appearance to the left cardiac lobe. An abscess about three inches in diameter was present in the posterior part of the lobe, and had ruptured into the pleural cavity on the diaphragmatic surface. This was probably responsible for the empyema.

Microscopic appearances. The majority of the lobules in the affected part show similar lesions. The degree of affection of the bronchi varies. Their lumina are completely filled with a mixture of necrotic debris and inflammatory cells. In some no cytological detail can be determined (Fig. 11) while in others desquamated epithelial cells, macrophages and polymorphs can be seen amongst the granular eosinophilic detritus (Fig. 12). The degree of damage to the bronchial wall also varies but in most cases the epithelium has either disappeared (Fig. 11) or only its necrotic remains are left (Fig. 12). The bronchial and bronchiolar walls show severe damage; sometimes the fibro-muscular wall encloses the necrotic luminar material while in other cases no trace of wall remains. Immediately surrounding this central bronchial zone, the alveoli are heavily infiltrated with polymorphs and macrophages. At the inner part of this area necrosis has supervened on the inflammatory cells leaving fused mass of deeply staining basophilic pyknotic nuclei. In the outer part there is relatively

good cytological morphology. The remainder of the lobule shows intense congestion of the alveolar capillaries and a cytological picture which varies from lobule to lobule. The majority however show a fairly heavy infiltration by macrophages. These cells have a homogeneous eosinophilic cytoplasm and coarsely reticulated round or oval nuclei. The size and shape of these cells varies and some are large and contain 20 to 30 nuclei usually arranged peripherally at one side while others have only one or two nuclei. Fibrin varies from a few strands to complete filling of alveoli but deposition of this substance is not a marked feature. In some lobules the necrotic central bronchiole is not surrounded by inflamed alveoli.

The pleura over consolidated areas is grossly thickened. Its outer surface is coated by a layer of fibrin; immediately subjacent to this the pleural mesothelial cells can be seen as a row of swollen cuboidal cells with large vesicular nuclei, often with more than one per cell. The stromal collagen fibres are swollen and separated by fluid exudate and the spaces irregularly invaded by mononuclears. Both the capillaries and the larger blood vessels are very congested but the main vascular change consists of enormous dilatation of the pleural lymphatics; this latter accounts for most of the thickening. The precipitated fluid in these lymphatics presents a moderate

admixture of mononuclears and fibrin. This process has not extended to the degree present in most cases of interstitial pneumonia (vide infra).

The bronchial nodes show a large number of pulmonary macrophages and fibrin deposition in the medullary sinuses (Figs. 13 and 14). There are scattered areas of fibrinoid necrosis in both the germinal centres and the medulla. This is thought to represent necrotising bronchopneumonia of fairly long standing; that is, about seven days.

Another case for which no details of history are available shows a much more acute process. At autopsy the lungs showed mainly congestion and some consolidation of the anterior lobes. Pus and abscess formation and gross evidence of necrosis were absent. The most regular histological feature is fibrinoid necrosis of the bronchiolar wall and the surrounding alveoli; structural details of the tissue can still be seen in "ghost" outline, the affected parts having lost their normal staining affinity and appearing diffusely eosinophilic with nuclear detail obscured. The surrounding tissue varies from normal to infiltration by macrophages of the type described above. This is thought to represent either an earlier or more acute stage of the process.

It is open to some doubt whether the last two main types

of bronchopneumonia can be sharply separated from each other since areas in some cases show both types of lesion to be present. However there is some evidence that the necrotising type is much more severe clinically and has a poorer prognosis. The latter is only to be expected in view of the destructive neture of the pathological process.

(c) Experimental work

An attempt was made to transmit this pneumonia to mice. In order to use the material when as fresh as possible, passages were started before the result of the bacteriological examination of the calf lung was known. The latter revealed the presence of Pasteurella septica in pure culture.

Five preparations of lung tissue were made by grinding the lung with sterile sand. (1) In normal saline a 10^{-1} suspension was made and centrifuged for two minutes at 3,000 r.p.m. The supernatant was used for passage. (2) A similar preparation was suspended in 40% glycerol saline. (3) A suspension was then made as in (1) above, except that 50,000 units of penicillin were added per 3 ml. of suspension. (4) Suspension (1) above was filtered through a Seitz EK filter. (5) Suspension (2) above was treated as preparation (4).

Results

Preparation (1)

Nine mice were each given 0.05 ml. intranasally (i.n.). All of the mice in this experiment showed bilateral acute lobar pneumonia at autopsy. Passages are indicated by arrows.

3 were killed when moribund after 1 day.

5 were killed when moribund after 3 days. → 6 mice all died in one day.

1 died in 2 days. → 2 mice died in 3 days

2 mice both died in one day. → 2 mice died in 1 day.

2 mice both died in one day.

2 mice both died in one day.

Bacteriological examinations were made at every second passage; a pure culture of P. septica was obtained in every case.

Preparation (2)

Six mice were given 0.05 ml. (i.n.). All were normal after seven days. Two lines of passage were initiated from two of these six mice. Each consisted of four passages to two mice. All were killed seven days after inoculation; no lesions were found. The original suspension yielded P. septica in pure culture but this could not be recovered from any of the

mice.

Two guinea pigs injected intraperitoneally with 0.5 ml. of this suspension died in one day. They had peritonitis with effusion and "septic" spleens from which P. septica was obtained on pure culture.

Preparation (3)

Four passages, each of two mice given 0.05 ml. (i.n.) and lasting seven days, were carried out. All of the mice remained healthy and showed no lesions either at autopsy or on microscopical examination. P. septica was not recovered at any stage.

Preparation (4)

This was carried out as for (3); the results were identical.

Preparation (5)

This, too, was carried out as for (3); no lesions were found in the inoculated mice.

No definite conclusions can be drawn from this work about the aetiological agent involved in this case of calf pneumonia. Pasteurella septica may have been the primary pathogen, or if it was not, may have been responsible for the acute necrotising

process. Seitz E.K. filtration and penicillin treatment of the suspension were sufficient to prevent infection of mice with P. septica but did not reveal any other agent transmissable to mice. The 40% glycerol saline suspension appeared to prevent Pasteurellar pneumonia in the mice but did not prevent septicaemia in the guinea pigs inoculated intraperitoneally.

ACUTE INTERSTITIAL PNEUMONIA

Six of the 52 cases show this lesion. In these six cases this is the basic and uncomplicated lesion; but in several of the other types of pneumonia, areas of interstitial pneumonia are also present and are thought to represent secondary intrapulmonary vascular spread of a severe inflammatory process.

Several of these animals were seen personally when alive. The youngest was five days old but cases have also been seen in adult cows six years old. The disease is usually only of a few days duration. The calf is acutely ill, febrile (105° to 106° F.) dehydrated, dyspnoeic, ~~anorexic~~ anorectic, and may show pain when the thorax is compressed. Purulent nasal discharge was not a feature of the cases seen.

Post mortem findings. As in other calf pneumonias the anterior

lobes are most constantly affected, although spread to involve almost the whole of the diaphragmatic lobes has been seen. The affected lobe does not collapse when the thorax is opened. It is deep red and tense with rounded lobe edges; the overlying pleura usually shows acute fibrinous pleurisy and adhesions between the parietal and visceral pleurae are common. The lung parenchyma is very friable. The outstanding feature is the exaggerated lobular delineation. This is caused by the strikingly prominent and thickened interlobular septa. These may be only oedematous or may be thick, yellow, dry and necrotic, depending on the stage of the process. The latter may have progressed so far as to give the appearance of pin point areas of surviving parenchyma containing a bronchiole, surrounded by a rectangular area of coagulative necrosis; or whole areas of lobes several inches square may have undergone complete coagulative necrosis. Suppurative softoning and the presence of pus in the bronchi are not features. The regional lymph nodes are usually intensely congested and may show flecks of necrosis.

Microscopic appearances. The clinical features, post mortem appearances and the pathogenesis of the disease are easily understood from a consideration of the morbid histological features. The following description is based on a series of

lesions selected from different cases and from different parts of the lung in one case. This process has not been described before in the literature.

Stage (1) (Fig. 15). The subpleural and septal lymphatics are grossly dilated. The valve cusps of the pleural lymphatics are pulled apart by this dilatation (Fig. 15). The fluid in the lymphatics is precipitated as a smooth homogenous lightly eosinophilic film. Within this, very fine spicules of deeper staining fibrin are deposited in an irregular fashion. The cellular content at this stage varies even within the same vessel (Fig. 15). At some places there are no cells while at others, corresponding to the position of heavier fibrin reticula, there are present small aggregates of cells, mainly monocytes and lymphocytes. Neutrophil leukocytes are not present in any number. The walls of the lymphatics and the septal stroma show minimal cellular changes and show only mild oedema. In the subpleural areas (Fig. 15) there is capillary engorgement. The adjacent alveolar tissue shows only slight changes viz. mural capillary congestion and the presence of an occasional macrophage in alveolar lumina. The bronchi and bronchioles show no inflammatory changes whatsoever.

Stage (2) (Fig. 16). The septa have become grossly thickened

at this stage and are easily visible to the naked eye. The lymphatics are markedly distended and completely occluded by a fine meshwork of fibrin in which are entrapped only a few cells. The walls of the vessels are thin and are uniformly eosinophilic; this together with the loss of nuclear staining affinity indicates incipient necrosis. The surrounding septal stromal tissue shows marked oedema and separation of fibres. Here too there is some loss of staining affinity and indications of necrosis. This tissue contains a few neutrophils and polymorphs but the cellular reaction is nowhere intense and is confined to the septa. Congestion and haemorrhage are minimal. The surrounding alveolar tissue shows only congestion and the presence of a few macrophages in occasional alveoli. The bronchi and bronchioles are completely normal (Fig. 16).

Stage 5. (Fig. 17). At this stage the inflammatory phenomena are still confined to the septa. It is difficult to see any clear line between the thrombosed lymphatics which are undergoing necrosis and the oedematous stromal tissue, the fibres of which are separate and have lost their normal sharp definition. The material between these fibres is granular and eosinophilic. An inflammatory cellular reaction has now become more prominent although it is still mainly focal in character. The infiltrate is composed of neutrophils and

macrophages in almost equal numbers. The alveoli and bronchi are similar to those described in Stage 2.

Stage 4. (Fig. 18). The septal tissues have here undergone complete coagulative necrosis there being complete loss of normal staining affinity of the formed elements. The septa are of the same breadth as in Stage 3, but are now composed of an almost amorphous palely eosinophilic granular material. Some "ghost" outlining of cells and vasculature remains. At the lobular edge of the septum there is a narrow band of intense cellular infiltration. The cells are mainly neutrophil polymorphs and their morphology is much clearer at the alveolar than at the septal side, which appears to indicate a rather rapidly advancing coagulative necrosis preceded by a narrow band of acute inflammation. In the alveoli immediately adjacent to the septa there is some deposition of fine fibrin strands and a light diffuse mural and luminar macrophage infiltration. The central alveoli bronchioles and bronchi are for the most part normal although an occasional bronchus contains a few polymorphs. There is no trace of any necrotising phenomena in the bronchial tree.

Stage 5. (Fig. 19). This is a marked intensification of Stage 4. The septa show almost complete eosinophilic

coagulative necrosis and the process has spread to involve the outer third of the lobules. The band of advancing cellular infiltration is much thicker and more highly cellular. The cells are almost wholly neutrophil polymorphs. The edges of this area are almost straight and seem to indicate a rather uniform process (Figs. 19 and 20). The inner alveoli are still mostly air containing although there is a greater degree of fibrin deposition and macrophage infiltration. Some bronchioles show a fairly heavy polymorph content while others (Fig. 20) are relatively unaffected. There is uniform engorgement of the alveolar capillaries.

Stage 6. (Fig. 21). This represents the penultimate stage of the process and shows complete necrosis of the septa and the greater part of adjacent alveoli. The surprising thing about this lesion is that, even at this stage, when the greater part of the affected lobe has undergone complete coagulative necrosis the adjacent alveoli show a very minor degree of inflammatory change. Bronchioles situated very close to the inflamed septa may show little or no cellular exudate or necrotic debris (Fig. 21).

Stage 7. (Fig. 22). The process proceeds until there are areas of complete necrosis involving almost whole lobes. Some

areas show "ghost" outlines of former structural elements while others are amorphous masses of eosinophilic debris.

The septal changes parallel those of the pleurae and subpleural tissues so that in early stage in the process a fibrinous pleurisy is established.

The main features of the pathogenesis of this pneumonia, then, appear to be thrombosis of the lymphatics of the pulmonary septa, their subsequent necrosis and inflammation and the spread of this process in a centripetal fashion to involve the lobules. The final result is not suppuration and abscess formation, but coagulative necrosis. The bronchi are relatively unaffected even at a late stage.

The process appears to be haematogenous in origin rather than aerogenous. In most cases however, no primary extrapulmonary focus of infection can be found and it is possible that the organism or organisms involved have a predilection site in the interstitial tissues of the lungs. The initial focus of infection has been found in some cases which are discussed under these separate headings (q.v.) viz. sepsis supervening in a peptic ulcer, omphalophlebitis, and omphaloarteritis. These pneumonia lesions have also been found in focal distribution in some cases of acute bronchopneumonia and this has been interpreted as intrapulmonary vascular spread of such a

pneumonia.

INCLUSION BODY PNEUMONIA

Three of the 52 cases showed this lesion; one only will be described.

Clinical history. This 10 day old calf had been ill for seven days, the only symptoms noticed being apathy, anorexia and the passage of greyish-white faeces. Apart from a few small pyloric ulcers, the only lesions were in the lungs.

Post mortem findings. A strip about 1 cm. wide on the anterior edge of both apical and cardiac lobes was crepitant and of a pink colour on section; the remainder of the lungs was consolidated. The normal well marked lobular pattern of calf lung was accentuated by thickening of the interlobular septa. A little white frothy fluid could be expressed from the bronchioles.

Microscopic appearances. The lumina of the larger bronchi contains some polymorphs but those are quite well preserved and show a sharp nuclear outline. There are occasional macrophages and giant-cells of the alveolar type described below.

The epithelial lining is intact and healthy with no areas of desquamation or papilliform projections. In the subnuclear region of many epithelial cells there are eosinophilic inclusion bodies and identical bodies are also present in the alveoli. The epithelial inclusion bodies are not associated with cellular proliferation in the main bronchi. The bronchial walls are unthickened and show no inflammatory infiltration.

The respiratory bronchioles show similar features of early purulent inflammation (Fig. 23). Here also, tissue destruction is not a feature, but in contrast with the large bronchi there are proliferative changes. Projecting from the walls are triangular syncytial masses of essentially similar structure to giant-cells seen in the alveoli.

The most striking lesion is epithelialisation of all the alveoli and the formation of giant-cells (Figs. 23, 24 and 25). The alveolar walls are completely lined by a single layer of cuboidal epithelium, so low that the nuclei cause bulging of the cell border. The nuclei of the alveolar epithelium are round or slightly oval with a very distinct, coarsely reticulated chromatin network (Fig. 25). The cytoplasm is grey or slightly basophilic in sections stained by haemalum and eosin and never shows the eosinophilia of pulmonary macrophages. Mucin stains do not reveal secretory droplets in the cells of the alveolar epithelium, but eosinophilic inclusion bodies are

common, usually lying at the poles of the nucleus or between these and the basement membrane (Fig. 26 and 27). These nuclei are usually clumped together in the centre in an overlapping mass in which cell boundaries are not discernible. The cytoplasm of the giant-cells is similar to that of the epithelial cells, and the giant-cells appear to have little phagocytic power since only an occasional polymorph is seen lying in a vacuole in their cytoplasm. However, the giant-cells contain many eosinophilic inclusion bodies and as described below, it is within the giant-cells that the inclusion bodies show their greatest range of size. The giant-cells may be desquamated and lie free in the lumen of an alveolus or bronchus (Fig. 23). There is no interstitial reaction due to macrophages or septal-cell proliferation. The marked thickening of the alveolar walls is produced solely by the epithelialisation and the congested capillaries.

In addition to the above changes there is a mild diffuse infiltration with polymorphonuclear leukocytes; tissue destruction is nowhere severe.

The Inclusion Bodies

Staining reactions. The inclusion bodies are strongly eosinophilic and retain their red colour when all dye has been washed

out of the erythrocytes. The best staining method was found to be eosin-phloxine-tartrazine method, but the bodies are easily seen with haemalum and eosin, or any of the Romanowsky combinations used; dilute Giemsa, Leishman, eosin-methylene blue or Maximow's haematoxylin-eosin-azur mixture. The Giemsa modification was best for delicate staining of the epithelium and giant-cells. The inclusions are strongly fuchsinophil in the picro-Mallory method, but other tissue components, also staining red, obscure the clarity of detail. They are not stained by Machiavello's and Castaneda's methods. The Periodic acid-Schiff technique does not stain them and affords a differentiation from mucin, which it stains brilliantly.

Morphology. The bodies range from 1-6 u in their long axes with a mean of about 3u. They are usually oval though larger pear-shaped forms are occasionally seen in giant-cells. Their structure appears homogeneous and the staining methods employed show no reticulation suggestive of fusion of elementary bodies. They appear singly or in groups, depending on the size of cell and seem to have no particular position in the cell although most lie between the nucleus and the basement membrane. The inclusions are confined to the cytoplasm of epithelial cells; they do not lie in vacuoles, in the nucleus, in phagocytes or outside cells. They do not seem to have any relation to the

presence or absence of nucleoli in the nucleus. The morphology and staining reactions of these inclusion bodies seem to be similar to those found in the lung in measles and in the pneumonia associated with canine distemper.

Experimental work

An attempt was made to transmit this pneumonia to mice. No calves were available at this time for inoculation.

Experiment (1). Pieces of pneumonic lung were ground with sterile sand and 10% wt./vol. suspensions were made in bacteriological broth. These were centrifuged for three minutes at 3,000 r.p.m. and the supernatants used for inoculation. Six mice were each given 0.05 ml. intranasally (i.n.) under ether anaesthesia. All remained well and were killed eight days after inoculation. Epithelialising pneumonia was not found on histological examination. Pooled material from these mice was passaged into four mice. These were killed 20 days later. Two showed some pulmonary collapse and septal cell reaction; neither epithelialisation nor inclusion bodies were found. A further similar passage was made to four mice. These did not show any lesion when killed 14 days later.

Experiment (2). A Seitz E.K. filtrate was prepared from the suspension described above. It was given intranasally to six mice. No lesions resulted and no further passages were carried

out.

Experiment (3). The filtrate described above was inoculated on to the chorio-allantoic membrane of six 11 day chick embryos. Two of these membranes, on harvesting, were oedematous and were twice the normal volume. Bacteria could not be cultured from them. Each of them was passaged as i.n. suspensions through three groups of mice, seven days elapsing between inoculation and killing. No specific lesions were found.

Histological examination of the chorio-allantoic membranes showed only oedema of the stromal tissues; no inclusion bodies could be demonstrated.

OTHER EPITHELIALISING PNEUMONIAS

Five of the 52 cases showed epithelialisation of alveoli without the presence of inclusion bodies; two cases will be described.

Case 1

Clinical history. This animal was one of nine calves aged four to 15 weeks which had been suffering for at least a fortnight from a disease which, according to an experienced veterinary practitioner, was clinically indistinguishable from

parasitic bronchitis caused by infestation with D. viviparus. At this time the faeces of these animals did not contain demonstrable Dictyocaulus larvae.

The animal in question developed severe dyspnoea and was killed when it was considered moribund.

Post mortem findings. The pleurae were thickened and the interlobular septa accentuated. The larger bronchi contained some blood-tinted frothy fluid but adult nematodes or larvae were not found after a thorough search. Pulmonary crepitation was diminished but selected portions floated in water. Pulmonary oedema was quite marked and small amounts of white frothy fluid could be expressed from the bronchioles. All lobes of the lungs were equally affected.

Microscopic appearances. Three distinct pathological processes are present:-

(1) the pulmonary changes associated with acute left-heart failure,

(2) early focal purulent bronchopneumonia, and

(3) alveolar epithelialisation with giant-cell formation.

The pulmonary changes in acute left-heart failure are these which were described by Hadfield (1938) as constituting the rheumatic lung. The alveolar walls are thickened by congestion and macrophage infiltration, there is some degree of

intra-alveolar haemorrhage and the alveolar ducts and the walls of some of the alveoli are lined by hyaline membranes (Fig. 28). Some lobules show early bronchopneumonia and in an occasional focus a small abscess has formed. These latter lesions are essentially scattered and focal. Throughout the lung lobules are found areas in which every alveolus has become lined with notably regular cuboidal epithelium. Proliferative changes are not so marked as the cases of inclusion body pneumonia but syncytial masses containing four or five nuclei are present. Inclusion bodies are not present in this case. Many of the lobules show mild bronchopneumonic changes and in some places the epithelial proliferation is almost obscured by the pyogenic reaction. Gross dilatation of the pleural and septal lymphatics is responsible for the apparent stromal thickening.

There is mild cellular infiltration into the walls of the large bronchi but their lumina do not contain pus and the epithelium is healthy and intact. Inclusion bodies are not present in this epithelium. There is no histological evidence of either adult or larval nematodes.

Case 2

In an outbreak of pneumonia, seven calves died of which two were submitted for pathological examination. Since they

show identical features only one case will be described. A similar case from another source has also been studied.

Post mortem findings. Morbid changes were confined to the lungs, both of which were deeply congested and oedematous. The apical, cardiac and intermediate lobes and the anterior half of the diaphragmatic lobe were consolidated and sharply demarcated from the posterior half of the diaphragmatic lobe. The pleural and cut surfaces of the pneumonic lobes felt shotty and were studded with small white foci, which were degenerating bronchi.

Microscopic appearances. The lumina of the larger bronchi contain a little pus and necrotic debris. Their epithelium shows some desquamation but inflammatory infiltration of the wall is light. Many of the terminal bronchioles and their surrounding alveoli have undergone fibrinoid necrosis, and although the structure of the various tissue elements can still be seen, the staining affinities, especially of the nuclei, have been almost wholly lost, the remaining ghost outlines being light pink (Fig. 29). The necrosis appears to have been sudden as judged by the minimal cellular response in these foci.

Congestion of the alveolar capillaries is severe; the vessels are wide and tortuous and oedema fluid is abundant in

the air spaces. This fluid contains many macrophages with pink vacuolated cytoplasm, and large round giant-cells with staining reactions identical with the phagocytes (Figs. 9 and 10). These macrophages which have from five to 30 nuclei arranged peripherally in the homogeneous eosinophilic cytoplasm are round, lie free in the air spaces and are not found in the areas of alveolar epithelialisation or of bronchiolar necrosis. They do not contain inclusion bodies and have no morphological similarity to the giant-cells described in the case of inclusion body pneumonia.

In some areas particularly around healthy medium-sized bronchi, there are fairly large foci of epithelialisation of alveoli (Fig. 30). The lining cells form a continuous sheet of regular cuboidal epithelium, the individual cells being rectangular and showing no tendency to proliferate. No inclusion bodies are present. These alveoli do not contain inflammatory exudate and there is some evidence that the process is a relatively chronic one, since the thickened alveolar walls are lightly infiltrated with plasma cells and actively dividing fibroblasts are present.

Neutrophil leucocytes can rarely be seen in the affected lobes, the consolidation being due to the severe exudative reaction and the mononuclear infiltration.

PULMONARY ASPERGILLOSIS

Two of the 52 cases showed this type of pneumonia. These cases came from different outbreaks; one outbreak was associated with a simultaneous outbreak in turkey poults. The other case showed a concurrent interstitial pneumonia as described above. This latter case only is described in detail.

Subject. Ayrshire heifer calf aged four weeks.

History. The calf was ill for three weeks; during that time it had shown loss of condition, poor appetite and dullness but no respiratory symptoms had been noticed. The rest of the calf herd were suffering, some from diarrhoea, others from persistent mild coughing. There were no records of rectal temperature. Antibiotics had been employed on the farm but there was no record concerning this particular animal or of prolonged course of treatment.

Post mortem findings. The left lung. There was patchy consolidation of the anterior lobes and the anterior strip of the diaphragmatic lobe. Scattered throughout the consolidated lobules were miliary white nodules which did not appear to have any anatomical relation to the bronchi.

The right lung. This showed similar changes involving the whole of the apical lobe, the middle third of the cardiac lobe,

the anterior half of the diaphragmatic lobe and the dorsal half of the intermediate lobe. In addition the cardiac lobe showed the marked changes of acute interstitial pneumonia.

Microscopic appearances. Scattered throughout the lung parenchyma are many focal lesions (Fig. 31); they have no particular anatomical localisation within the lobule but they are confined to the alveolar tissue. The most highly developed nodules consist of a central deeply basophilic area which appears to consist of closely packed pyknotic nuclei and fungal mycelia which have undergone necrosis (Fig. 32). Immediately exterior to this is a zone consisting of a light infiltration of neutrophils and macrophages intermixed with a heavy branching mycelium. Exterior to this again is a ring of collapsed alveoli in the walls of which are many large pale "septal cells". These latter form the greater part of this zone. The septal cells often contain fungus and this can also be seen penetrating the alveoli immediately exterior to the nodule.

Other small nodules are present which consist of foci of swollen septal cells which contain fungal elements. In a few places necrosis has taken place so that almost the only recognisable formed elements are fungal. The mycelia (Fig. 33) vary in their staining reactions, some being basophilic and

some eosinophilic; all are stained by the periodic-acid-Schiff method.

Typical acute interstitial pneumonia of a moderately severe degree is present in the right cardiac lobe. No fungal elements are discernable.

The second case seen showed essentially similar lesions but of a smaller distribution and without any other complicating pneumonia.

CUFFING PNEUMONIA

This name was first applied as a term of convenience by the present author to a type of pneumonia which appeared to be characterised by expanding hyperplastic lymphoid sheaths around most of the bronchi and bronchioles of affected parts of the lung. The first cases studied were the 18 which occurred in the present series. Later a larger scale investigation carried out on parasitic bronchitis revealed that cuffing pneumonia was widespread in the field and had interesting relationships with parasitic bronchitis; it also lent support to the view suggested by the present cases that the clinical signs were related to the expanding lesion. The first report of this disease (Jarrett et al. 1955) contains an account of some

of its clinical and epidemiological features.

Of the 13 cases occurring in this series, five have been selected to demonstrate the development of the characteristic lesions.

Case 1

History. After an illness lasting about one day this calf suddenly developed mania and died. Many other animals in the herd were ill or had already died of pneumonia.

Post mortem findings. Post mortem examination revealed only a few subendocardial petechia and radial vascular congestion of the renal cortex and medulla. The lungs were mildly oedematous but no gross lesion was apparent.

Microscopical findings. The lumina of the bronchi are free from cells or debris and the epithelium is intact and does not show proliferative changes. The most striking lesion in this case is in the fibrous tissue surrounding bronchi of all sizes where the lymphoid elements show hyperplasia (Fig. 34). For several reasons this appears to be an actual hyperplasia and not an infiltration. With haemalum and eosin staining, and more particularly with Maximow's haematoxylin-eosin-azur method,

it can be seen that cells of both early and late stages in the lymphoid series are present chiefly in foci with a reticulin framework like that of a lymph node. The small nodules have a sharp outline and the lymphocytes are not invading the surrounding fibrous tissues (Fig. 35). Plasma cells are not present at this stage. In the peribronchial tissue these areas are localised to one or two points and do not form vascular or bronchial cuffs. At this stage the increase in volume of the peribronchial tissue is not sufficient to cause compression of adjacent alveoli.

The capillaries of the lung are very congested and a mild degree of pulmonary oedema is present in most but not all lobules. A few mononuclear cells are probably derived from the interstitial tissue which is more cellular than normal. These cells have a varied morphology; they may be histiocytes or the so-called pulmonary septal cells. Signs of acute inflammation are completely absent from the lungs. Epithelial proliferation is not present either in alveoli or bronchioles and inclusion bodies are not demonstrable in any of the cellular foci or bronchial epithelium.

The pleurae and septa are thickened, mainly because of the great dilation of lymphatic vessels. The only lesions in other organs are hepatic centrilobular congestion and a few

small intertubular round-cell foci in the renal cortex.

Case 2

History. This animal was selected from a group of calves all of which showed dyspnoea and paroxysmal coughing. They had all been reared indoors with no access to grass. Dictyocaulus viviparus larvae could not be demonstrated in their faeces. Clinically, the case was one of moderate severity. It was killed in order to ascertain with which type of pneumonia the calves were affected.

Post mortem findings. Both left and right apical lobes were congested but air was present in the alveoli. Selected blocks of tissue from these lobes floated in water. The small bronchi were unusually distinct and their walls appeared thickened. Pus did not appear on the cut surface when the lungs were squeezed.

Microscopical appearances. In sections taken from the apical lobes, the bronchi and bronchioles are surrounded by a narrow cuff of lymphoid cells. Reticulum cells, lymphoblasts, lymphocytes and plasma cells can be seen enmeshed in a reticulin framework. This cuff evenly surrounds each bronchiole; discrete lymphoid follicles are not present (Fig. 36). Serial

sections show that this cuff extends evenly along the bronchioles forming a sheath (Fig. 37).

The surrounding alveoli are not compressed and show no inflammatory infiltrate. The bronchial and bronchiolar epithelia are intact and the bronchial lumina free from exudate.

Case 3

History. This calf belonged to the same herd as case 1. It was dyspnoeic but its respiratory distress was not developed to an extent which precluded eating. It was killed for diagnostic purposes.

Post mortem findings. The lesions were confined almost completely to the apical lobes and the mediastinal lymph nodes. The latter were moderately hyperplastic and pale grey; the former showed obvious cuffing of the bronchioles with a varying degree of collapse of the surrounding lobules. The anterior lobes were deep red and less than normal in volume. Pus could be expressed from some of the smaller bronchi. There was no gross purulent exudate in the larger bronchi.

A few collapsed lobules were present along the course of the main diaphragmatic bronchi; the affected lobules were immediately adjacent to the large bronchi.

Microscopical appearances. The bronchi of the affected lobes are completely surrounded by lymphoid cuffs which show the anatomical structure of lymph nodal tissue, i.e. germinal follicles with "Flemming centres" surrounded by cortical tissue consisting of lymphocytes packed between sinuses (Figs. 38 and 39). The reticulin framework is also similar to fully developed lymph node tissue. Mitotic figures are numerous in the lymphoid tissue.

In this tissue there are many cells with an oval or indented nucleus and cytoplasm which contains many small basophilic inclusions. These stain with Giemsa, Machiavello and Castaneda staining, but they also stain metachromatically with toluidin blue, are periodic-acid-Schiff positive and stain with methylene blue dissolved in phosphate buffer at pH2. They are considered to be residual granules of discharged mast cells and not specific inclusion bodies. No inclusion bodies are demonstrable with eosin-phloxine-tartrazine, picro-Mallory or eosin-methylene-blue.

The bronchial lumina show mild purulent bronchitis; purulent exudate is absent from the alveoli and while some show partial collapse, many are fully expanded.

There is some oedema of the interlobular and subpleural connective tissue and the lymphatics in these areas are dilated.

Case 4

History. This calf came from the same farm as case 2. It was more severely affected clinically and was purchased and slaughtered in order to study the lesions.

Morbid anatomy. The only lesions found were in the lungs and mediastinal lymph nodes. All anterior lobes and the anterior borders of the diaphragmatic lobes were affected. The pulmonary tissue was collapsed, deep red and its volume was less than normal. The cut ends of the bronchi and bronchioles were surrounded by grey cuffs and appeared to pout from the cut surface. Muco-pus could be expressed from these bronchi.

The broncho-mediastinal lymph nodes were grossly enlarged and formed a confluent mass subjacent to the oesophagus. The cut surface of this tissue was pale and homogeneous. There was neither congestion nor necrosis.

Microscopical appearances. All the bronchi and bronchioles in the affected areas are surrounded by large lymphoid cuffs. The histological details are similar to those described in the preceding cases but differ in degree. In this case the hyperplastic lymphoid tissue presumably exerted considerable pressure in both an inward and an outward direction because bronchial and alveolar lumina are markedly diminished (Fig. 40). Polymorpho-

nuclear infiltration is mild in the bronchi and absent from the alveoli. Many of the cells in the lymphoid cuffs are plasma cells.

Case 5

History. This calf was received about a fortnight after case 1 and from the same herd: during these two weeks the losses in the herd had become heavier, sulphonamide and penicillin treatment having been of no avail.

Post mortem findings. At autopsy the only lesions were seen in the lungs. Each bronchus was surrounded by an even, grey cuff, several millimetres wide, which compressed both the bronchial lumen and in the surrounding alveolar tissue. This cuff extended from the hilum to the terminal bifurcations where a transverse section revealed an appearance like a bunch of grapes. Plugs of pus could be expressed from the bronchi. Every lobe was affected in this way.

Microscopical appearances. The lesion is a marked development of those seen in cases 1 to 4. A wide cuff of round cells surrounds each bronchus on cross section (Figs. 41 and 42) and longitudinal and serial sections show that it is a continuous sheath throughout the whole bronchial tree following each

terminal ramifaction. (Fig. 43 shows this lesion; it has been taken from another case in which collapse had not supervened, in order to illustrate the lesion more clearly.) The cellular elements are very closely packed together, but pyronin-methyl green staining shows that many of them have the characteristic morphology and staining reactions of plasma cells. The cuff is so extensive that the vessels accompanying the bronchus have become embedded in cells.

Compression by the cuff is exerted both inwards and outwards. The lumina of the bronchi are often reduced to an irregular slit which is packed with inflammatory debris, necrotic cells and clumps of bacteria. The epithelium does not appear to be undergoing hyperplasia and no inclusion bodies can be demonstrated in the cells. The cuff surrounding the bronchus now occupies about three-quarters of the lobule and there is almost complete collapse of all alveoli. The edges of the lymphoid tissue are sharp and there does not appear to be a direct infiltration of the adjacent alveoli. These collapsed alveoli however, contain mononuclear cells with a distinct nucleus and fairly abundant cytoplasm. The alveolar walls are congested but do not contain the numbers of mononuclear or septal cells seen in case 2 and it is possible that these are the cells now lying in the remains of the air spaces.

Polymorphonuclear consolidation or degenerated foci are nowhere present. The reaction is hyperplastic and not necrotising.

Dilated lymphatics are present in the interlobular septa and in the subpleural tissues; this together with vascular engorgement and some fibrosis has produced marked pleural thickening (Fig. 41). The bronchial lymph nodes show a diffuse cellular hyperplasia; the medulla, which is normally occupied by large sinuses and few cells, is encroached upon by the actively dividing tissue.

The liver is normal but the kidney shows some intertubular lymphocyte infiltration which is more marked than that in case 5.

The cases of this group show a rather unusual type of pathological process. If the cases are accepted as showing different stages of the same process, the development of the lesion appears to represent hyperplasia of the small amount of lymphoid tissue normally present in small foci in the bronchial walls of the calf. (These foci are especially marked, in the normal animal, in the angle of bifurcation of the bronchi.) The hyperplasia progresses until a bronchial sheath is formed extending from the main bronchi of the affected lobe to the terminal bronchiolar ramifications. This sheath may occupy

the greater part of the lobule when viewed in cross section compressing both alveoli and bronchus. The alveoli become collapsed and infiltrated with mononuclear or septal cells; the bronchus is narrowed and may be invaded by pyogenic organisms. The latter infection appears to be of a low grade of virulence and leads to bronchiectasis rather than pulmonary abscesses. There is usually a striking absence of acute inflammation from the lung parenchyma; in the present cases there are no foci of alveolar necrosis or consolidation by polymorphonuclear leucocytes.

There are many histological similarities between this condition and grey lung virus disease of mice (Niven, 1950) and a pneumonia of cotton rats (Andrewes and Niven 1950). In grey lung virus disease the lesions are confined to the lungs and are briefly: a septal cell or mononuclear reaction primarily interstitial but coming to involve the alveoli; marked pulmonary oedema; the formation of a sharply defined peribronchial and perivascular cuff which is composed first of lymphocytes, then mainly of plasma cells; and the absence of pyogenic reaction until the later stages of the disease when bacterial invasion may supervene. In the murine disease, as in the bovine, epithelial hyperplasia is not a feature and inclusion bodies are not demonstrable.

Gulrajani and Beveridge (1951) have shown that a virus pneumonia of pigs is of widespread distribution in Britain. They have not published an account of the morbid histology of this condition but cases which I have studied show a marked peribronchial lymphoid hyperplasia similar to that in cuffing pneumonia. In my cases of pig pneumonia however, this hyperplasia has not progressed to the extent of producing pressure collapse of surrounding alveoli (Fig. 44).

It is not prudent to transfer the conclusions of experiments on one species to another species, and the fact that certain rodent and porcine pneumonias, almost certainly of virus etiology are morphologically similar to the bovine lesions, may be purely accidental since species reaction to the same organism is often very variable. However, bacteriological examination of cases of cuffing pneumonia (for which I am indebted to Messrs. Michna and Grindlay of the Glasgow Veterinary School) failed to reveal any constant bacterial pathogen and some cases were bacteriologically sterile. The mixed flora obtained included C. pyogenes, B. coli, Proteus vulgaris and Lancefield negative Streptotocci; these are common organisms in bovine pneumonia and are frequently obtained from apparently normal lungs. It was decided to attempt transmission of this pneumonia to both laboratory

animals and to calves; the latter are very expensive experimental animals and it was possible at this stage to use only small numbers.

Experiments Using Laboratory Animals

Mice

Several attempts were made to passage this pneumonia to mice. One such experiment is summarised below.

130 newly weaned white mice were divided into four groups of 20 and five groups of 10. The groups of 20 were inoculated with preparations of affected calf lung; the groups of 10 were controls.

Inoculated group

1. 20 mice were given, intranasally (i.n.) under ether anaesthesia, 0.05 ml. each of a 10^{-2} suspension of affected calf lung suspended in bacteriological broth.
2. 20 mice were given a similar dose intraperitoneally (i.p.).
3. 20 mice were given 0.05 ml. (i.n.) of a filtrate (Gradocol membrane A.P.D. 0.8 u) prepared from the inoculum used for group 1.
4. 20 mice were given a similar dose i.p.

Control group

5. 10 mice were given 0.05 ml. of a 10^{-2} suspension of normal calf lung in bacteriological broth i.n.
6. 10 mice were given 0.05 ml. of sterile broth i.n.
7. 10 mice were given 0.05 ml. of sterile broth i.p.
8. 10 mice were killed for normal histology at the start of the experiment.
9. 10 mice were killed for normal histology at the end of the experiment.

Results

The mice were killed 30 days after inoculation.

Group 1. One mouse showed no lesions: two showed marked peribronchial and mild perivascular cuffing; the remainder showed mild peribronchial and perivascular lymphoid cuffing of most bronchi and bronchioles.

Group 2. showed a similar result to group 1.

Group 3. All mice showed well developed peribronchial and perivascular cuffing.

Group 4. showed a similar result to group 3.

Group 5. Two mice showed well developed cuffing lesions; the remainder had mild lesions.

Group 6. All mice were normal.

Group 7. Four mice showed a moderate degree of cuffing.

Group 8. Five mice showed mild cuffing.

Group 9. Three showed marked and five moderate, cuffing.

In a pilot experiment the control group (10 mice) had shown no peribronchial and only occasional perivascular lymphoid cuffing. The mice used in the experiment described above were bred especially for the purpose, the does used being bought in for the purpose. Until this time there was no record of any endemic pneumonia in the animal house but this may have been chance since the mice were not used extensively for histological work. It was surprising to find such a large proportion of mice showing lung lesions. It was immediately suspected that grey lung virus disease was responsible for the lesions. An identical experiment was carried out using a different source of mice but the results were similar.

Similar experiments were also carried out using normal saline phosphate buffer at pH 7.2 and serum broth as the suspending media. The results were the same.

These experiments were terminated at this point since facilities to exclude grey lung virus disease were not available. If strict isolation had been available it might have been possible to get rid of the grey lung virus by dosing the breeding stock with aureomycin since Niven (1950) has shown that virus cannot be recovered from mice thus treated. It

would then have been reasonable to expect the young to be uncontaminated.

Up to the present time, experimental calves have not been available to attempt to make passages from mice to calves.

Guinea pigs

When lungs of guinea pigs which had been injected intranasally and intraperitoneally with affected calf lung, were examined histologically, they were found to have perivascular and peribronchial lymphoid cuffing (Fig. 45) together with areas of partial collapse; the latter showed a marked increase of mononuclear cells in the alveolar walls. At first it was thought that the bovine disease had been transmitted but it was soon realised that uninoculated guinea pigs of the herd suffered from a spontaneous pneumonitis with morphological characteristics similar to grey lung virus disease of mice.

No calves were available at this time to attempt to passage guinea pig material to them.

Ferrets

Three ferrets were inoculated, two intranasally and one intraperitoneally with fresh lung suspension from a case of cuffing pneumonia. There were no lesions seen microscopically in their lungs. Repassage to calves was not attempted.

Experiments Using Calves

Due to three factors, (1) the expense involved, (2) the initial absence of facilities for complete isolation, and (3) the very limited subsequent isolation accomodation, the initial transmissions to calves which come within the scope of this work, had perforce to be small in number. They were designed to demonstrate that this disease was transmissable and to see if the clinical signs were attributable to the expanding peribronchial lymphoid cuffs.

The technique used was as follows. Small pieces of affected lung tissue were removed aseptically at autopsy. These were ground in a mortar with sterile sand and suspended at 10^{-1} or 10^{-2} dilutions in bacteriological broth. Young calves usually about one week old were used. The hair of the calf was clipped in the midline of the neck lateral to the trachea. The area was swabbed with "Cetavlon" or tincture of iodine. A needle held in one hand was inserted through the skin behind the trachea and, holding the trachea in the other hand, was pushed forward into the trachea. The inoculum was then injected quite quickly, the calf's nostrils being held closed to diminish coughing.

The first two passages were made in calves in a communal house. The calves contracted pneumonia and shortly afterwards

the other calves in the house began to cough. The disease appeared to spread by droplet infection and further passages were carried out in small houses carrying only three calves in each. Each passage lasted approximately 28 days.

The following table illustrates the line of passage.

MH/1 Field case with well developed lesions.
Purchased and slaughtered for passage.

↓

5 calves Four calves showed well developed lesions and marked clinical signs of dyspnoea: one died of intercurrent infection with F. necrophorus (calf diphtheria).

↓

3 calves All showed typical clinical and pathological signs. Some polymorph reaction in the alveoli was present in one case. The case used for passage was bacteriologically sterile.

↓

4 calves Three calves had the typical clinical and pathological picture; one calf died of purulent bronchopneumonia after 20 days and showed no signs of cuffing lesions.

↓

6 calves All calves showed typical clinical signs. Four were given to another worker for an experiment concerned with parasitic bronchitis; the remaining two were slaughtered and had cuffing lesions.

↓

6 calves Three calves were inoculated with suspension and three with the supernatant fluid after centrifuging

the suspension at 5,000 r.p.m. for three minutes. The three injected with suspension were positive; two of the three which got supernatant were ~~positive~~ positive and the remaining calf was healthy. Two of the calves which received suspension showed concomitant purulent bronchopneumonia which did not wholly correspond anatomically to the areas of cuffing.

12 calves In this experiment dilutions of 10^{-1} to 10^{-4} were given to four groups of three calves respectively. The results are tabulated below.

10^{-1}	Calf	1	Negative
	"	2	Good positive
	"	3	Died three days after inoculation with purulent bronchopneumonia.
10^{-2}	"	1	Good positive
	"	2	Good positive
	"	3	Was clinically ill from the fourth day after inoculation and showed severe bronchopneumonia with no cuffing when killed at the 28th day.
10^{-3}	"	1	Cuffing pneumonia present but confined to collapsed areas in the apical lobes.
	"	2	Cuffing pneumonia present but confined to collapsed areas in the apical lobes.

	Calf	3	Died of suppurative omphalophlebitis 10 days after inoculation; showed early cuffing lesions.
10^{-4}	"	1	Mild positive cuffing pneumonia.
	"	2	Good positive cuffing pneumonia.
	"	3	Good positive cuffing pneumonia.

The experiment was terminated here because of contamination of the lungs with C. pyogenes. It was decided not to risk the chance of transmitting purulent bronchopneumonia.

These experiments were of a purely "pilot" nature to see if the disease could be reproduced serially. It is of interest to note that one passage was made with a suspension which appeared to be bacteriologically sterile and that no organisms could be cultured from several of the infected calves. The calves which showed cuffing pneumonia did not show symptoms usually until about 12 to 14 days after inoculations; those which had bronchopneumonia became ill a short time (two days in one case) after inoculation and did not show cuffing lesions. The bronchopneumonic calves were febrile and showed a polymorphonuclear leukocytosis; the cuffing cases were consistently afebrile. In general the degree of cuffing pneumonia corresponded to the respiratory symptoms. Three calves inoculated with normal lung did not show lesions when killed 28 days later.

From these experiments it was concluded that cuffing pneumonia was possibly a specific disease and justified further investigation.

Cold agglutinins

In the human subject it is often possible to demonstrate cold agglutinins in the serum of patients suffering from atypical pneumonia. In view of this fact eight random samples of adult cow blood and two from calves in the fourth week of the experimental disease were taken and their sera were tested for cold agglutinins. A 5% suspension of washed ox erythrocytes was prepared and put up against the various sera, the latter in doubling dilutions of 1/2 to 1/16. 0.15 ml. of sera were used. The tubes were placed in the refrigerator and read at one, two, four and 24 hours. No cold agglutinins were demonstrated

ASPIRATION PNEUMONIA

Aspiration pneumonia did not occur among the 100 consecutive cases upon which this work is based; it is thought worth while including it however, for classification purposes, since it was found in two experimental calves. These had been bought

in a market and housed in isolation boxes. They had probably been suckled since great difficulty was encountered on attempting to pail feed them. An inexperienced stockman immersed their noses, on several occasions, to try to make them drink. They died after a febrile illness lasting 24 to 36 hours.

Post mortem findings. Lesions were confined to the lungs. The right apical lobe and patches from half an inch to one inch diameter scattered throughout the other lobes, were dirty yellow in colour, non-crepitant and friable; they were obviously areas of coagulative necrosis. The bronchi around the necrotic areas exuded a dirty blood tinged fluid. The unaffected parts of the lungs were congested. The bronchial nodes were hyperaemic.

Microscopic appearances. The affected areas vary in size from lesions involving only a few alveoli to foci encompassing several lobules; a small focus, destroying about one-third of a lobule is illustrated in Fig. 46. The lesion consists of an area of coagulative necrosis in which the "ghost" outline of tissue components can be seen, surrounded by an irregular band of alveoli filled with polymorphonuclear leukocytes. The alveoli outside this zone show partial collapse, mural congestion and a light luminal infiltration of polymorphs and macrophages.

Where the lesion involves a septum, dilatation, thrombosis and necrosis of septal lymphatics occur. This probably facilitates spread from one lobule to another. Fig. 46 also shows the lesion extending into a respiratory bronchiole of an adjacent lobule.

PULMONARY ABSCESSES

Three of the 53 cases are classified thus; small focal abscesses complicating other pneumonias are excluded.

Case 1

Subject. Ayrshire heifer calf aged six weeks.

History. The calf had been noticed to be ill for two weeks. The only symptoms reported were wasting and inappetence. The temperature was normal, there was no diarrhoea and signs of respiratory disease were said to be absent. The animal was slaughtered because of the wasting; several other calves in the herd were suffering from pneumonia.

Post mortem findings. The animal was undersized and showed muscular wasting. Lesions were confined to the thorax. On opening the thoracic cavity, a large sac was found immediately

behind the pericardium, extending from slightly to the left of midline to the right thoracic wall. This sac was connected, by dense adhesions, to the left lung, the diaphragm, the pericardium and to the right parietal pleura. It was apparently continuous with the anterior lobes of the right lung. The wall of the sac was 5 mm. thick, composed of well developed fibrous tissue and lined by a layer of necrotic debris. It was filled with greyish-red, blood tinged pus containing a few creamy necrotic or inspissated fragments. Over 2,000 ml. of pus were removed.

In its lower part the sac had a thick wall as described above; near its dorsal end it was lobulated, the divisions being the remaining partially necrotic lung tissue, probably organised blood vessels. The long axis of the cavity turned from vertical to horizontal, running anteriorly as far forward as the upper part of the cardiac lobe. The remainder of the lung did not seem to be affected in any way. This was confirmed histologically. The pericardium was adherent to the abscess wall and in that area showed a plastic pericarditis surrounded by strong fibrous adhesions to the epicardium. The rest of the pericardium was normal.

This lesion was tantamount to solution of a complete lobe which, apparently, did not cause any flagrant clinical signs.

Another strange feature was the absence of any trace of pneumonia in the adjacent lung tissue. No evidence of the origin of the process was found. Corynebacterium pyogenes was isolated from the pus.

Case 2

Subject. An Ayrshire heifer calf of undetermined age.

History. No detailed history was furnished apart from the fact that the animal was slaughtered as a "wasting bovine". The calf was obviously stunted in growth the head being large in relation to the rest of the body. The coat was staring and rough, the abdomen tucked up and the perineum soiled with faeces and denuded of hair.

Post mortem findings. Lesions were confined to the thorax. The left cardiac, the left diaphragmatic and the right cardiac lobes were united to the adjacent areas of the parietal pleura by strong fibrous adhesions which could not be broken down without stripping the pleura from the thoracic wall. These areas corresponded to abscesses in the substance of the lung. Several other abscesses were present, all lobes being affected except the left apical. The abscesses had thick sclerotic fibrous walls and contained thick creamy light green pus. (C. pyogenes was isolated from this pus.) The immediately

adjacent lung tissue was dark brown and collapsed and the septa were thickened and prominent. Active pneumonia was absent. The regional nodes were enlarged, pale and hyperplastic. There were no abscesses in other organs. The umbilicus was healthy.

Microscopic appearances. Each abscess wall consists of concentrically arranged, heavily collagenised fibrous tissue. The innermost layer is of necrotic fibrin; immediately subjacent to this is a narrow area which is lightly infiltrated with plasma cells, lymphocytes and polymorphs. There is no pneumonia in the surrounding tissue.

Case 3

Subject. Ayrshire heifer calf aged about 10 days.

This case was one of "navel ill" or suppurative omphalophlebitis. The syndrome is described later. Briefly this case showed (1) an abscess involving the tissues around the umbilical ring, (2) suppurative thrombosis of the umbilical vein, (3) multiple hepatic abscesses, (4) suppurative polyarthritis, and (5) pulmonary abscesses. The pulmonary abscesses were scattered throughout every lobe of the lungs and ranged in size from miliary to one inch diameter. There was no obvious confluent pneumonia. The lungs were difficult to

handle at autopsy, the tissue being very friable as a result of the number of abscesses; the latter had no obvious walls and since they consisted of liquefied tissue, the lobes tended to break when the organs were lifted. The pus was non-mucoid but contained numerous necrotic flecks. The immediately surrounding lung tissue was congested. On slitting the bronchi some were seen to contain purulent fluid but this was not constant. The abscesses were not obviously related anatomically to the bronchi.

Microscopic appearances. The abscesses are composed of a central area containing polymorphs in various degrees of degeneration and liquefied tissue debris in which no trace of former structure can be seen; surrounding this is a zone of alveolar infiltration by polymorphs and fibrin deposition. The alveolar walls are undergoing necrosis. Exterior to this the alveoli are irregularly invaded by polymorphs and foamy macrophages. There does not appear to be any anatomical relationship to either septa or bronchi although many of the latter contain inflammatory debris.

BRONCHIECTASIS

Three of the 52 cases showed this lesion. During the course of another investigation carried out by the writer,

involving the examination of a large number of lungs from bovines of all ages, it became obvious that this is an important condition in cows leading to their rejection from commercial herds because of continued poor condition. It seems possible that many of these cases have their origin in calfhood pneumonia.

Case 1

Subject. Ayrshire female calf of unknown age but obviously stunted in growth and being about the same height as a calf of two to three weeks of age.

History. All of the calves on the farm were showing persistent coughing with an occasional animal developing an acute pneumonia. On account of its poor condition, this calf was slaughtered for diagnostic purposes. There was no history of purulent or foetid nasal discharge.

Post mortem findings. Lesions were confined to the right apical lobe. The lobe was dark brown in colour and there was complete collapse of the alveolar areas. The septa showed fibrous thickening and the bronchi were grossly dilated and bulged from the surface of the lung. This gave the lobe the appearance of several tubes of constant diameter separated by thin bands of fibrous tissue. On section, the bronchial walls were thickened and fibrous and the lumina were filled with

viscid muco-pus. The bronchial nodes were grossly hyperplastic.

Microscopic appearances (Fig. 47). The lumina are filled with pus in which little cytological detail can be distinguished. The bronchial epithelium is of the low cuboidal type and lies on top of a wall thickened by fibrosis and mildly infiltrated with a few macrophages, lymphocytes and plasma cells. There is no evidence of hyperplastic lymphoid activity in the walls or peribronchial areas. The alveoli are completely collapsed and do not contain any inflammatory cells. The septa are thicker than normal due to an increase in fibrous tissue. The process does not appear to be an active one.

Case 2

Subject. Ayrshire heifer calf aged five weeks.

History. This calf was one of several which died of cuffing pneumonia in an outbreak involving most of the calves in the herd.

Post mortem findings. The lungs showed the lesions of cuffing pneumonia, but in addition there was bronchiectasis of the right apical lobe. The bronchi were not so markedly dilated as those in the preceeding case but the process was involving the smaller as well as the larger lobes and this gave the lobe a more reticulated appearance.

Microscopic appearances. The bronchial and bronchiolar lumina are filled with degenerated pus. The epithelium is of the low columnar type. The main feature is the presence, in the peribronchial area, of lymphoid cuffs containing large "germ centres". There is surrounding alveolar collapse and some septal fibrosis. Acute inflammatory changes are absent.

This appearance approximates to that of human follicular bronchiectasis (Whitwell, 1952). It seems reasonable in this case however, to relate the bronchiectasis primarily to the cuffing pneumonia. It is worth while noting that the right apical lobe of the bovine is supplied by a bronchus which arises in the trachea several inches anterior to the bifurcation of the bronchi and that this bronchus descends almost vertically from its point of origin. It is possible that bronchial drainage from this lobe is inferior to that of the other lobes.

Case 3

Subject. Ayrshire heifer calf of unknown age; probably about 10 weeks.

History. This calf was one of several in a herd which died of cuffing pneumonia. The history was typical of that disease.

Post mortem findings. The apical lobes showed typical lesions of cuffing pneumonia. At the posterior end of the left main

dorsal diaphragmatic bronchus there was a saccular dilatation filled with pus. The dilatation was two inches broad and one and a half inches long. The wall of the bronchus at this point was thin and flaccid. There was no surrounding pneumonia and no obstructive lesion proximal to the dilatation. Microscopic appearances. The wall of the bronchus has lost its epithelium and is lined by a thin layer of fibrinoid material. The tissue immediately subjacent to this is relatively vascular fibrous tissue with a moderate infiltration of plasma cells and macrophages. There is no associated lymphoid hyperplasia or pneumonia.

No reasonable explanation of the cause of this lesion was found. It is possible that a foreign body had been present and was subsequently discharged.

DISCUSSION

A striking point which emerges from a study of the literature of calf pneumonia is the paucity of information on the detailed pathology of the disease. Most workers refer to calf pneumonia as if it was a single entity; a few describe briefly the histology of some of the cases with which they worked (e.g. Smith, 1921; Langham, Thorp, Ingle and School

1942; Levi and Cotchin, 1950) but no one has attempted to classify any reasonable number of cases on a detailed histological basis. In addition several of the types of pneumonia described in the present work have not been previously described at all. Most of the papers published have dealt with etiological factors; none of these arrived at any definite conclusion as to primary causation. It seemed to the present author that until various morphological criteria were established the comparison of different workers' results would be extremely difficult, if not impossible; in addition it was considered that a study of the histopathology might throw some light on the etiological factors involved.

The main purpose of this work, therefore, is to suggest a classification based on morphology of the various types of calf pneumonia. A few pilot experiments on etiology were carried out but considerations of expense, accommodation and labour prevented any large scale investigation of the type required for the successful rearing, in isolation, of experimental calves for this purpose. It is felt that too little attention has been paid by most workers to the obtaining of completely normal calves of an age suitable for experimentation.

The 67 cases recorded here may be insufficient for a complete classification of calf pneumonias but the histopathology

was so strikingly different in many cases to justify at least a partial subdivision.

The pneumonias associated with "white scour" have been discussed in the section on that disease. It is possible that pulmonary lesions are an integral part of the fully developed "white scour" syndrome. In addition it seems almost certain that one or more of the "specific" pneumonias may complicate this disease since "white scour" causes a very marked weakening of the affected animal's general condition.

In bronchopneumonia of the young bovine few really marked differences from the typical condition in other species were noted. In the calf there is probably more macrophage and mesenchymal giant-cell reaction than in other species; however it is considered that the number studied in this series is insufficient to make any definite differentiation between cases of this group. No factors concerning the possible etiology of simple "typical" bronchopneumonia emerged from this study. A careful search was made for basophilic and eosinophilic intracytoplasmic and intranuclear inclusion bodies in all cases, without success. One exception with regard to etiology was aspiration pneumonia, the etiology of which appears obvious. Under the present conditions of rearing calves artifically such cases must be not uncommon.

Acute necrotising bronchopneumonia might be reasonably thought to have a basis of aspiration. This pneumonia, however, has been seen in enzootic form and has involved calves which had not been force-fed in any way.

An original description of interstitial pneumonia and its probable pathogenesis is given. The histological features all point to this condition originating in the pulmonary septal vasculature and spreading from there to the lung parenchyma. The primary cause of this lesion is not apparent. In some cases it appears to develop from a septicaemia originating in a focal septic lesion such as umbilical or urachal abscesses or breakdown of a peptic ulcer. These are, of course, sporadic cases but the disease also occurs in outbreaks where no common septic focus is obvious. It was also found in small areas in lung showing other pneumonias; this has been interpreted as intrapulmonary vascular spread following involvement of septa in a purulent process.

The description given of inclusion body pneumonia is also original; no account of this condition in calves appears in the literature. It is well known that epithelialisation of alveoli can be caused by many and varied stimuli. Osteever et al. (1943) list at least 12 different causes, most of which are of an irritative non-necrotising nature. Many of these

can be excluded in the cases here described, leaving for consideration bacterial pneumonia, lipoid pneumonia, collapse and virus infection.

Greever et al. state that although some epithelialisation may be found in unresolved cases, they never saw it in acute lobar pneumonia. None of my cases shows the intra-alveolar fibrosis or other features of an unresolved pneumonia. There was no evidence of lipoid phagocytosis or of epithelium in collapsed foci, all the affected alveoli being fully distended.

The alveolar epithelialisation with proliferation to form giant-cells containing eosinophilic inclusion bodies closely resembles that seen in lungs from cases of human measles, giant-cell pneumonia of infants and canine distemper. In measles and distemper there is a tendency for the proliferative process to be concentrated around the bronchioles; in the calf, on the other hand, the epithelium has lobular distribution. This might be explained by the fact that in the calf the bronchiolar or lobular unit is small and much more isolated anatomically from other lobules than in the dog and man. Moreover in measles the virus pneumonia is not the main manifestation of the disease which affects also the cutaneous and lymphatic systems. The virus of canine distemper is localised in the keratinised appendages and the brain. Only

pulmonary lesions were found in the calves described here.

In measles, where the exact date of exposure to infection is often known, the virus pneumonia is said to begin about the seventh day and to disappear on the fourteenth day when purulent bronchopneumonia may supervene (Roberts, personal communication). It is possible that in calves, too, a purulent process may obscure such a primary lesion so that in many cases only the later stages of the disease are seen.

It would be rash to postulate a virus etiology for these cases of calf pneumonia on morphological grounds alone, but the possibility must be considered since the cases described present features almost identical with those of two proven virus diseases.

Inclusion bodies could not be demonstrated in the other epithelialising pneumonias described. It is impossible to say, in the cases examined, if these represent a stage in the development or resolution of inclusion body pneumonia or whether they are part of a different process. It was interesting to note in one of these cases the formation of hyaline membranes in alveolar ducts and alveoli; I have seen this lesion commonly in older bovines suffering from dyspnoea, especially in Dictyocaulus viviparus infection. It appears to be identical to the human "rheumatic" or "acute heart failure" lung.

It is unknown if the cases of aspergillosis described were primary or secondary infections; no accurate history of the use of antibiotics could be obtained. There was, however, on one farm, a simultaneous outbreak in turkey poults. The lesions in the calf do not appear to have been previously described.

The etiological aspects of cuffing pneumonia are discussed in the section on that disease. There is no description in the literature (except that of Jarrett et al. 1953 and 1954, and Jarrett 1954) of this disease although some of the cases described by Smith (1921) and Levi and Cotchin (1950) might have fallen into this group. The essential feature of this condition is a peribronchial lymphoid hyperplasia unaccompanied by any fibrotic or chronic inflammatory changes. It is easily transmissable to experimental calves but the etiological factor or factors involved have not yet been determined. The condition appears to be one of the commonest and most economically serious, pneumonias of the bovine. The clinical and pathological similarities of cuffing pneumonia and virus pneumonia of pigs are very interesting.

Bronchiectasis and pulmonary abscesses are of importance largely because they are common residual lesions after pneumonia has resolved. The affected animal shows a poor growth

rate but, because of return of respiratory function to normal, is often kept alive and under treatment for a considerable time. Such animals rarely become economically worth retaining. Bronchiectasis is a lesion commonly seen in the knackeryard in "cast" or wasting bovines.

CONCLUSIONS

This work has demonstrated that there are several at least morphologically distinct pneumonic diseases of the calf. It is thought that the classification suggested might form a basis for an enquiry into the various etiological agents involved.

"NAVEL-ILL"

Introduction

"Navel-ill" is a term applied in veterinary medicine to young animals of all species which show an abscess in one or more of the umbilical structures, i.e. the subcutaneous and muscular tissues of the umbilical ring, the umbilical vein or veins, the umbilical arteries and the urachus. This primary lesion may lead to suppurative omphalophlebitis or arteritis, liver abscesses, pyaemia, septicaemia or peritonitis. It is also common in calves, however, to find no demonstrable cause of death, the only lesion being an umbilical abscess. It is of interest, in regard to the last point, that I have found in several hundred healthy experimental calves used in an experiment outwith the scope of this work, many animals of all ages up to several months, which had localised abscesses of the umbilical ring; and many young normal bull calves of up to one week old, sent to Glasgow Corporation abattoir, show this lesion. In the N.V.M.A. Report on the Diseases of Live-stock (No. 12. 1947) it is stated with regard to septicaemic diseases of young calves that, "The mode of entry of the organisms into the blood stream is not clearly established, although there is a strong presumption that they do so through the wall of the alimentary tract in white scour and that in

some cases of joint-ill the infection is disseminated from a focal infection of the umbilicus. The status of these diseases is rendered uncertain by the fact that the organisms which are associated with them are not infrequently isolated from normal animals, and, although they may be present in large numbers and in pure culture in association with the disease, the general failure to reproduce symptoms and lesions by artifical infection, must lead to the conclusion that the primary causes of these diseases are unknown." This is an accurate summary of the present state of knowledge since it draws attention to the fact that a precise relationship between an umbilical abscess and generalised disease is not always demonstrable.

Earlier writers (e.g. Hutyra et al. 1938) did not draw a sharp line of demarcation between scour, septicaemia and navel-ill; and the above quotation leaves the impression that there are no cases in which a definite diagnosis can be made. This is far from being the case. Navel-ill appears to be a disease, in foals as well as in calves, often directly attributable to poor post-parturient hygiene. Jordan (1933) discussing calf mortality statistics for 1931 and 1932 attributed about 50% of calf deaths to navel-ill. Since that time there have been great improvements in Scotland in dairy hygiene and navel-ill is no longer a serious cause of calf mortality. In the present

series of 100 autopsies only nine (9%) had umbilical abscesses. Of these, four probably died of other causes. It must also be borne in mind that in an outbreak of "white scour" or pneumonia many calves may be ill and several die and only one be sent for autopsy. The actual incidence of navel-ill must therefore be considerably less than 9%.

The "fully developed" picture of navel-ill consists of an umbilical abscess, suppurative thrombophlebitis, liver abscesses, pneumonia and purulent polyarthritis ("joint-ill"). All variations are found between this and a simple sclerosed quiescent abscess of the external umbilical ring.

Results

Table 12 shows the distribution of lesions throughout the various organs in my nine cases.

The nine cases are summarised below and the etiological significance of the navel abscesses are discussed.

Case 1

This five week old calf was ill for only two days; it developed dysentery and showed signs of abdominal pain. No others in the herd were affected. At autopsy the only lesions found were a sclerosed abscess of the external umbilical ring and severe haemorrhagic enteritis of the colon. Bacteriological

examination (by Mr. Michna, Glasgow University Veterinary School) failed to reveal any organisms in the internal organs and only B. coli from the bowel contents; Coryne. pyogenes were recovered from the umbilicus.

It is considered unlikely that the umbilical lesion played any part in the disease process.

Case 2

No clinical details were supplied. The umbilicus was swollen and incision revealed a large subcutaneous abscess four inches in diameter. The umbilical vein was thickened and oedematous and contained a mass of septic thrombus; the vein terminated in the liver in a small abscess of one inch diameter. The lung showed marked interstitial pneumonia involving the greater part of all lobes. There was a localised peritonitis over the internal umbilical ring; there was adhesion between the latter and the duodenum. It is considered that the umbilical lesion was responsible for the other lesions in this case.

Case 3

No clinical details were submitted. There was an umbilical abscess of two inches diameter in direct continuity with the umbilical vein; the latter showed septic thrombophlebitis

of the distal two inches of its length. The liver, spleen and kidneys were normal. The lungs showed consolidation of, and abscesses in, three lobes. The left fore fetlock joint and the right fore knee joint were markedly swollen and contained pus under pressure. There was no erosion of the articular cartilages. The periarticular tissues were acutely inflamed. Coryne. pyogenes was recovered from the umbilicus, lung and joints. The umbilical lesion is a possible source of pyaemia in this case; in view of the fact that the umbilical vein was affected, it is strange that there was no lesion in the liver.

Case 4

This calf was three days old when it died suddenly; previous illness was not noticed. 10 calves had recently died on this farm from white scour; there was diarrhoeic staining of the perineum in this case at autopsy. At the external umbilical ring there was a small abscess of one inch diameter. The umbilical vein and internal organs were normal. Coryne. pyogenes was isolated from the abscess; Proteus vulgaris and a group D streptococcus were isolated from the lungs. It is possible that this calf died of neonatal "septicaemia" and that the umbilical lesion was an incidental finding.

Case 5

No clinical details were supplied. There was an umbilical abscess and marked suppurative omphalophlebitis. The lower left part of the liver was studded with abscesses of about 1 cm. diameter. The lungs showed marked bilateral interstitial pneumonia. There was a small abscess (7 mm. diameter) of the right cerebral hemisphere. There was no pyaemic nephritis but, in the medullary rays of the kidney, there was perivascular infiltration by plasma cells and lymphocytes. Only Proteus vulgaris was isolated from the umbilicus and internal organs. It is considered that the primary focus of infection in this case was the umbilicus.

Case 6

This calf was three weeks old; the farmer had not noticed any symptoms. The umbilicus was swollen and the surrounding tissues were acutely inflamed. The whole of the umbilical vein showed suppurative thrombophlebitis. Both umbilical arteries were thickened and filled by septic thrombus in their distal two inches. All lobes of the liver were enlarged and riddled with abscesses; one of these was four inches in diameter. Fibrosis was absent and the inflammatory process was obviously still actively spreading. There was a tangle of adhesions in the porta hepatis area between the liver and the

small intestine. Diaphragmatic adhesions were also present. The spleen was about twice normal in size; the pulp was soft and congested. There was a diffuse acute peritonitis.

The umbilical lesion is considered to be primarily responsible in this case.

Case 7

This calf was three weeks old. No other history was available. There was no actual umbilical abscess but the umbilical arteries were adherent to the internal ring. The arteries appeared to be normal. At the anterior pole of the bladder was a large (three inches diameter) urachal cyst filled with green pus. Adhesions were present between this, the urinary bladder and the umbilical ring. A peptic ulcer which showed no evidence of acute change was present at the pylorus. The cause of death was not determined. C. pyogenes was recovered from the urachal pus but not from the organs.

It is doubtful if the urachal lesion was responsible for death.

Case 8

No clinical details were submitted. The umbilicus was swollen and permeated by abscess tracks containing greenish pus; the surrounding tissues were acutely inflamed.

Suppurative omphalophlebitis was present throughout the length of the vein. The liver was enlarged and riddled with small abscesses. The spleen was enlarged, congested and pulpy. There was purulent arthritis, without erosion, of both carpi and stifles. The umbilical lesion was obviously primary in this case.

Case 9

This calf was aged five weeks. It had shown respiratory symptoms for several days. There was thickening and fibrosis of the umbilical ring; a small encapsulated abscess was present in the subcutaneous tissue over the ring. At the anterior pole of the bladder there was a vestigial urachus which contained an encapsulated abscess of 1 cm. diameter. The anterior lobes of the lung showed marked cuffing pneumonia; the diaphragmatic lobes were emphysematous.

The umbilical lesion was considered to be incidental.

It would appear from these findings that in only five of the nine cases the umbilical lesion was responsible for initiating a pyaemia.

In these five cases the lesions were all of an acute advancing type which showed little or no fibrosis. In view of this it is interesting to note that the affected calves

Table 12

The distribution of lesions and the age of the calf in nine cases of suppurative omphalitis.

Case	Age Days	Umbilicus	Umb. vein	Umb. artery	Urachus	Liver	Lungs	Spleen	Kidneys	Brain	Joints	Other
1	35	+	-	-	-	-	-	-	-	-	-	-
2	?	+	+	-	-	+	+	-	-	-	-	Localised peritonitis
3	?	+	+	-	-	-	+	-	-	-	+	-
4	3	+	-	-	-	-	-	-	-	-	-	-
5	?	+	+	-	-	+	-	-	+	+	-	-
6	21	+	+	+	-	+	-	+	-	-	-	peritonitis
7	21	-	-	-	+	+	+	-	-	-	-	Peptic ulcer
8	?	+	+	-	-	+	-	+	-	-	+	-
9	35	+	-	-	+	-	-	-	-	-	-	-

were all several weeks old and it appears unlikely that the lesions would be steadily progressive from birth. It is possible that some factor such as sucking the umbilicus, a "stable vice" not uncommon in penned, pail-fed calves may provide a persistently exposed umbilicus and allow pathogenic agents a nidus for infection.

ACUTE LEAD POISONING

Two cases were diagnosed as acute lead poisoning. There was no history of illness in either case, the animals being found dead. Post mortem and histological examination failed to reveal any structural abnormality.

Portions of liver and kidney were submitted to Mr. J. S. S. Inglis of the Department of Animal Husbandry, University of Glasgow Veterinary School who carried out the chemical analyses for lead. In both cases the levels found were considered pathognomonic of acute lead poisoning. The results are given below in Table 13.

The N.V.M.A. Publication No. 12 (The Husbandry and Diseases of Calves) states that lead poisoning is a not uncommon condition in calves. The commonest source appears to be lead paint which the calves ingest from old doors or from orchards recently

Table 13

The lead content of the livers and kidneys of two calves dead of lead poisoning.

Organ	Case 1	Case 2
Liver	74 parts per million	120 p.p.m.
Kidney	125 parts per million	308 p.p.m.

sprayed with lead arsenate solution: the former are commonly used for penning calves in a cow byre; the latter conditions might easily obtain since the piece of grass nearest to the house is commonly used for calves which are still being partly fed by hand.

TUBERCULOSIS

Two calves of four to six weeks of age were submitted for autopsy, from one farm, with a history of unthriftiness and persistent diarrhoea. The farm was attested (i.e. deemed free from tuberculosis as judged by the tuberculin test) and there was no history of any other disease among the young stock. These two calves were the only animals being milk fed at the

time. (On receiving the report that the calves were tuberculous, steps were immediately taken to discover the source of infection on the farm. It transpired that one cow had first given a "doubtful" reaction to the intradermal test but had "passed" on retesting. This animal was suffering from a chronic mastitis which had failed to respond to antibiotic therapy. The milk was examined and found to contain acid fast bacilli. The cow was slaughtered under the Tuberculosis Order and the diagnosis of tuberculous mastitis confirmed. The herd was then retested and seven animals reacted to the test; the attestation certificate was therefore withdrawn.)

Post mortem findings. The calves showed identical lesions; one only will be described. Lesions were confined to the alimentary tract, mesenteric nodes and peritoneum.

Throughout the length of the jejunum and ileum there were irregular ulcers ranging in size from pinhead to several inches long. The edges were uneven and the shallow craters lined with red crumbly material. The bowel wall at these points was thickened and oedematous. Fibrosis was not a feature. The mesenteric nodes were grossly enlarged some being three inches instead of the normal half inch diameter. In some places they were adherent to the adjacent bowel. On section the nodes were replaced by a mass of caseous material. The process

extended locally to the surrounding mesentery.

Microscopic examination confirmed the post mortem diagnosis of acute caseating tuberculous enteritis and mesenteric lymphadenitis.

The bovine type of Myco. tuberculosis was isolated from this case.

It seems probable that infection was via the infective milk from the cow with the mastitis. It is possible that the milk from this cow was not being added to the pooled milk of the herd (this is common practice since the organisms present in the common type of mastitis, e.g. Str. agalactia impair the keeping of the milk and also the milk is often partially clotted) and rather than waste it, it was fed to the calves.

In the N.V.M.A. Publication No. 12 (op. cit.) it is stated that tuberculosis is chiefly of the thoracic type in the calf and that only when the dosage is very high do alimentary lesions occur. In this case pulmonary lesions were absent and the history is compatible with several large oral doses of bacilli.

SULPHONAMIDE POISONING

One case occurred in this series to which a diagnosis of possible sulphonamide poisoning was given.

Subject. Ayrshire heifer calf aged four weeks.

History. The calf had been ill from the first week of life when it showed dullness and scouring. In the next three weeks it gradually lost its appetite and became emaciated. It received sulphathiazole in standard dosage for three days under veterinary supervision; in the subsequent three weeks the farmer administered phthalylsulphathiazole each day without veterinary authority. The farmer did not admit to administering any more sulphathiazole. The calf was sent in for necropsy without any clinical details of the few days before death. No blood sample was available.

Post mortem findings. There was intense pulmonary congestion with diffuse consolidation of the anterior lobes. The heart and liver appeared normal; the spleen was congested. Infarction of the polyarteritis nodosa type was not seen. The kidneys looked normal; there was no gross crystalline deposit.

Microscopic appearances. The lungs show an acute purulent bronchopneumonia. The heart, liver and central nervous system are normal. The spleen shows many small areas of focal necroses with a cellular exudate consisting of polymorphs and

plasma cells. Some of these foci involve the walls of arterioles; others appear to lie at the periphery of the malphigian bodies unconnected with a blood vessel. Throughout the spleen and lymph nodes there is a marked erythrophagocytic reaction; the phagocytes appear to be increased in number and they contain both intact and fragmented erythrocytes (Fig. 48). The kidneys show the most striking changes. An acute interstitial nephritis is present (Fig. 49). This is almost wholly confined to the cortex and the intensity varies from place to place. In some foci only a few cells surround the glomeruli external to Bowman's capsule. In others the reaction is quite marked in this position and has spread to between surrounding tubules. Some of the larger aggregates show central necrosis involving a tubule. The exudate consists largely of polymorphs and plasma cells. In the medullary rays there is some round cell cuffing of small vessels but frank polyarteritis nodosa is absent. The epithelium of many tubules is swollen and excessively eosinophilic in H. & E. staining; necrotic cells are being shed into the lumina. Many eosinophilic casts are present in the tubules and some of the former contain crystals (Fig. 50); these are birefringent under polarised light (Fig. 51).

Sulphonamide intoxication may be broadly divided into two

groups: (1) showing massive crystalluria, and (2) the "anaphylactic" type. The changes found in the latter group can occur either singly or in combination and are (1) haemolytic anaemia, (2) agranulocytosis and leucopenia, (3) interstitial nephritis, (4) nephrosis, and (5) polyarteritis nodosa.

No blood sample was obtained from the present case so that anaemia was not diagnosed; the presence of excess erythrophagocytosis is however presumptive evidence of haemolytic anaemia. Interstitial nephritis, a degree of nephrosis and birefringent crystals in the tubules, were present. While no definite diagnosis can be made in this case it is thought that these facts and a consideration of the history justify a tentative diagnosis of sulphonamide poisoning. It is impossible to say whether or not death was due to this condition since there was also a fairly severe bronchopneumonia. Nevertheless, the condition of the animal must have been adversely affected by the presumed poisoning.

The practice of allowing farmers to use sulphonamides without supervision is well established. Some of the diseases subjected to this lay treatment, e.g. calf scours, have normally a high mortality rate and it is seldom that trouble is taken to find the exact cause of death. It may be that the condition is not uncommon in calves.

CYSTIC KIDNEYS

One case was encountered which might be classified thus although the "cysts" were not massive.

Subject. Ayrshire heifer calf aged 10 days.

History. There was no history of illness; the calf had been eating normally and was found dead by the owner.

Post mortem findings. The only features of note were the kidneys and the peri-renal fat. The latter was yellow, translucent and gelatinous. The kidneys were similarly affected and were larger and heavier (250 gm.) than normal (100 gm.). They were firm and of yellow-brown colour. The cortex and medulla showed no sharp line of demarcation; the component tubules were obviously grossly dilated but this appeared uniform. No single large cysts were present. The inner part of both medullae were grossly fibrosed. The heart showed left ventricular hypertrophy; the left ventricular wall was 4 cm. thick. Unfortunately, no C.S.F. was obtained for urea estimation.

Microscopic appearances. On cursory examination the general appearance is not unlike that of chronic nephrosclerosis. There are alternating bands of uniformly dilated tubules and thinner areas of fibrosis (Fig. 52). This intertubular fibrous tissue is quite cellular (Fig. 53). In some areas the fibrosis is more marked than in others (Figs. 54 and 55). In the

fibrotic areas, the atrophic tubules contain deeply staining eosinophilic hyaline casts. In the inner medulla most of the tissue is fibrous with a few collecting tubules scattered throughout. The glomeruli are unaffected (Fig. 56). The afferent arterioles and the vasculature in general, do not show hypertensive change; in some of the medullary rays there are a few foci of perivascular lymphoid cuffing. Two small abscesses are also present in the cortex of one kidney but they do not appear to be connected with the general process.

This condition is interpreted as being of the nature of congenital cystic disease.

(It is interesting to note that I have seen three heifers, one and a half years of age, from the same farm and sired by the same bull which had what appeared to be an advanced state of this condition. Pathological fractures and osteodystrophia fibrosa ("renal rickets") were present.)

PEPTIC ULCERATION

Four of the 100 cases showed this lesion. According to Hutyra and Marek (1949) gastric ulceration is not uncommon in the calf. They quote several workers as stating that the incidence is between 60% and 98% in young cattle. These

figures must apply to erosions, etc., and not to true peptic ulcer: no pathological description is given of the lesions. The etiology is unknown.

Two of the present cases appeared to be actively advancing and were associated with pneumonia: two appeared to be purely incidental findings. One of each type will be described.

Case 1

Subject. Ayrshire heifer calf aged three weeks.

History. The calf was one of 14 which died in an outbreak of pneumonia.

Post mortem findings. The calf died from acute necrotising bronchopneumonia which is discussed elsewhere and is not thought, in this case, to have any connection with the ulcer. The alimentary tract was normal apart from the presence, in the abomasum, of an ulcer. It was situated on the lesser curvature, two inches from the pylorus. It measured 2 cm. long by 1 cm. wide and had raised firm rounded edges and a depressed crater. The latter was lined by whitish granular debris. There was no indication of haemorrhage, surrounding inflammation or incipient perforation. The lesion appeared quiescent. A transverse band of puckered mucosa extended from each side of the ulcer.

Microscopic appearances. The lesion is typical of a peptic ulcer. At the edges normal mucosa overhangs the crater (Fig. 57). The latter is lined by fibrin, cellular debris, and polymorphs with pyknotic nuclei (Fig. 58). Immediately subjacent to this is a layer of young granulation tissue which shows no sign of acute inflammatory change. The vessels in this area are healthy (c.f. case 2). The musculature, although encroached upon is not heavily affected.

Case 2

Subject. Ayrshire heifer calf of unknown age but still on a milk diet.

History. No detailed history was supplied other than that the calf had pneumonia.

Post mortem findings. The calf died of severe acute interstitial pneumonia. An ulcer was situated on the lesser curvature of the abomasum, about three inches from the pylorus. It measured 1½ cm. long by 1 cm. wide. The crater was markedly depressed and both it and the immediately surrounding area appeared acutely inflamed. The edges did not overhang markedly and were only slightly raised.

Microscopic appearances. The ulcer is penetrating the whole of the mucosa and submucosa are encroaching upon the muscle

layers (Fig. 59). The crater is lined by fibrinoid necrotic debris and polymorphs and the whole thickness of the lesion is involved in an acute inflammatory reaction. Both the large and small (Fig. 60) vessels in the area show obliterative septic thrombosis and inflammation of their walls. That this acute process is superimposed on a true peptic ulcer can be seen on the left hand edge of Fig. 59; in this area the normal mucosal and submucosal elements are replaced by young connective tissue. It is considered possible that this lesion may have been primary to the interstitial pneumonia. In the human subject pyaemic spread to the liver may supervene as a complication of peptic ulceration (Cappell 1951).

CALF DIPHTHERIA

Calf diphtheria is an acute infectious disease caused by Fusiformis necrophorus. It is characterised by large ulcers and the formation of diphtheritic membranes on the mucosae of the tongue, gums and cheeks; these may coalesce and local spread may take place to the pharynx and larynx and distant spread to the lungs. The disease is well described in the literature (e.g. Hutyra et al. 1938). The condition responds well, if treated early, to penicillin, and nowadays is

seldom seen in the laboratory.

The two cases in this series were young Ayrshire calves of about one week old which were in a batch of calves bought in from a market for experimental purposes. They were rejected and slaughtered since they were unsuitable for the purpose for which they were required.

Case 1

This calf had a large ulcer one and a half inches long on the dorsum of the tongue. It was covered by a diphtheritic membrane and penetrated three-quarters of an inch into the substance of the organ. No other tissues were involved. Histological examination showed the process to be of an acute necrotising nature. Cellular reaction was minimal even at the advancing edge of the lesion. The subjacent muscle fibres were swollen and hyalinised.

Fusiformis necrophorus was recovered on pure culture from the lesion.

Case 2

In this calf the lesions were bilateral and involved the lateral surface of the gums and the adjacent cheeks. The intervening space was distended by diphtheritic debris. On the left side erosion of the cheek had occurred and a fistula

had formed to the exterior. The histological characters were similar to the last case; F. necrophorus was recovered on culture.

INTERVENTRICULAR SEPTAL DEFECT

This calf, aged three weeks, was submitted with a history of weakness and a "cardiac murmur". No accurate clinical data were obtained.

Post mortem findings. There was no cyanosis apparent on the carcase. The lungs were normal and appeared fully distended. The only lesion found was in the heart. There was an inter-ventricular septal defect one and a half inches long and one inch wide. The defect edges were smooth, rounded and covered by endocardium. The foramen ovale was patent but there was neither dextra-position of the aorta nor pulmonary stenosis. The heart was normal in weight and did not appear to have under-gone hypertrophy. The other organs were normal, in particular there was no marked hepatic venous congestion.

Septal defects appear to be not uncommon in the young of the domestic animals; cases have been recorded in the calf by Britton (1942), Kingman (1945) and Blood and Steel (1946).

CONGENITAL HYDROCEPHALUS

This calf was one day old when it was seen and destroyed by the veterinary surgeon. It was unable to stand and the eyes did not respond to light stimuli.

Post mortem findings. The forehead rose steeply behind the nose instead of the usual sloping face. The skull was bulbous rather than elongated and the frontal and parietal sutures were inperfectly closed. On removing the top of the skull the cerebral hemispheres were grossly enlarged, the convolutions flattened and the sulci shallow. On section the lateral ventricles showed the greater distension, the overlying brain substance being markedly thinned. The aqueduct of the Sylvius was almost completely stenosed; the fourth ventricle appeared unaffected. The case appeared similar to the typical condition in the human infant.

APPENDIX TO PART 2

Post Mortem Technique

The following routine was used in the necropsies described in this series.

(1) The external appearances were noted, including the general bodily condition, body development, state of dehydration, etc. The nose, eyes and external genitals were examined for the presence of discharges, the lips and buccal mucosa for ulceration or inflammation, and the anus and perineum for signs of scouring. The umbilicus was always carefully palpated.

(2) Deep incisions were made in the axilla and inguinal region, so that the calf would lie firmly on its back on the table, with all limbs projecting horizontally.

(3) A mid line incision was made in the skin from the mandibular symphysis to the pubis. The umbilicus was incised and the umbilical vein examined.

(4) A puncture through this incision was made into the abdominal cavity, and the index and second finger of the left hand inserted into the abdominal cavity. Using these two fingers as a guide, and to protect the abdominal viscera, a probe pointed bistoury was employed to open the abdominal cavity along the line of the skin incision.

(5) A lateral incision of the flank following the line of the last rib was made on each side. This exposed the abdominal viscera.

(6) The skin and muscles over the chest wall were reflected and the ribs and sternum removed by rib shears.

(7) The tongue, pharynx, larynx and cervical trachea were dissected out and were removed from the body along with the lungs and heart by cutting the thoracic aorta away from its dorsal attachments.

(8) The abdominal viscera were removed as follows:-

The rectum was incised as far back in the pelvis as possible. The mesorectum was cut away back to the root of the mesentery. An incision was made from the root of the mesentery round the dorsal border of the spleen and through the cardiac end of the oesophagus. On cutting the coeliac axis, the liver, stomach, intestine and spleen were freed. The abdominal aorta was then opened up as far as the internal iliac bifurcation. The renal arteries were opened and the kidneys removed.

(9) The pelvic viscera were dissected out.

(10) The calf was now turned over and an incision made in the skin from the muzzle to behind the axis. The skin was reflected away from the skull bones. Four saw cuts were made in the skull. The anterior transverse cut was made between the

anterior ends of the orbit and the posterior cut was made just anterior to the occipital crest. These were connected by two longitudinal incisions. The top of the skull was then prised up and the midline dural attachment broken down. The cerebrum was now exposed. The tentorium cerebelli was incised. A scalpel blade was inserted into the atlanto-occipital articulation and the spinal cord cut transversely. The complete brain was then removed by cutting through the cranial nerves in turn.

(11) An incision was made into each joint to expose the articular surfaces.

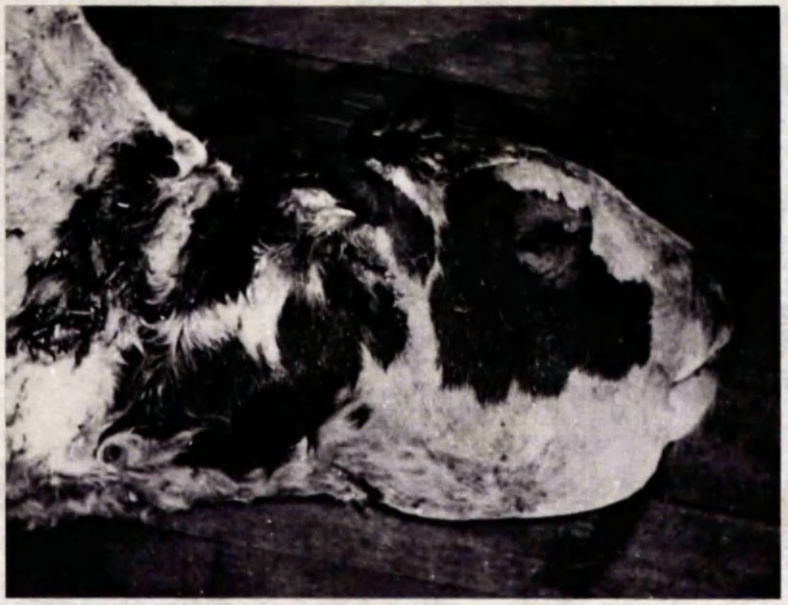


Fig. 1. Head of typical dropsical calf showing convex profile and oedema of the face and throat.

Fig. 2. Dropsical calf. Born alive and showing oedematous bullae on ears and swollen limbs.

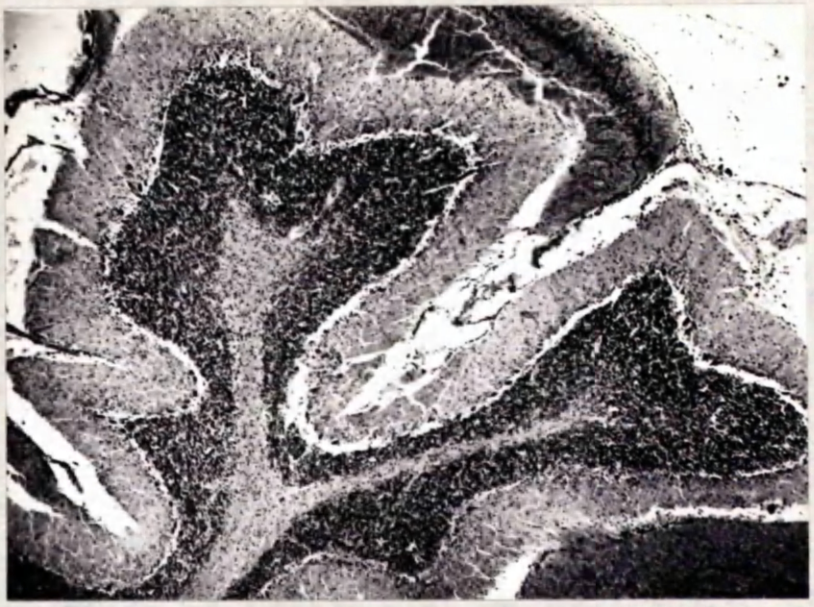


Fig. 3. Calf cerebellum: subarachnoid haemorrhage. H. and E. x 18.

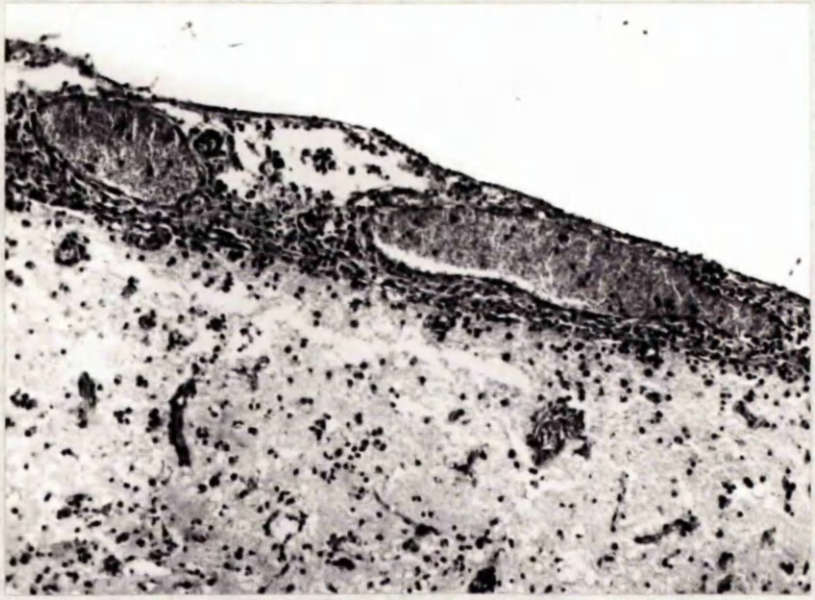


Fig. 4. Calf cerebrum. Purulent meningitis spreading to produce marginal encephalitis. H. and E. x 120.

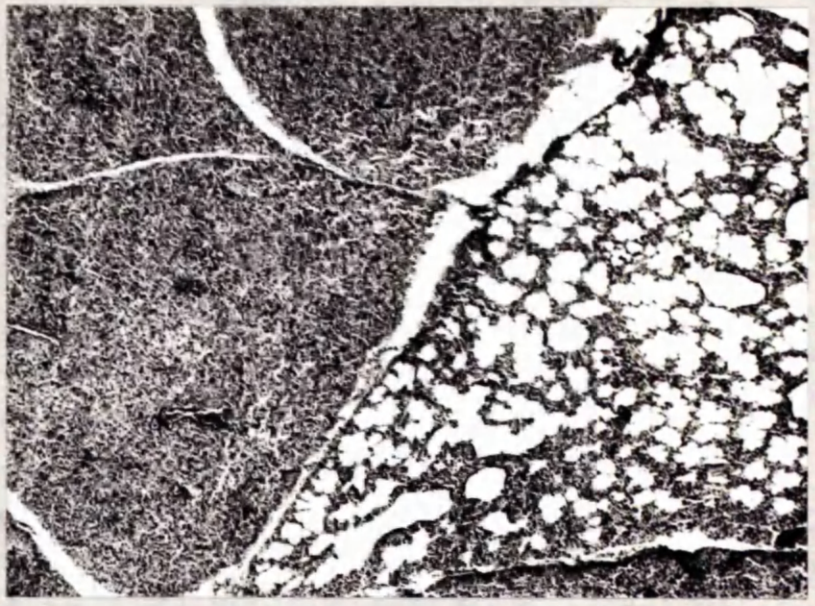


Fig. 5. Calf lung. Foci of necrosis and inflammation in the alveolar walls of a collapsed lobule. H. & E. x 35.

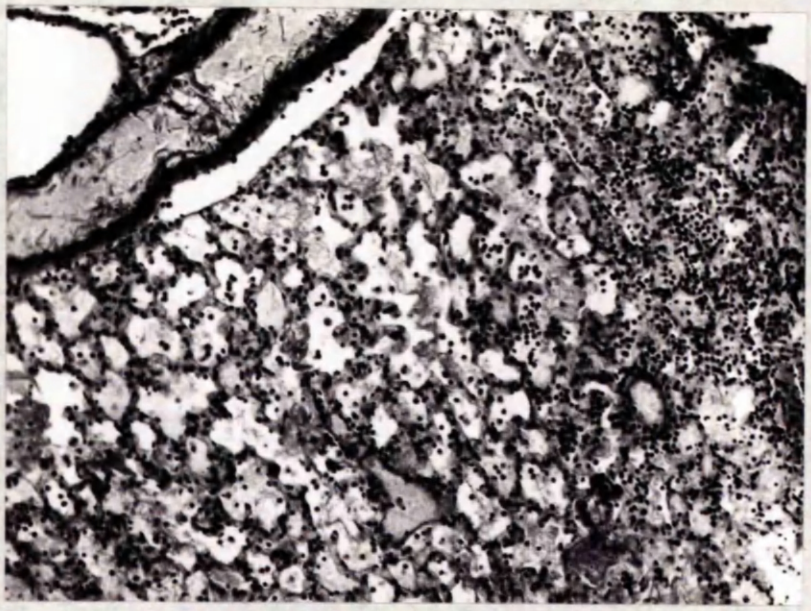


Fig. 6. Calf lung. Increase of cells in alveolar walls; early oedema and infiltration of alveoli; dilatation of septal lymphatics. H. and E. x 120.

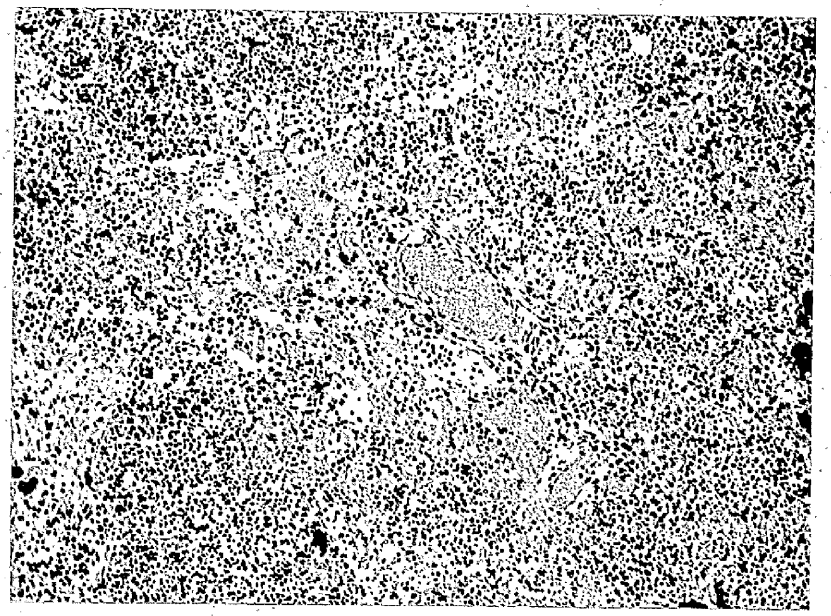


Fig. 7. Calf lung. Early inflammation involving alveoli in a case of "white scour". H. and E. x 100.

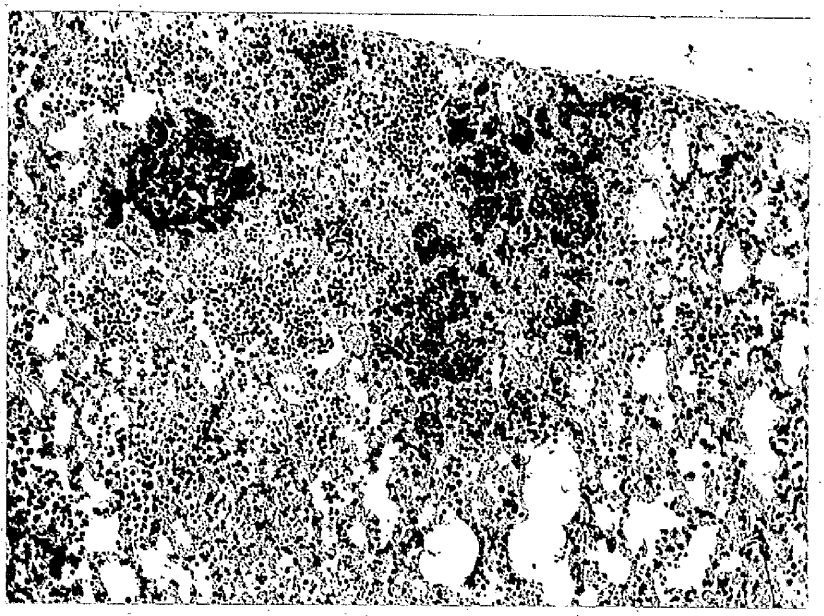


Fig. 8. Calf lung. Inflammatory exudate in terminal bronchi and spreading to alveoli. H. and E. x 100.

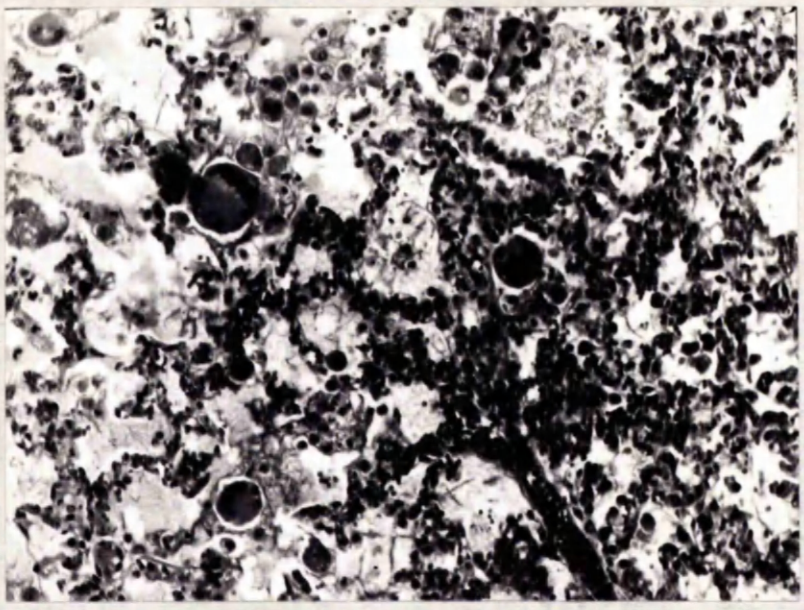


Fig. 9. Calf lung. Multi- and mono-nucleated macrophages in alveoli; alveolar oedema and mild fibrin deposition. H. and E. x 125.

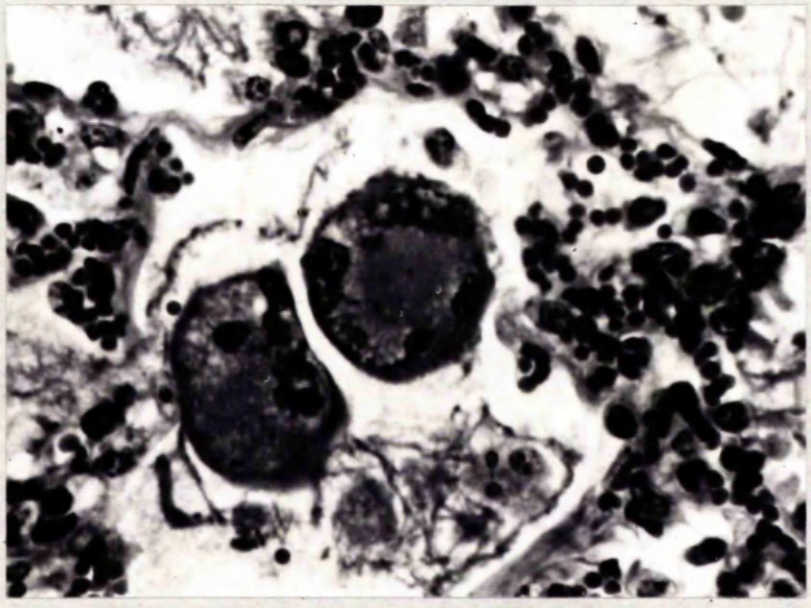


Fig. 10. Calf lung. Detail of multinucleated phagocytes of Fig. 9. H. and E. x 400.

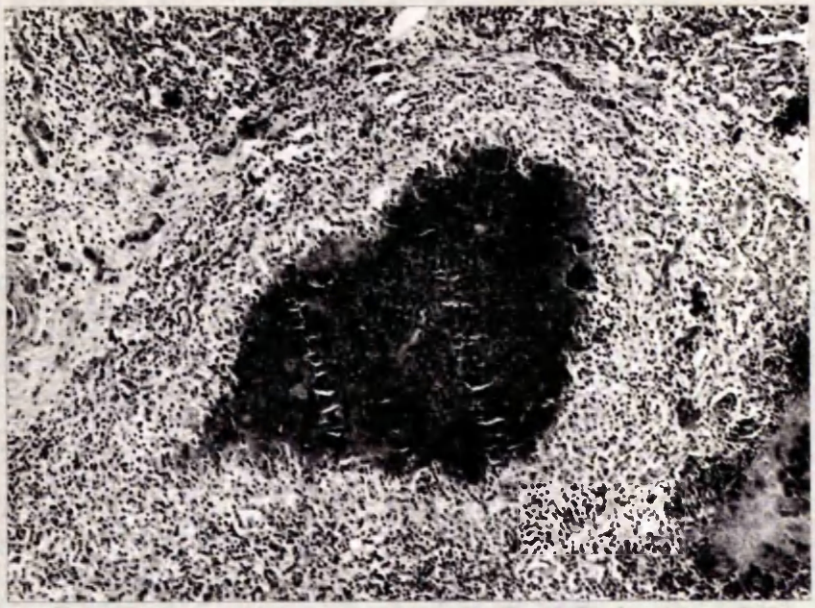


Fig. 11. Calf lung. Bronchial lumen filled with inflammatory debris; necrosis of part of bronchial wall. H. and E. x 50.

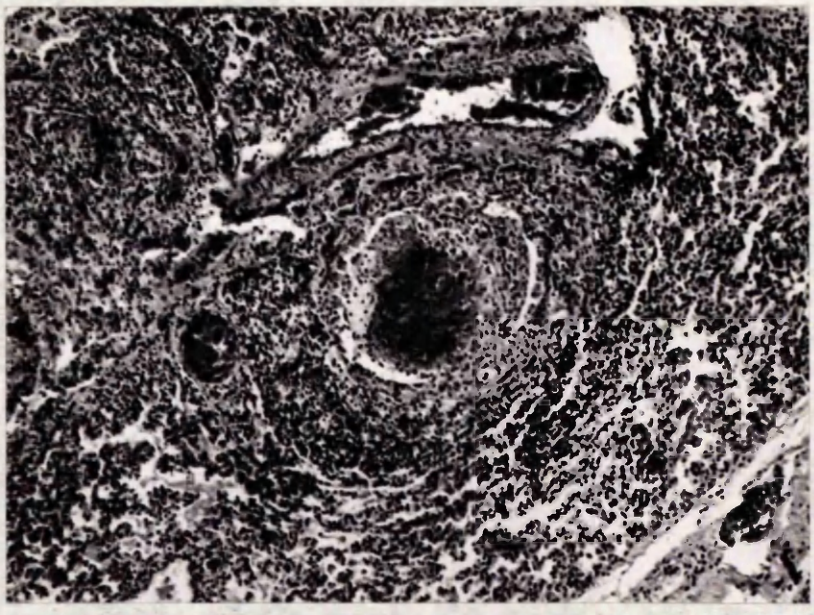


Fig. 12. Calf lung. Bronchiolar lumen filled with inflammatory exudate and with the mural structures still recognisable. The surrounding alveoli are relatively unaffected. H. and E. x 50.

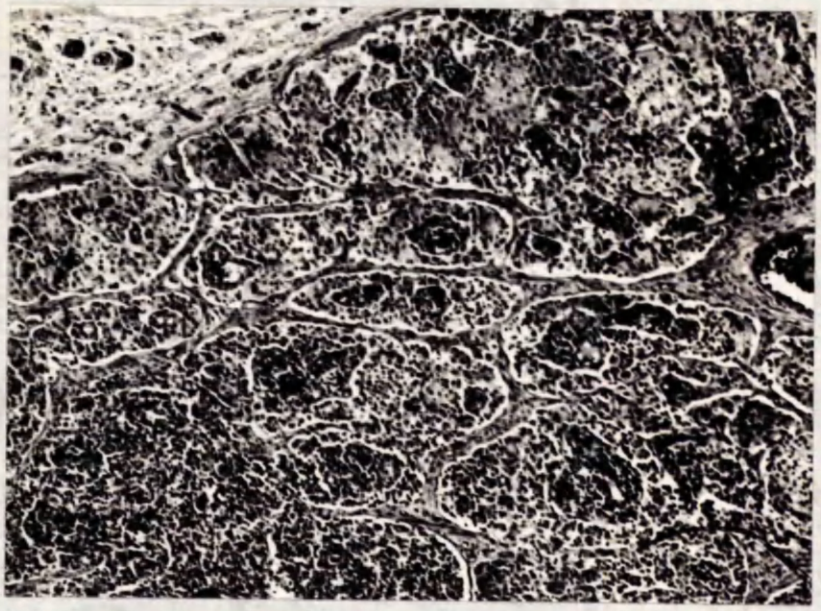


Fig. 13. Calf bronchial node. Medullary sinuses filled with pulmonary macrophages. H. and E. x 60.

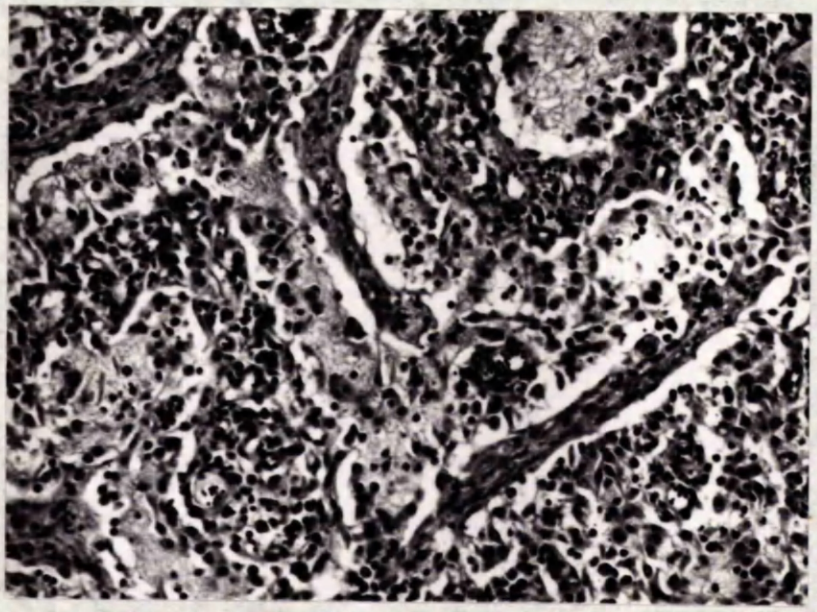


Fig. 14. Calf bronchial node. Detail of Fig. 13. Sinuses with macrophages and fibrin strands. H. & E. x 180.

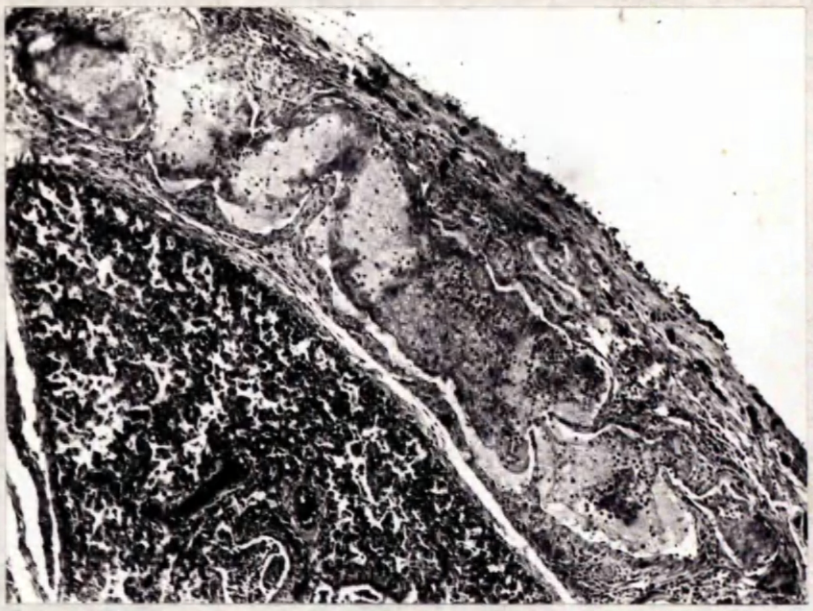


Fig. 15. Calf lung. Dilatation, thrombosis and infiltration of subpleural lymphatics. Note lymphatic valves. H. and E. x 60.

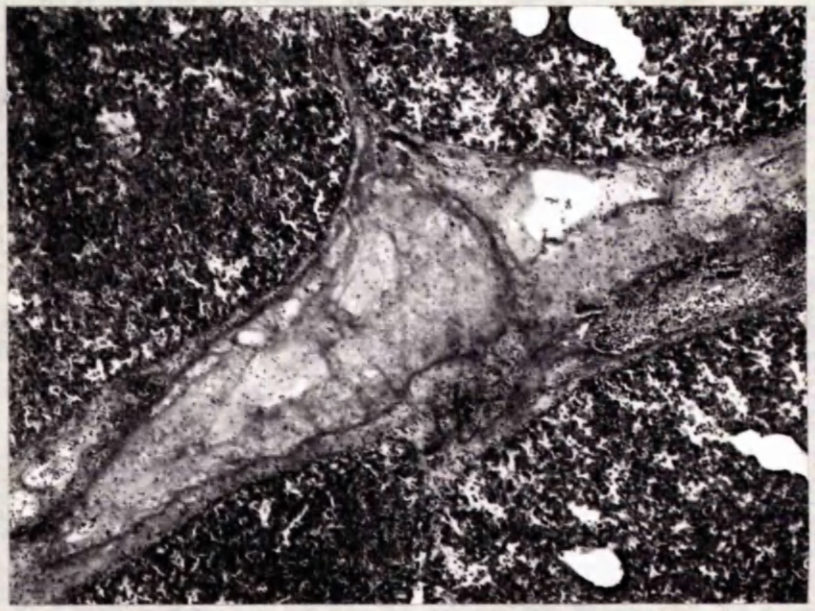


Fig. 16. Calf lung. Interstitial pneumonia, stage 2. H. and E. x 35.

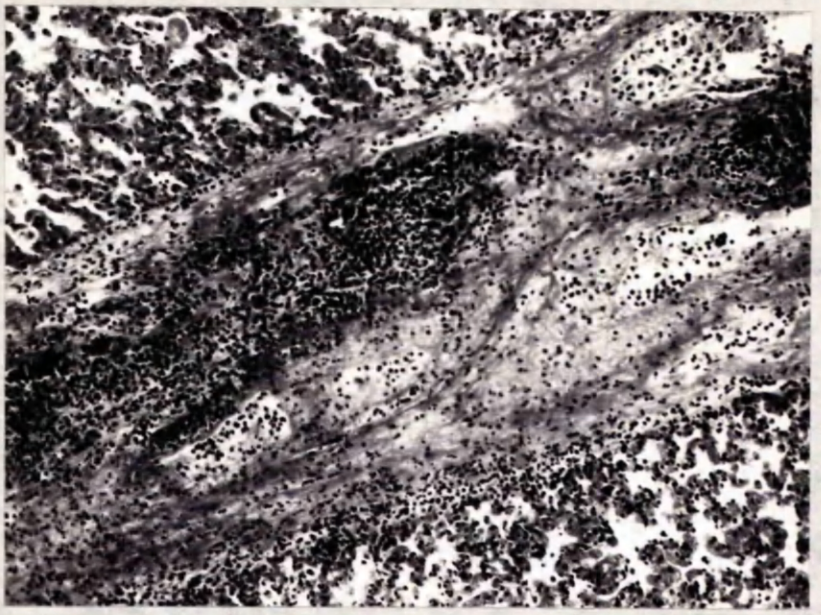


Fig. 17. Calf lung. Interstitial pneumonia, stage 3. H. and E. x 100.

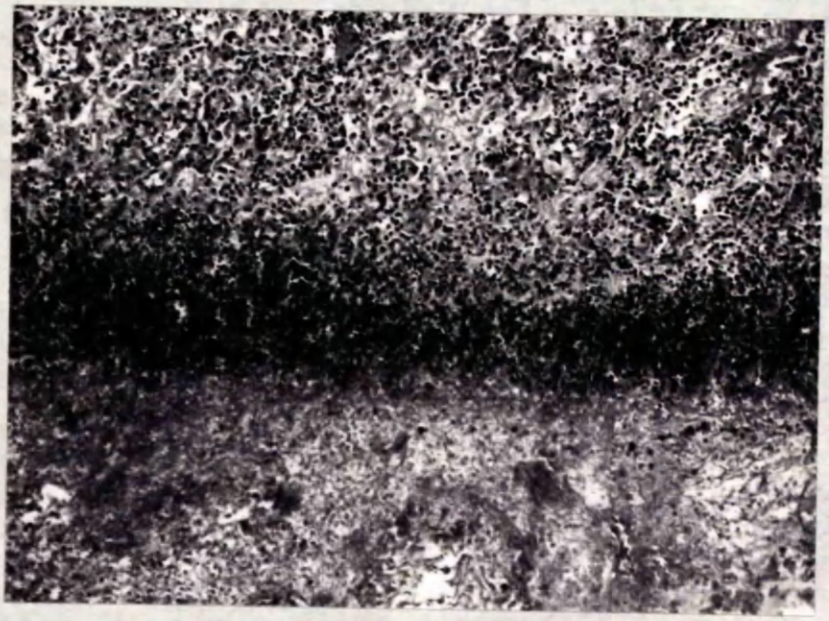


Fig. 18. Calf lung. Interstitial pneumonia, stage 4. H. and E. x 100.

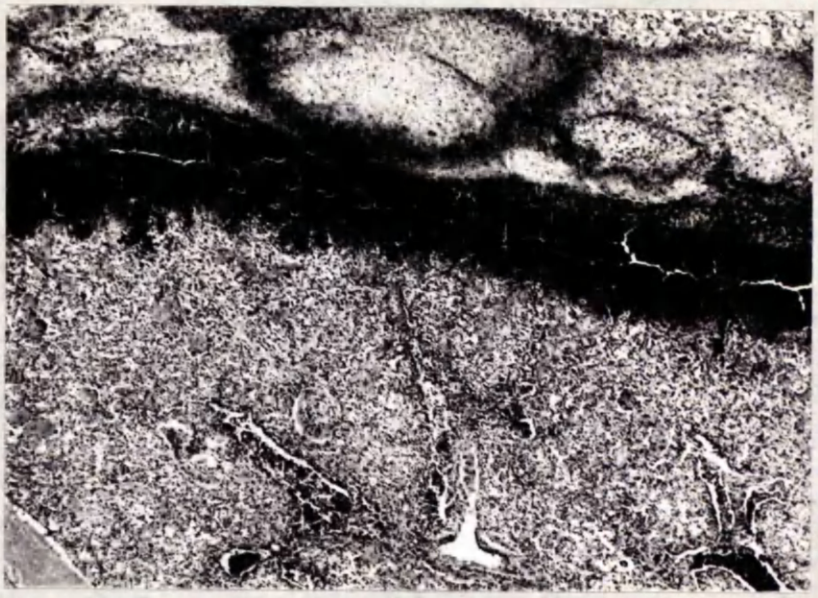


Fig. 19. Calf lung. Interstitial pneumonia, stage 5. H. and E. x 35.

Fig. 20. Calf lung. Interstitial pneumonia, stage 5. H. and E. x 120.

Calf 21. Calf lung. Interstitial pneumonia, stage 6. H. and E. x 35.

Fig. 22. Calf lung. Interstitial pneumonia, stage 7. Surviving tissue in centre. H. & E. x 8.

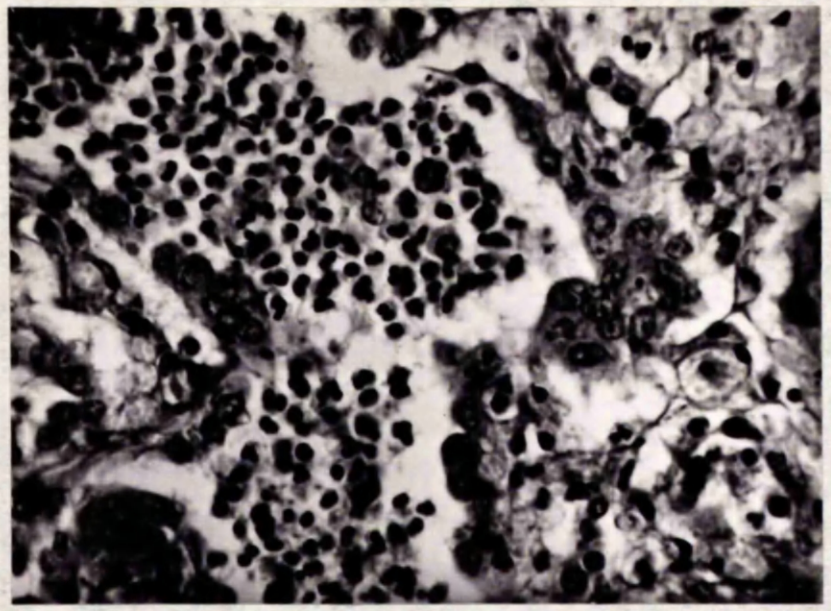


Fig. 23. Calf lung. Epithelial giant-cell formation in respiratory bronchiole and alveoli. H. and E. x 410

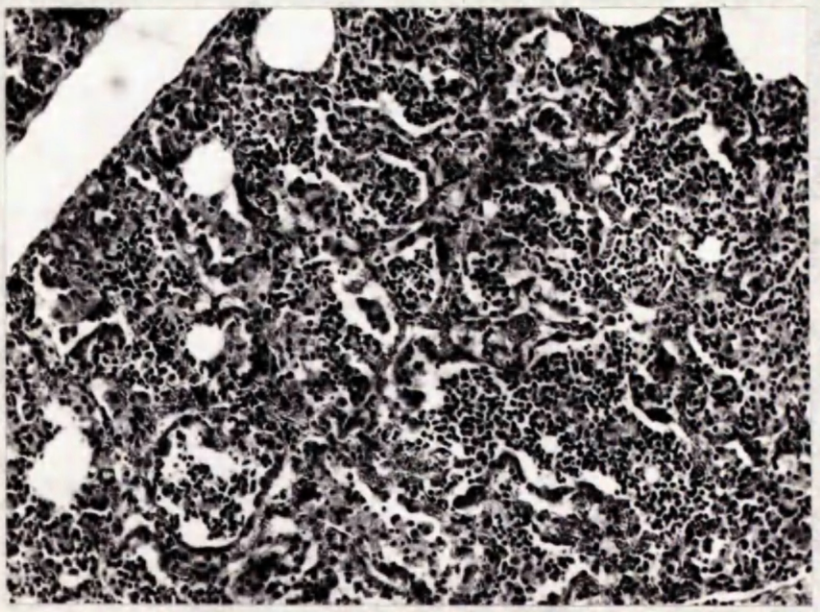


Fig. 24. Calf lung. Epithelialisation of alveoli involving greater part of lobule. Moderate superimposed polymorph infiltration. H. and E. x 100.

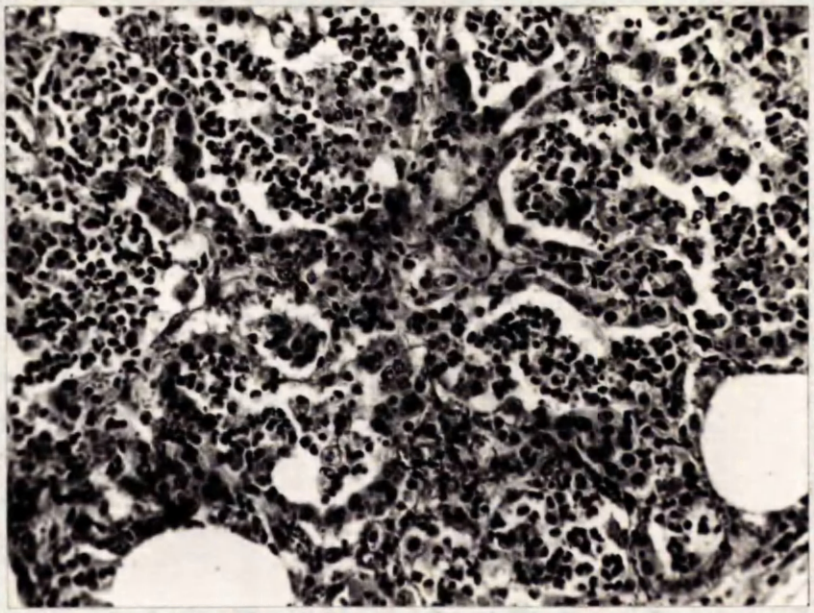


Fig. 25. Calf lung. Detail of lobule in Fig. 24. Note epithelial giant-cell formation. H. and E. x 150.

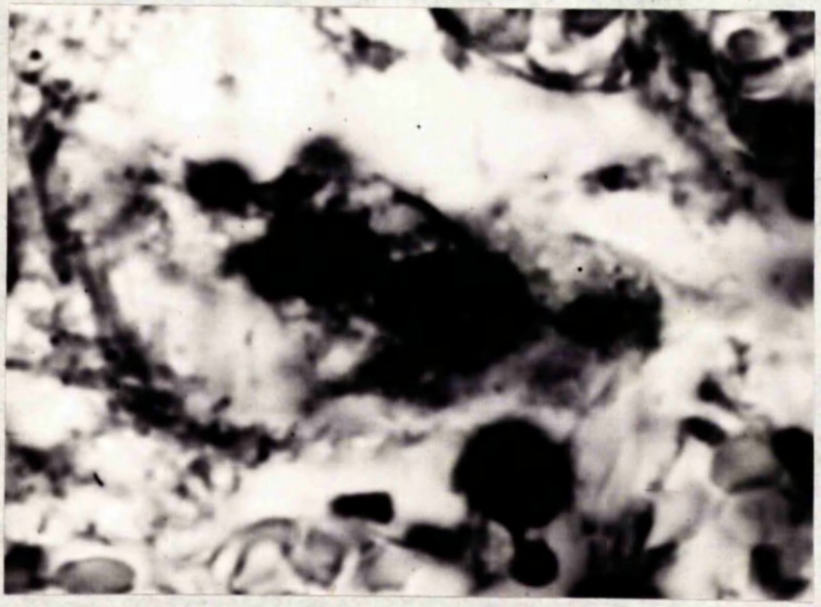


Fig. 26. Calf lung. Inclusion bodies in proliferated pulmonary epithelium. Eosin-phloxine-tartrazine x 1,400

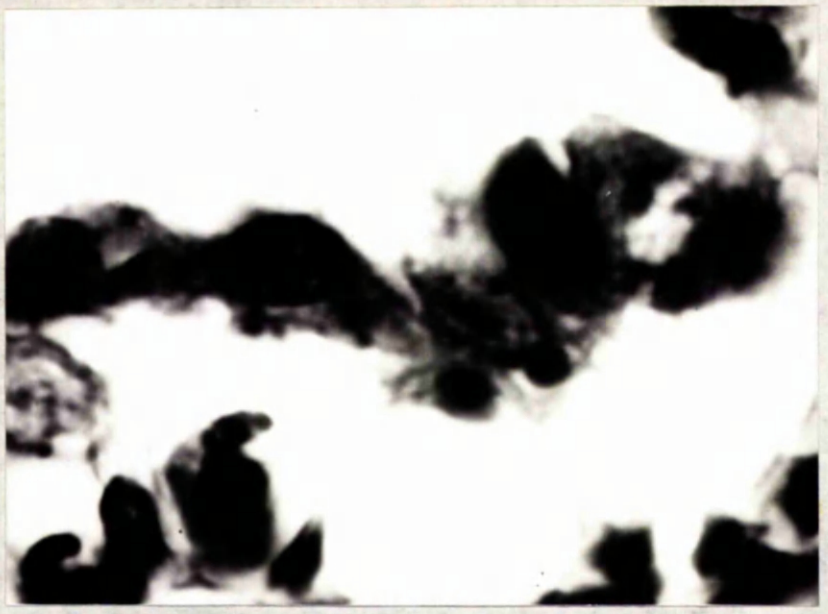


Fig. 27. Calf lung. Polymorphs in alveolar lumen; alveolar epithelium with intracytoplasmic inclusion bodies. Eosin-phloxine-tartrazine x 1,400.

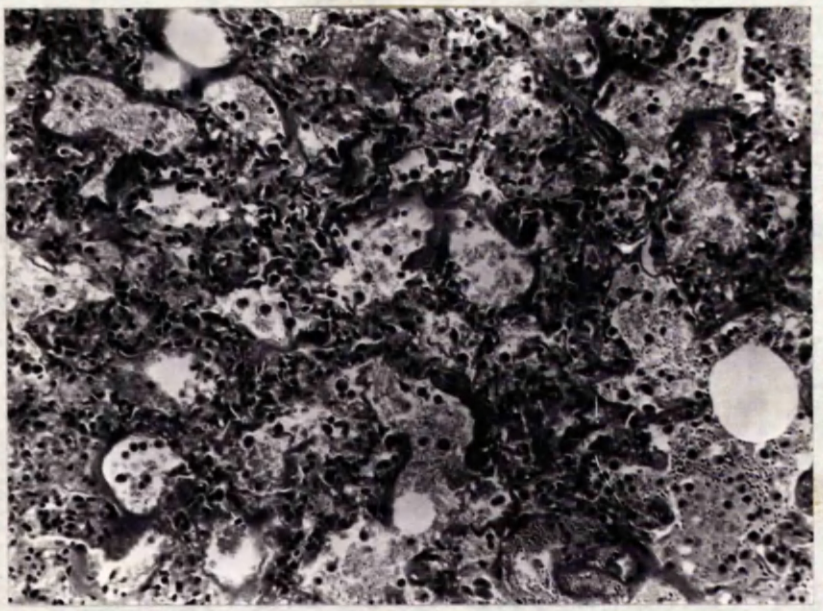


Fig. 28. Calf lung. Hyaline membrane formation, oedema and macrophage infiltration. H. and E. x 90.

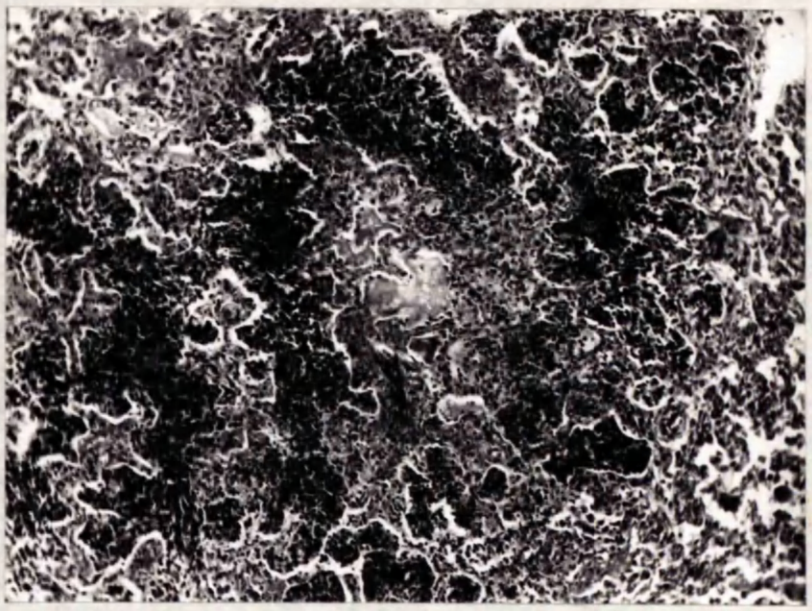


Fig. 29. Calf lung. Fibrinoid necrosis of terminal bronchiole; centrifugal spread of exudate to alveoli. H. and E. x 80.

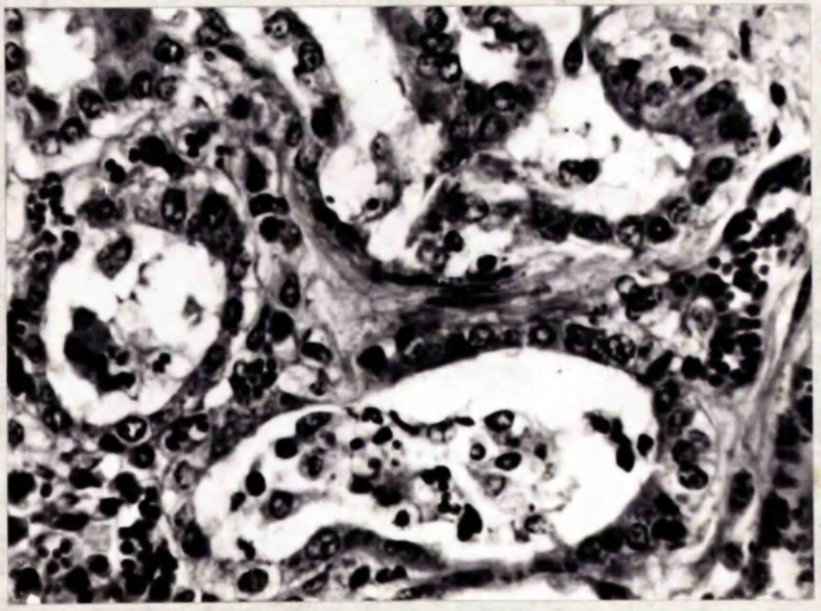


Fig. 30. Calf lung. Regular cuboidal epithelium in peri-bronchial alveoli. H. and E. x 400.

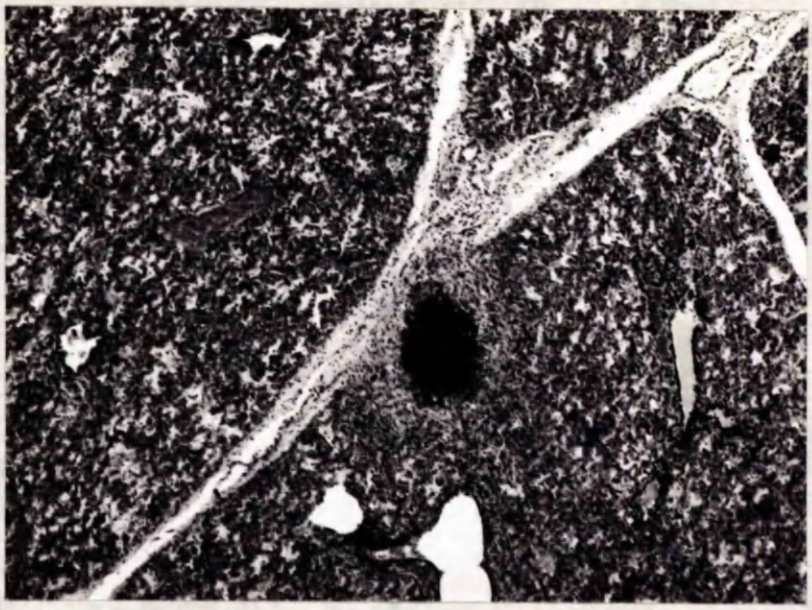


Fig. 31. Calf lung. Aspergillotic focus at periphery of lobule. H. and E. x 35.

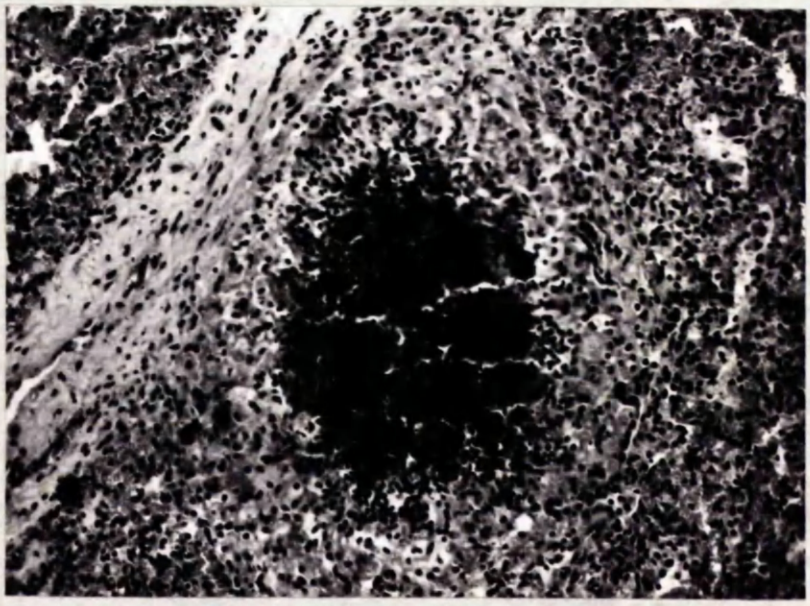


Fig. 32. Calf lung. Detail of aspergillotic focus. H. and E. x 120.

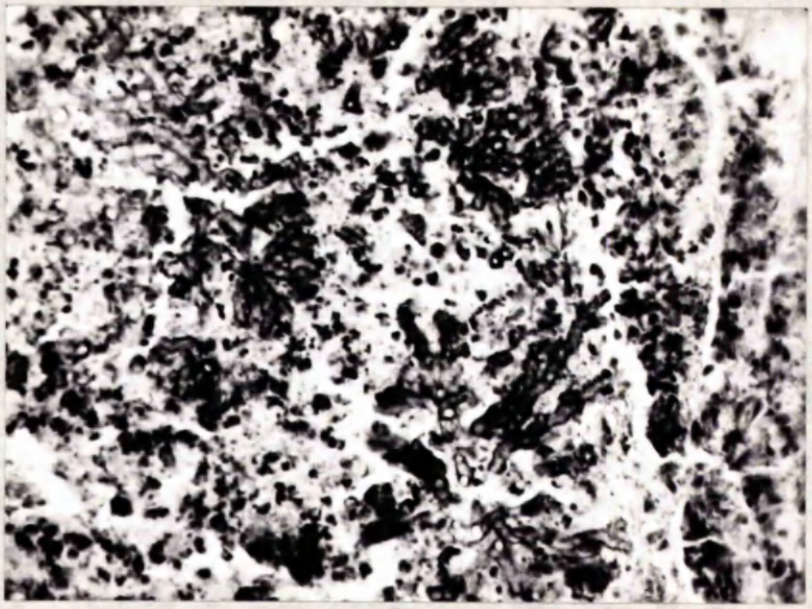


Fig. 33. Calf lung. Branching fungal mycelia in aspergillotic focus. Periodic acid-Schiff x 500.

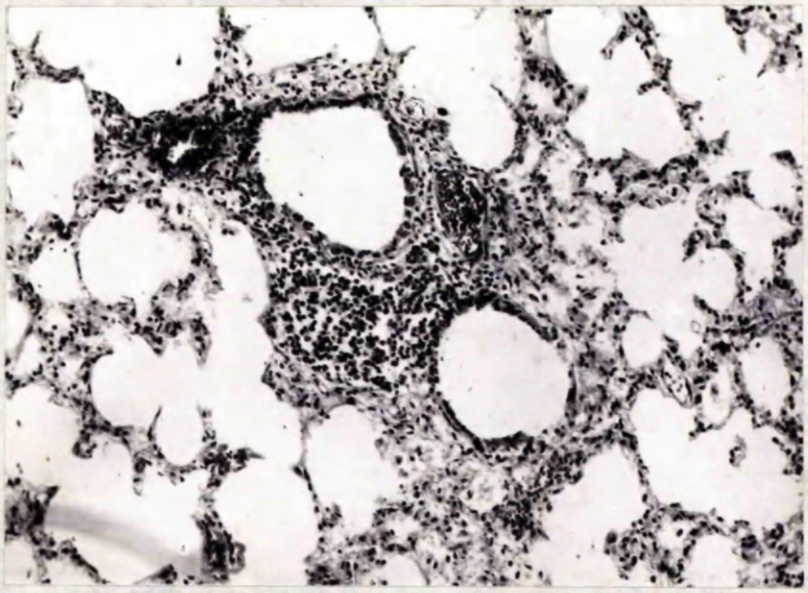


Fig. 34. Calf lung. Early accumulation of lymphocytes in peribronchial tissue. H. and E. x 80.

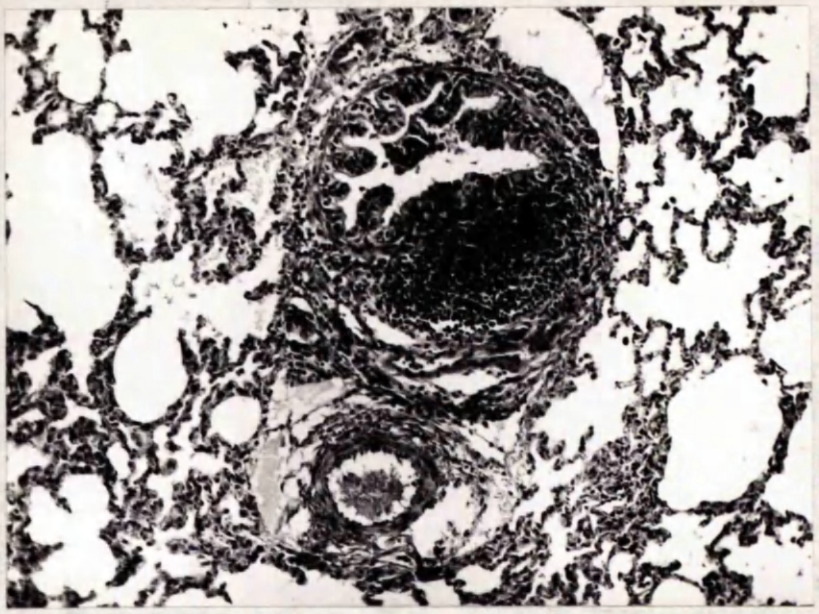


Fig. 35. Calf lung. Proliferating nodule of lymphoid tissue in bronchial wall; absence of infiltration. H. and E. x 80.

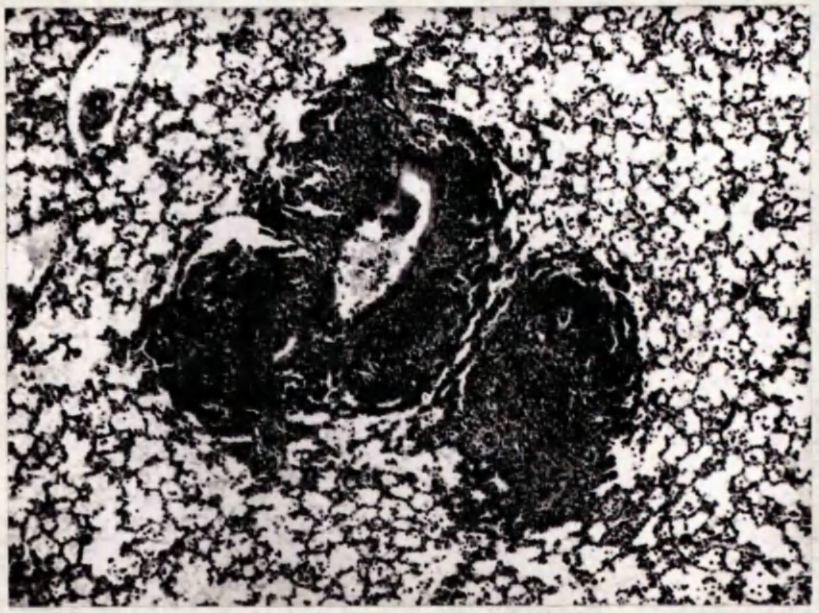


Fig. 36 Calf lung. Extension of lymphoid tissue to form peribronchial cuff; alveoli fully expanded and free of exudate. H. and E. x 50.

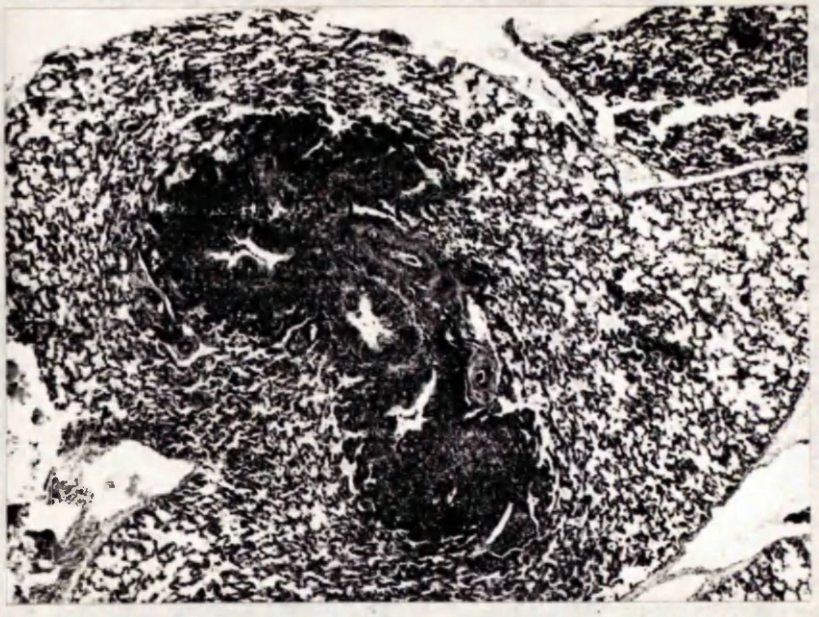


Fig. 37. Calf lung. Bronchus cut several times in course: sheath-like nature of cuff; early compression of alveoli. H. and E. x 40.

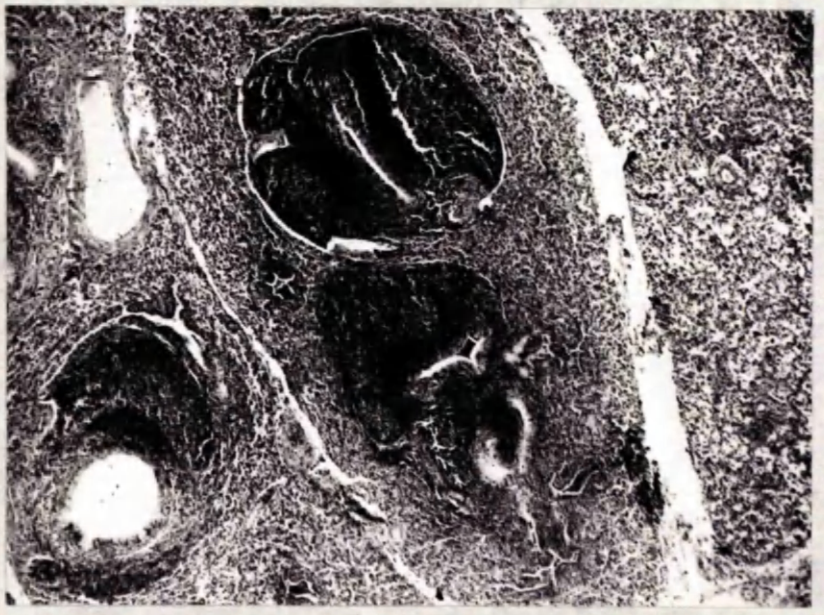


Fig. 38. Calf lung. Germinal follicles in peribronchial cuff; compression collapse of bronchi and alveoli; absence of polymorph exudate. H. & E. x 35.

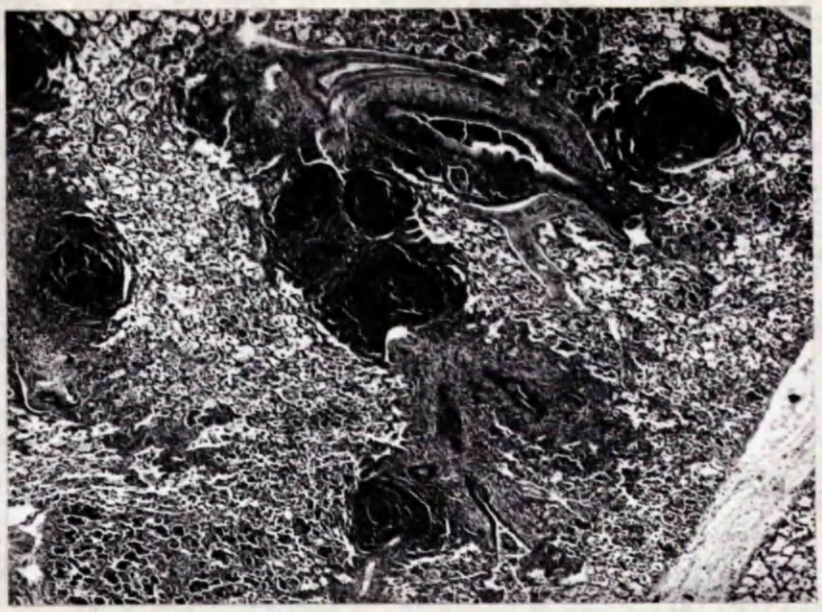


Fig. 39. Calf lung. "Flemming centres" in peribronchial tissue. H. and E. x 30.

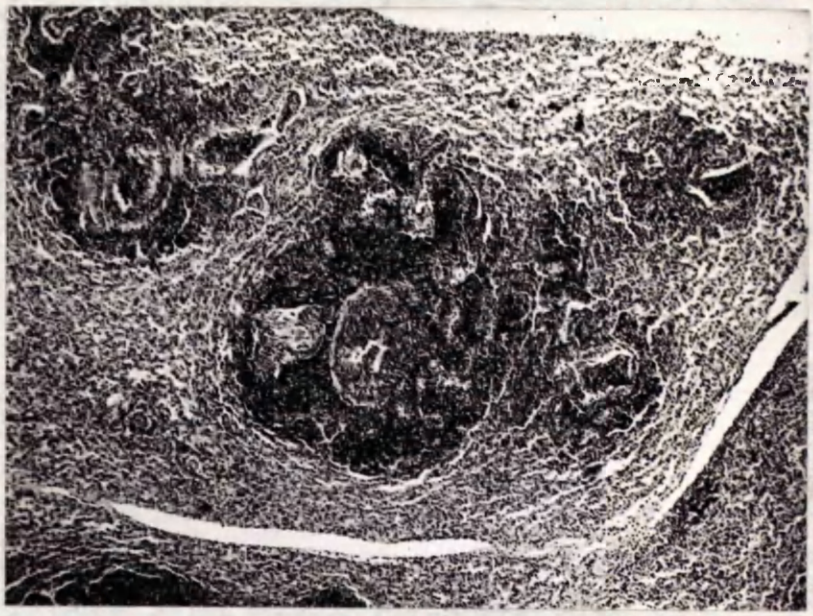


Fig. 40. Calf lung. Peribronchial cuff causing almost total collapse. H. and E. x 30.

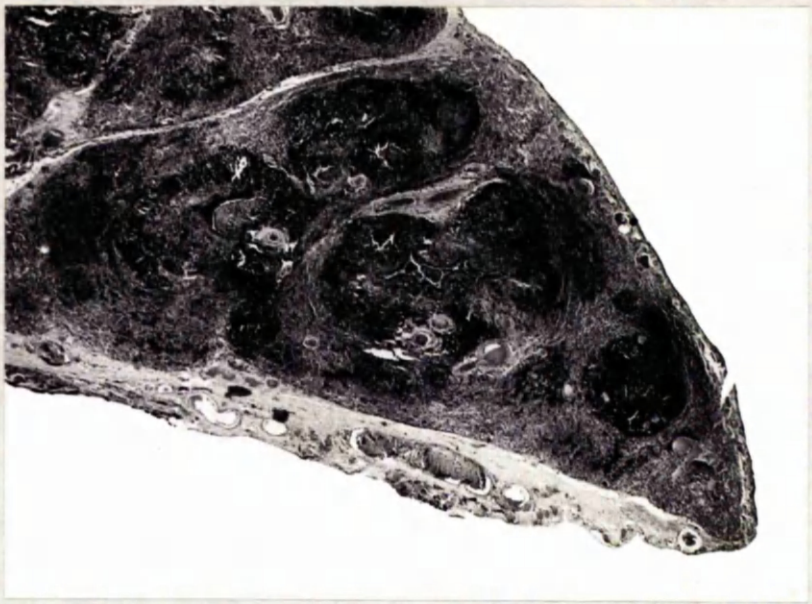


Fig. 41. Calf lung. Expansion of cuff to fill greater part of lobule; consequent total collapse of alveoli; exudate in bronchial lumina; thickening of pleura. H. and E. x 5.

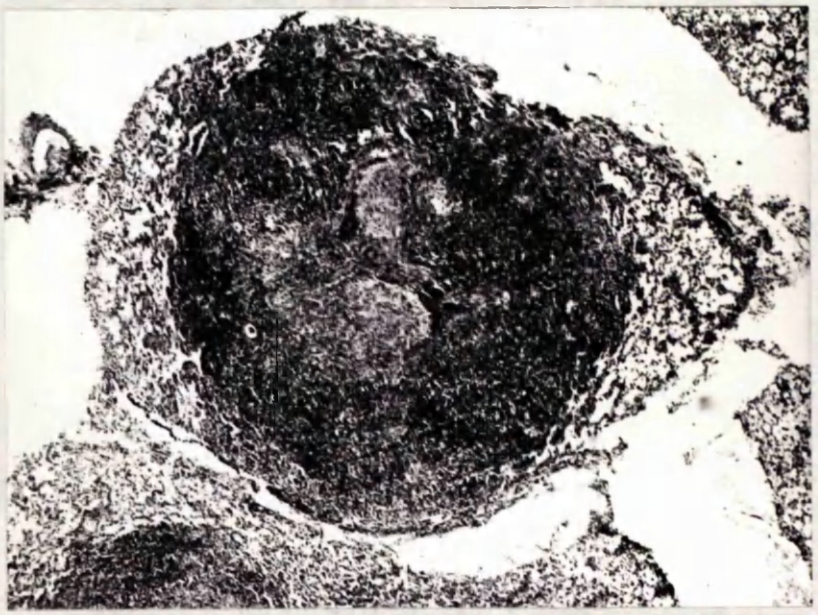


Fig. 42. Calf lung. Lobule almost completely replaced by lymphoid cuff. H. and E. x 30.

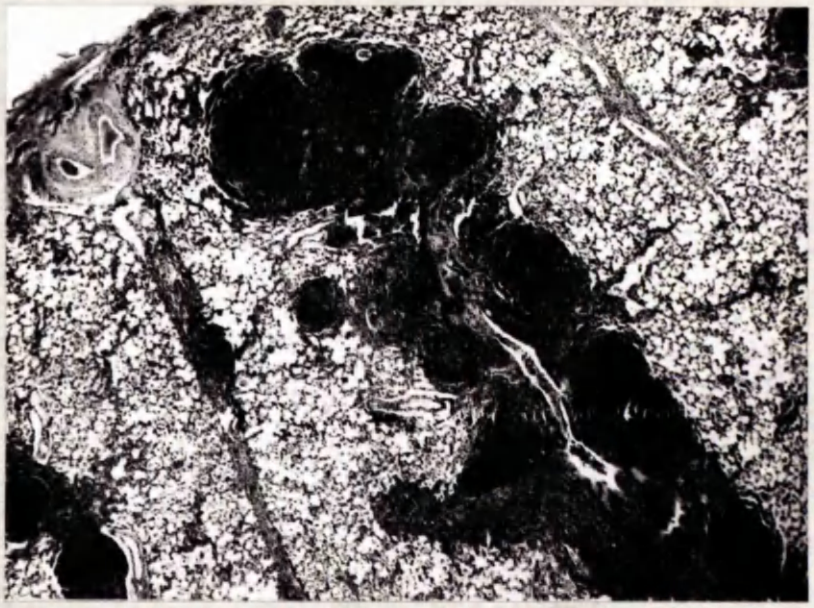


Fig. 43. Calf lung. Longitudinal section of bronchus with germinal centres in sheath of lymphoid tissue: absence of infiltrate in alveoli. H. & E. x 35.

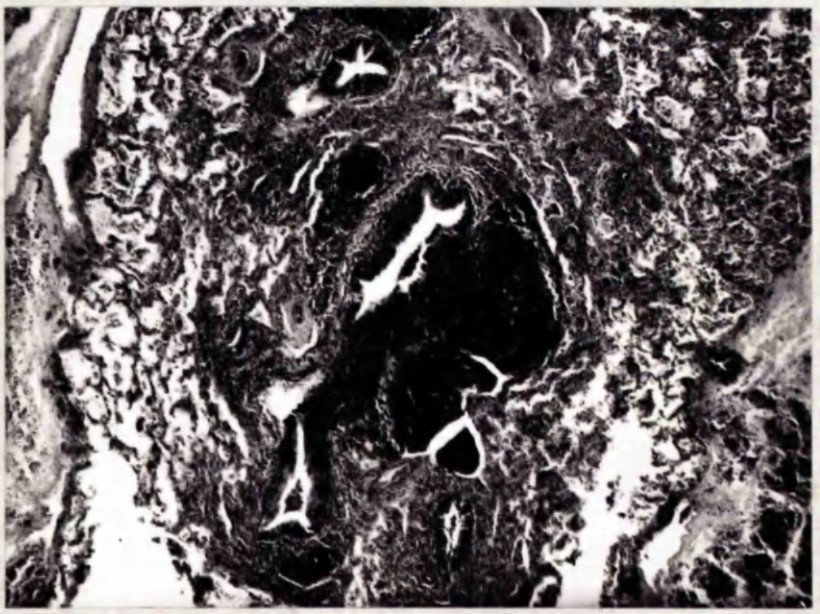


Fig. 44. Pig lung. Peribronchial lymphoid hyperplasia in virus pneumonia. H. and E. x 30.

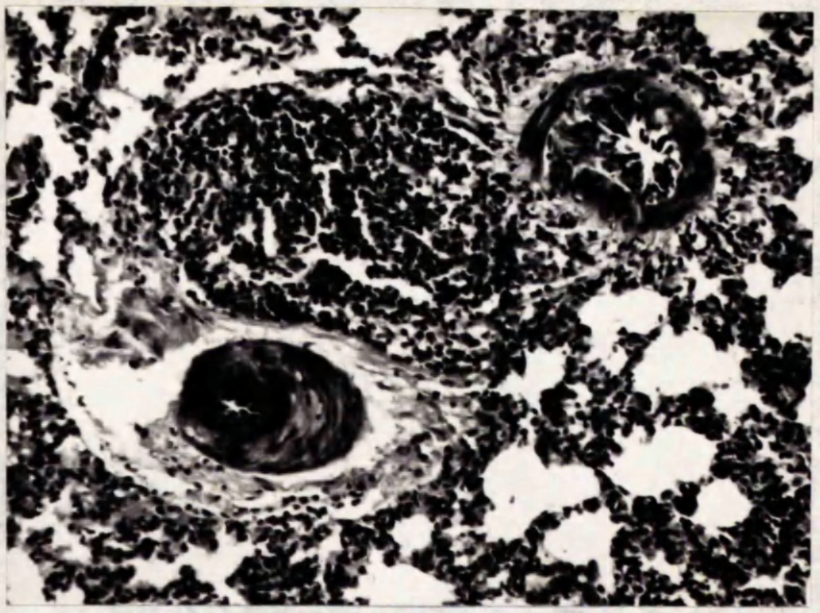


Fig. 45. Guinea-pig lung. Excess lymphoid tissue between bronchiole and blood vessel. H. and E. x 125.

Fig. 46. Calf lung. Coagulative necrosis with surrounding inflammation: expansion of process to terminal bronchiole of adjacent lobule. H. & E. x 35.

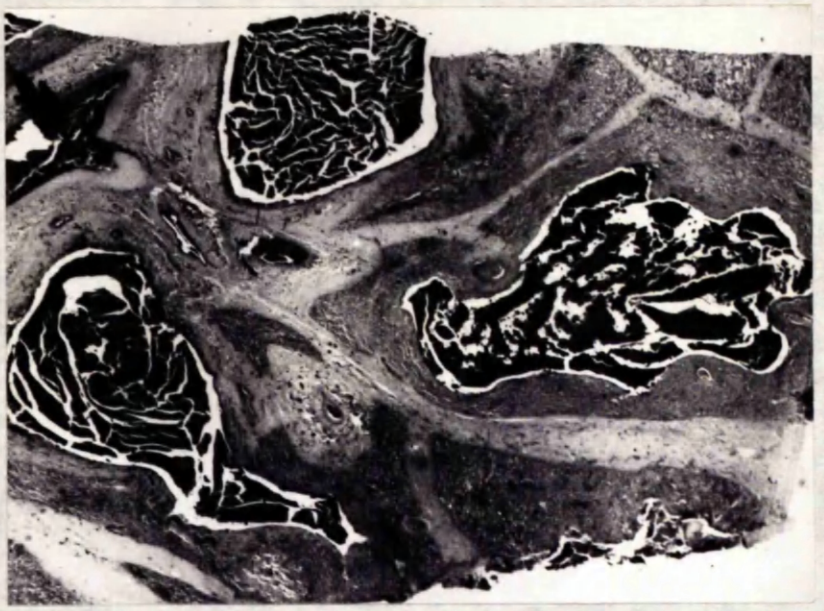


Fig. 47. Calf lung. Tubular bronchiectasis; old muco-pus in lumen; alveolar collapse; septal thickening and fibrosis. H. and E. x 8.

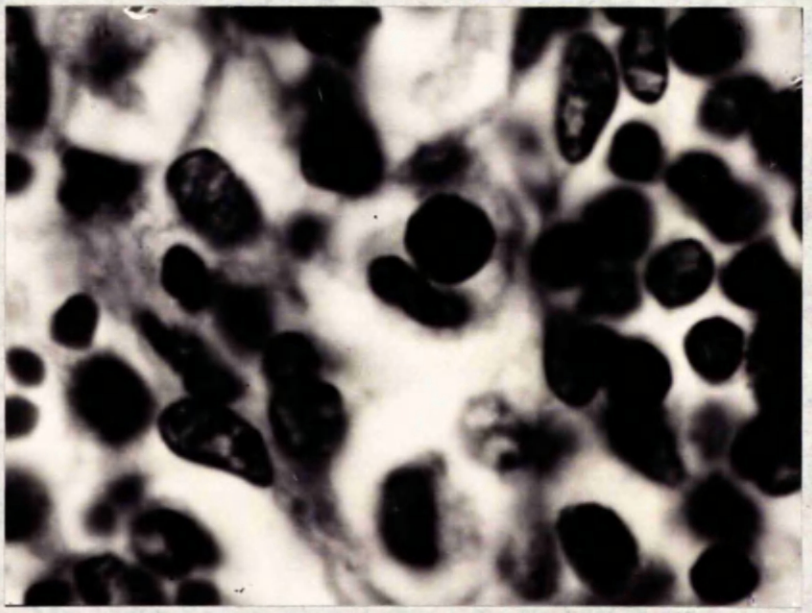


Fig. 48. Calf lymphatic tissue. Erythrocyte in phagocyte. Eosin-phloxine-tartrazine x 1,200.

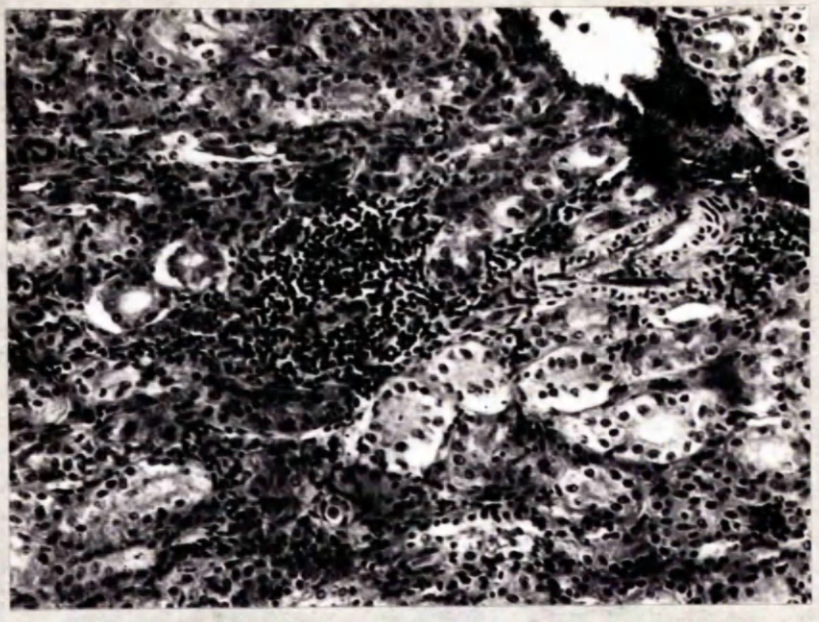


Fig. 49. Calf kidney. Interstitial nephritis. H. and E. x 130.

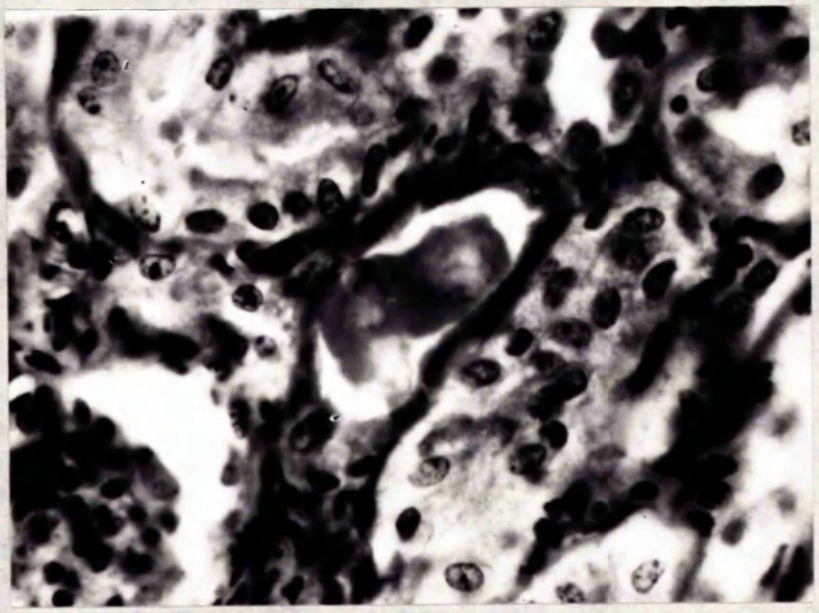


Fig. 50. Calf kidney. Tubule with eosinophilic cast containing crystals. H. and E. x 900.

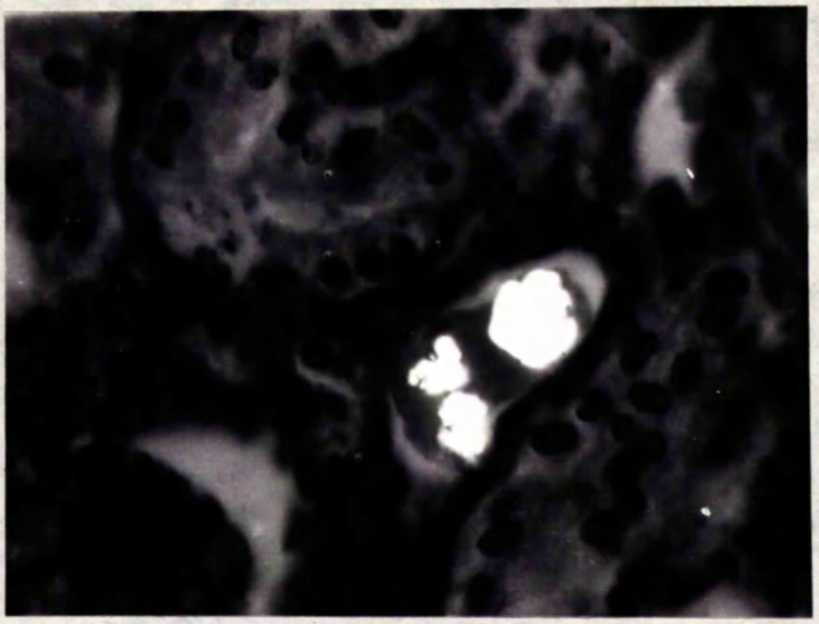


Fig. 51. Calf kidney. Same field as Fig. 50 photographed through polaroid lens and condenser filters. Birefringent crystals in tubule. H. and E. x 900.

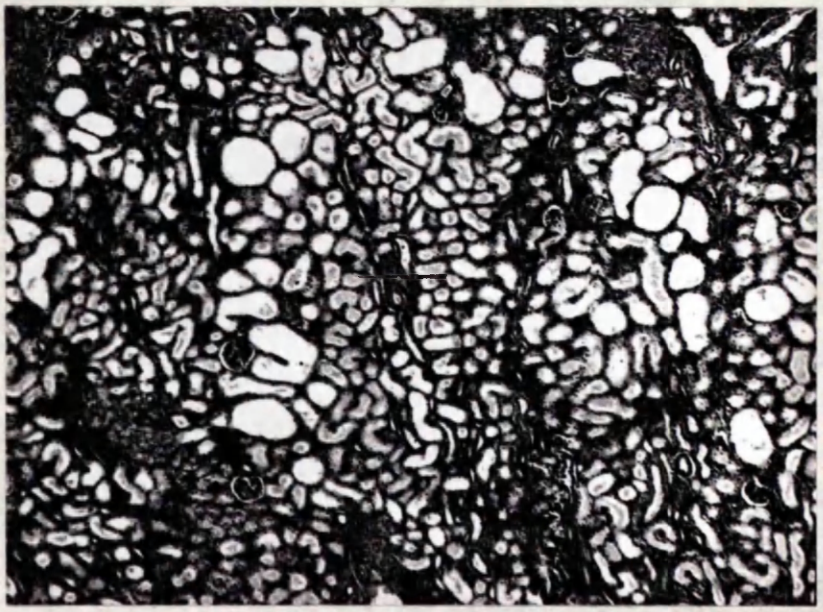


Fig. 52. Calf kidney. Dilated tubules. H. and E. x 35.

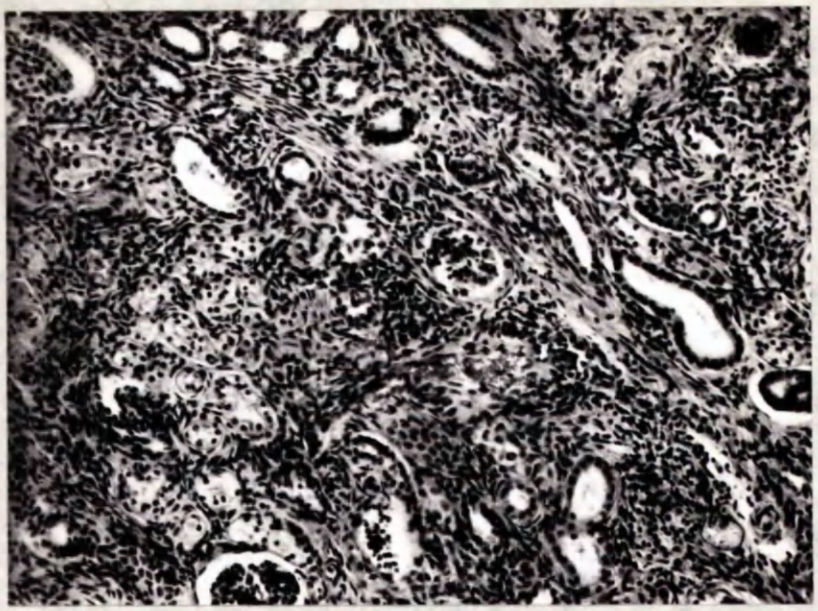


Fig. 53. Calf kidney. Area of intertubular fibrosis. H. and E. x 120.

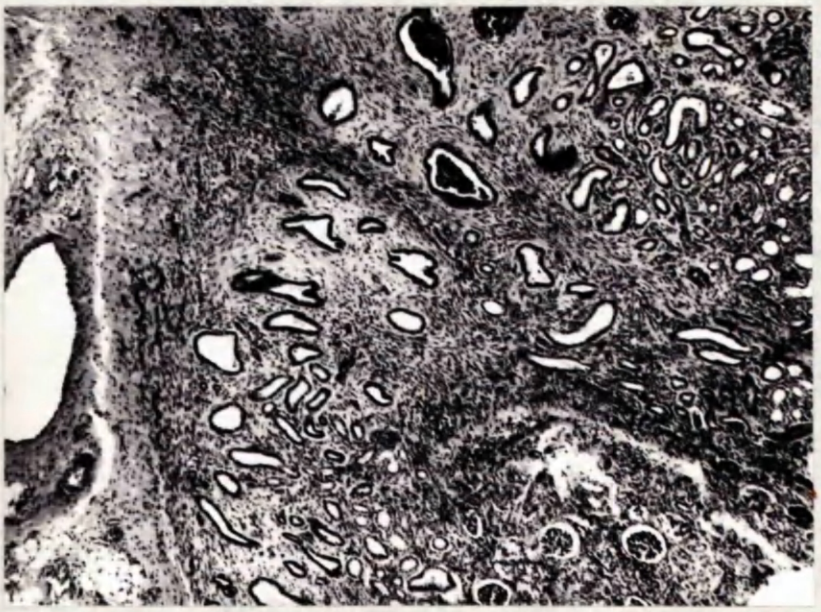


Fig. 54. Calf kidney. Area of agenesis showing marked fibrosis and excess epithelial proliferation in tubules. H. and E. x 40.

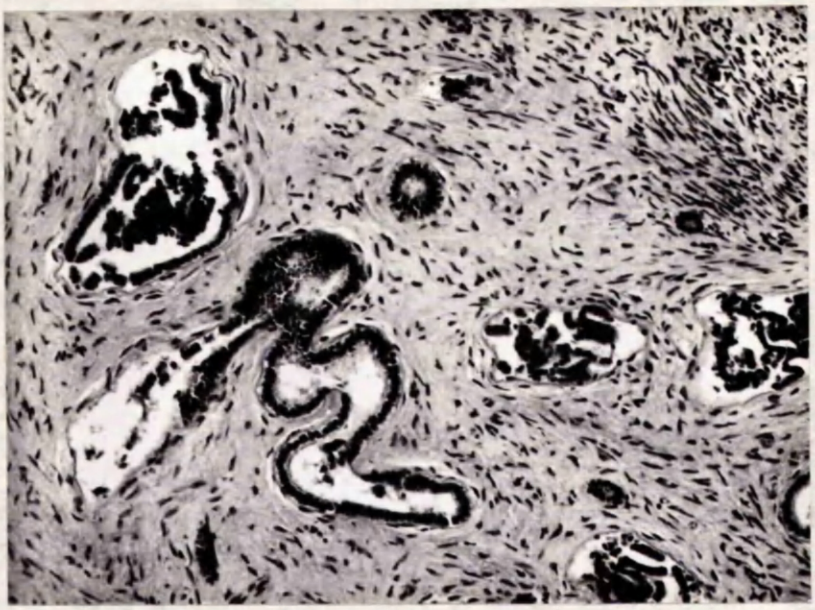


Fig. 55. Calf kidney. Detail of agenetic area in Fig. 54. Intertubular fibrosis and epithelial overgrowth. H. and E. x 120.

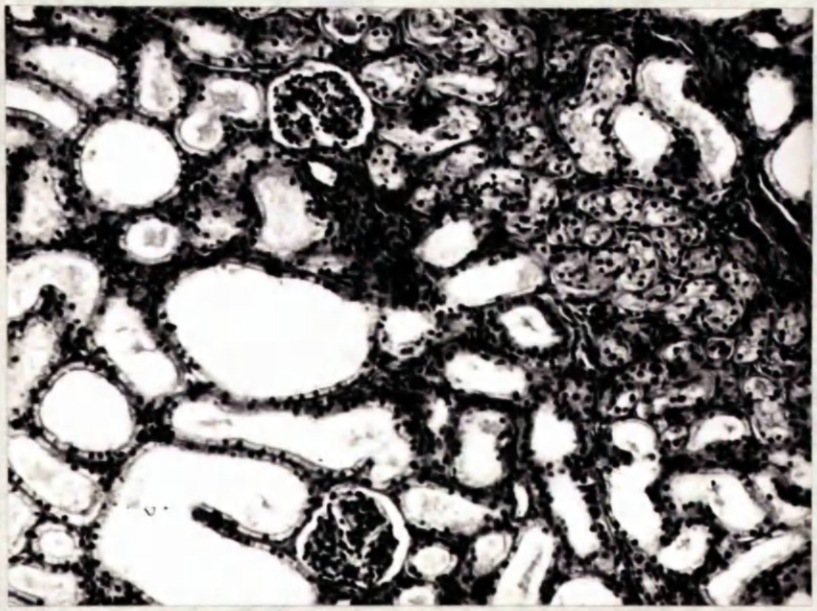


Fig. 56. Calf kidney. Normal glomeruli and dilated tubules. H. and E. x 120.

Fig. 57. Calf abomasum. Edge of peptic ulcer. Overhanging edge; desquamation of epithelium; fibrinoid necrosis of crater; replacement of muscle with fibrous tissue. H. and E. x 35.

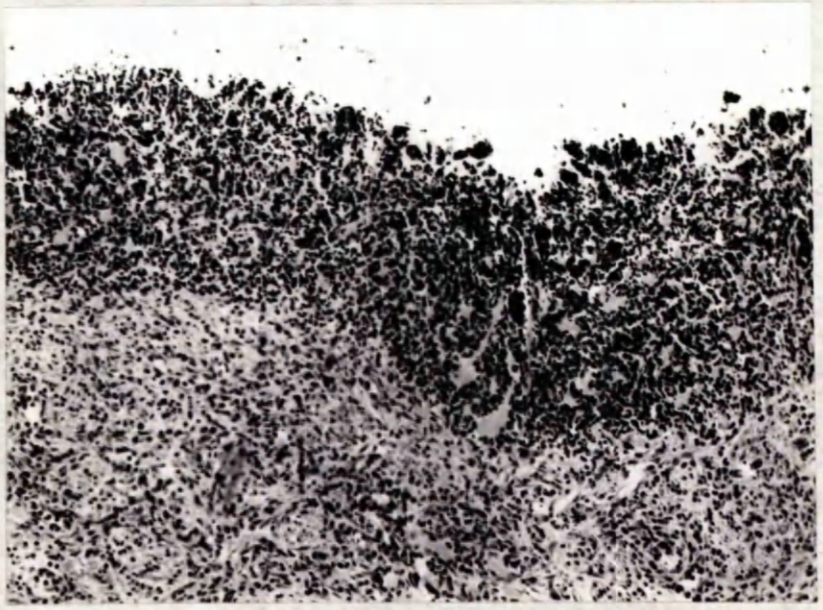


Fig. 58. Calf abomasum. Crater of peptic ulcer. Fibrinoid necrosis polymorph infiltrate and subjacent granulation tissue. H. and E. x 100.

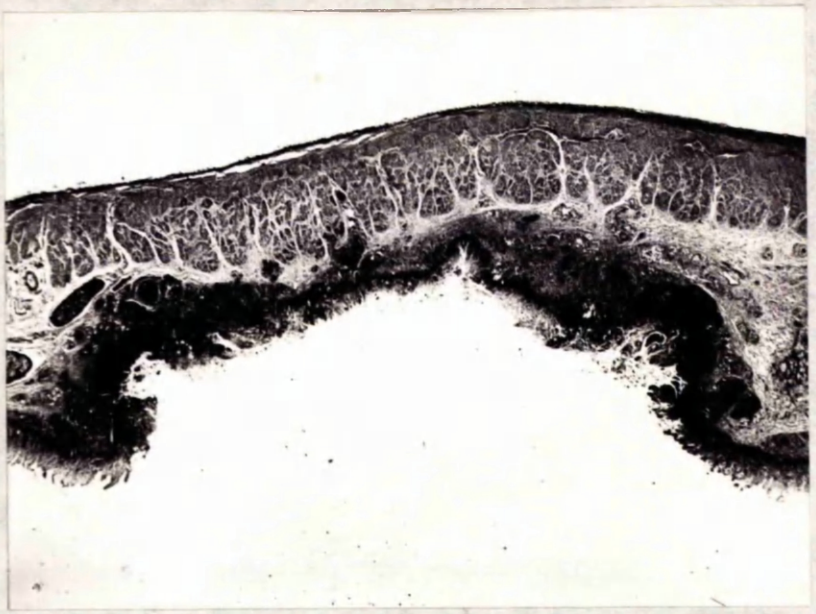


Fig. 59. Calf abomasum. Peptic ulcer. Acute exacerbation with inflammatory reaction penetrating the granulating base. H. and E. x 8.

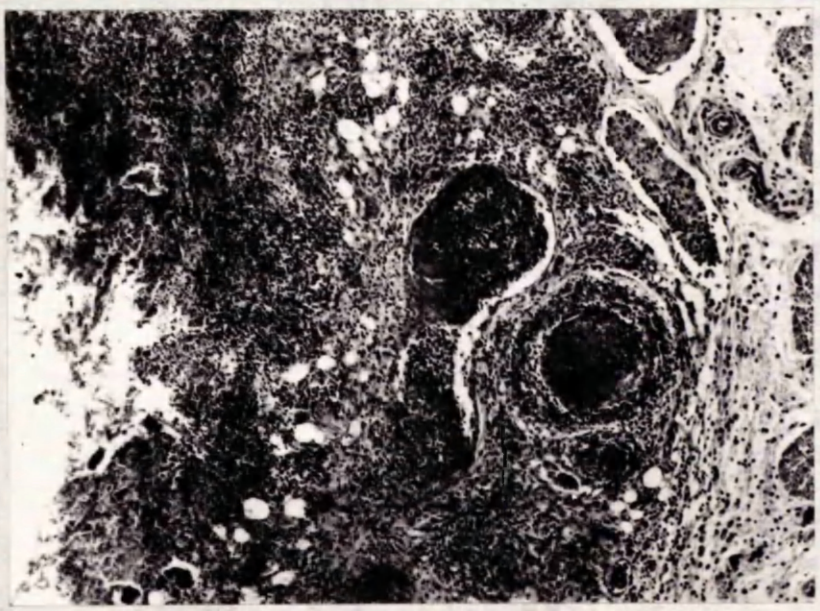


Fig. 60. Calf abomasum. Septic thrombosis of vessels in floor of ulcer. H. and E. x 35.

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SUMMARY

The thesis consists of two parts. The first is an original description of the pathology of bovine Hydrops foetalis; the second is a study of the pathology of the diseases of young calves found in 100 consecutive necropsies.

Bovine Hydrops foetalis is a disease, now known to be transmitted by double autosomal recessives in Mendelian fashion, which has received considerable attention in the last few years since the offspring of some of the best bulls in the country were affected and the numbers of affected calves had increased. In view of the advances in knowledge of the human disease since 1939, when it was found to be due to haemolytic disease of the foetus caused by iso-immunisation of the mother, it was considered worthwhile comparing the human and bovine conditions utilising the techniques employed in the diagnosis of the former.

The animals studied were 15 parents which had given birth to hydropi calves and six hydropic calves. The serological tests used were the "saline" and "albumen" agglutination tests, "direct" and "indirect" Coombs' tests and a haemolytic test. Haematological examinations were made on the blood of some of the calves. It has been proved conclusivel that the pathogeneses of the two diseases are different since in the bovine there is no serological evidence of iso-immunisation of pregnancy and no haematological or pathological evidence of haemolytic anaemia; the latter are the two basic processes in the human disease.

The only constant pathological findings, apart from oedema, were cardiac hypertrophy and a marked serum albumen deficiency. It is suggested/

suggested that the pathogenesis of the disease might be either of placental vascular origin (an obliterative process or an anterio-venous "shunt") or a congenital defect in albumen metabolism. Unfortunately no placentas were available for study.

An experimental attempt to produce iso-immunisation of pregnancy in three cowsfailed.

In Part 2 a detailed pathological description is given of 100 calves which died from natural causes. The three main diseases of calves in this area were found to be pneumonia, "white scour" and suppurative omphalophlebitis. The main part of the work is a study of calf pneumonia. This disease group is commonly regarded as one condition but detailed histo-pathological examination has shown that there are at least nine morphological types. Original descriptions are given of acute interstitial pneumonia, inclusion body pneumonia, epithelialising pneumonia, pulmonary aspergillosis and "cuffing" pneumonia. On the basis of morphological findings an original classification of calf pneumonias is given.

Studies have been carried out on the transmission of some of these pneumonias to laboratory animals and to experimental calves.

The pathenogenetical and etiological implications of the histological findings are discussed in relation to pneumonias of man and other animals.

The pathology of 36 cases of "white scour" is described. The three most important findings were (1) the pathology of the disease is not "specific", (2) 15 of the cases showed concurrent pneumonia, and (3) 11 showed lesions of the central nervous system (meningitis and/

and subarachnoid haemorrhage). As is the case in the human infant, the clinical syndrome of "gastro-enteritis" in the calf is not associated with inflammatory changes in the alimentary canal.

Several other diseases are described of which two, a type of renal agenesis and a form of sulphonamide poisoning, have not been previously reported. The role of peptic ulcers in initiating pyaemia is described.

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