Blood loss, blood and fluid replacement, and the control of blood pressure are discussed.

The technique of induced hypothermia by the method of surface cooling is described, and some relevant problems are considered.

The importance of maintaining a normal blood chemistry, with particular reference to the blood pH and pCO₂, is stressed.

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CANICOLA FEVER IN MAN THROUGH CONTACT WITH INFECTED PIGS

BY

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Leptospiral infections in man resulting from contact with infected pigs have been reported from different parts of the world but have not previously been recorded in Great Britain. Thus the benign human leptospiroses known as "swineherd's disease" and "seven-day fever of Queensland" have followed contact with pigs infected with *Leptospira pomona* (syn. *L. suis*) and *L. mitis* (syn. *L. hyos*) respectively, while van Thiel (1948) quotes two published cases of Weil's disease where it seemed likely that the patient had contracted the disease through slaughtering pigs infected with *L. icterohaemorrhagiae*.

Neither *L. pomona* nor *L. mitis* has so far been isolated from man or pig in this country, but occurrences of *L. icterohaemorrhagiae* infection in swine in two rat-infested piggeries in the south-east of Scotland have been reported by Nisbet (1951).

One other type of leptospira—namely, *L. canicola*—has been isolated from swine. Williams *et al.* (1953) found during the investigation of an extensive outbreak of human canicola fever in a rural community in South Georgia that dogs, cows, and swine showed evidence of infection with *L. canicola*. All the human cases had bathed in the water of a creek to which animals had access, and, although the original source of infection remained obscure, it was the first record of *L. canicola* infection in animals other than dogs.

Previously it had been generally accepted that dogs were the only natural carriers of *L. canicola* (van Thiel, 1948) and that infection in man resulted directly or indirectly from contact with these animals. The disease in the dog varies in severity, but, whatever the degree of illness, the infection usually leads to leptospiuria, which

may persist for many months if recovery occurs, thereby providing a source of contamination for other dogs and for man. While the number of known cases of human canicola fever has been steadily increasing, its true incidence is difficult to assess, since it is a disease which must very often escape diagnosis. In some instances of human disease the history would seem to leave little doubt that infection was transmitted from a dog, but others have been recorded where no apparent connexion between patient and dog could be established (Broom, 1951) and where an alternative source of infection seemed probable. It may be that pigs are more frequently infected with *L. canicola* than is commonly supposed, and, if so, the question arises whether they may not act as reservoirs of infection to persons who feed and handle them. Investigations into a number of obscure cases of human canicola fever which occurred between 1950 and 1955 among piggery workers in and around the City of Edinburgh gave rise to a series of interesting results which point to the probable role of pigs in the transmission of canicola infection to man. These form the basis of the present communication.

Laboratory Methods

Agglutination-lysis tests were used for serological diagnoses. The methods of setting up the tests and interpreting the results were those developed by the staff of the Institute of Tropical Hygiene in Amsterdam, and are described in detail by Wolff (1954). Live cultures of leptospires were used, and the sera were diluted from 1 in 10 to 1 in 30,000. Titres of 1 in 100 and over are regarded as indicating past or present leptospiral infections. A few titres as low as 1 in 10 to 1 in 30 have been recorded, but they are to be treated with reserve since their significance is doubtful.

The isolation of leptospires from the organs of infected animals at necropsy was attempted by grinding small pieces of tissue in Korthof's medium in a Waring blender and inoculating tubes of medium with three or four drops of the emulsion so produced. Latterly, however, we were more successful in obtaining positive cultures by inoculating duplicate tubes of Korthof's or Stuart's medium with small pieces of kidney tissue punched out with a Pasteur pipette, after the surface had been seared with a red-hot scalpel blade (cf. Wolff, 1954). The tubes were incubated at 28° C. and examined at weekly intervals up to six weeks before being discarded as negative.

In addition to culture, hamsters approximately 3 weeks old were inoculated intraperitoneally with 0.5 ml. of tissue emulsions or with 0.5 ml. of centrifuged urine deposit suspended in 1 ml. of Korthof's medium.

Microscopical examinations of cultures, urine, and heart blood from experimental animals were made with dark-ground illumination using a 2-mm. objective.

Clinical Observations

The first case to be investigated occurred in November, 1954, when a man employed on a piggery (Farm A) was admitted to hospital with a feverish illness of eight days' duration characterized by severe frontal headache. Blood taken from the patient agglutinated *L. canicola* to a significantly high titre. Although, on inquiry, no history of recent illness was forthcoming, blood from four out of five other persons living and working on the farm gave positive agglutination findings. The results of these tests and other relevant features are shown in Table I.

There were three dogs on the farm, and, to determine whether they might have been responsible for the infection, specimens of blood and urine were obtained. Dark-ground examination of the urine failed to reveal leptospires. Two of the sera agglutinated *L. canicola* to titres of 1 in 30 and 1 in

TABLE I.—Details of Personnel Living and Working at Farm A

	Age	No. of Years Working with Pigs	Remarks	Serum Titre of Agglutination Against	
				<i>L. canicola</i>	<i>L. ictero-haemorrhagiae</i>
Mr. A. . .	23	4 months	Case of canicola fever	(1) 1/30,000 (2) 1/30,000	1/1,000 1/3,000
Mr. W. D.	60	45 years	Owner of piggery (no significant previous history)	1/1,000	1/300
Mrs. W. D.	50	Intermittently over a number of years	Wife of owner (no significant previous history)	1/10,000	1/300
Mr. J. D. . .	30	15 years	Son (no significant previous history)	1/3,000	1/300
Mrs. J. D.	30	No association with pigs	Daughter-in-law	Negative	Negative
Mr. B. . .	40	20 years	Piggery worker (no significant previous history)	1/3,000	..

100, while none of them agglutinated *L. ictero-haemorrhagiae*. These low agglutination titres and the absence of leptospirae in the urine did not point to the dogs as the direct source of infection, and, as the only person in the piggery whose blood failed to agglutinate leptospirae was also the only one of the six persons concerned who had no contact with pigs, it occurred to one of us (J. N.) that the pigs might be harbouring the organisms and serving as a reservoir of infection. Consequently, blood samples were taken at random from 75 of the animals and submitted for serological examination. The results are shown in Table II.

TABLE II.—Results of *Leptospira* Agglutination Tests with Pig Sera from Farm A

	Total Tested	Titres of Agglutination							
		Neg.	1/10	1/30	1/100	1/300	1/1,000	1/3,000	1/10,000
<i>L. canicola</i>	75	17	1	11	24	7	8	4	3

Thus evidence of infection with *L. canicola* based on positive serological findings was present in 46 of the 75 pigs tested (61%), while in 12 others a low degree of agglutination was obtained. Although, in the cases of the positive sera, cross-reactions occurred with *L. ictero-haemorrhagiae* the titres never exceeded those with *L. canicola* and were usually much less. Twelve sera were also tested against *L. pomona* and *L. mitis* with negative results.

The interesting results obtained at Farm A were a stimulus to further study and, as a first step, inquiries were directed to another piggery (Farm B), in connexion with which a confirmed case of canicola fever had occurred two months previously. Specimens of blood were obtained from this man and his nine fellow workers, and also from 98 pigs taken at random on the farm. The results of leptospira agglutination tests, with other details, are given in Tables III and IV.

Table III shows that in four out of nine persons working at the piggery there was serological evidence of previous infection with *L. canicola*. Apart from the original patient, none of these workers, in spite of careful interrogation, gave a history of an illness suggestive of canicola fever.

It will be seen from Table IV that 40% of the pigs tested had antibodies to *L. canicola* present in their sera to a significant extent.

Inquiries were now extended to 10 other piggeries, and specimens of blood were obtained from 31 workers. Serological tests in 21 were negative, but the other 10 were positive and their agglutination titres with other relevant information are set out in Table V.

It should be mentioned that at three of the piggeries all eight workers examined were free from evidence of infection. No pigs were examined on these farms. The 10 cases with positive sera were among the 23 employees at the remaining seven farms. It is also of interest that at one of the latter farms 12 pigs out of 31 tested were found to have sera positive to *L. canicola*.

Summarizing the results shown in Tables I to V, it appears that of a total of 47 blood specimens taken from persons employed or living at 12 pig farms, 19 (40%) were found to contain antibodies to *L. canicola* in amounts sufficient to signify a past infection with that organism. Five of the persons concerned had had previous illnesses diagnosed at the time on clinical and serological grounds as canicola fever, while an additional five gave histories of undiagnosed illnesses, the symptoms of which, in retrospect, suggested canicola fever. As regards the pigs, 86 out of 173 (50%) at Farms A and B showed evidence of infection with

TABLE III.—Details of Personnel Living and Working at Farm B

	Age	No. of Years Working with Pigs	Remarks	Serum Titre of Agglutination Against	
				<i>L. canicola</i>	<i>L. ictero-haemorrhagiae</i>
Mr. F. . .	17	1	Case of canicola fever	(1) 1/3,000 (2) 1/10,000	1/300 1/1,000
Mr. W. N.	50	40	No significant symptoms	1/1,000	Negative
Mr. I. N.	17	1	" "	1/30	"
Mr. M. . .	33	6	" "	1/3,000	"
Mr. S. . .	26	Intermittently for several years	" "	Negative	—
Mr. J. . .	50	14	" "	"	—
Mr. R. . .	50	10	" "	"	—
Mr. W. . .	40	20	" "	"	—
Mr. McN.	17	1	" "	1/3,000	1/30
Mr. T. . .	30	1	" "	Negative	Negative

TABLE IV.—Results of *Leptospira* Agglutination by Pig Sera from Farm B

	Total Tested	Titres of Agglutination						
		Neg.	1/30	1/100	1/300	1/1,000	1/3,000	1/10,000
<i>L. canicola</i> ..	98	54	4	21	11	5	1	2

TABLE V.—Details of 10 Piggery Workers Whose Sera Agglutinated Leptospirae

Name	Age	No. of Years Working with Pigs	Remarks	Titres of Agglutination Against		
				<i>L. canicola</i>	<i>L. ictero-haemorrhagiae</i>	<i>L. pomona</i>
Mr. D. McD.	42	Many	History suggestive of canicola fever 7 years ago	1/10,000	1/300	Negative
Mr. W. McD.	47	"	History of illness diagnosed as ?tuberculous meningitis 7 years ago	1/1,000	1/30	"
Mr. M. S. . .	20	3	No record of illness	1/300	Negative	"
Mr. E. N. . .	40	17	History of severe influenza 4 years ago	1/300	1/10	"
Mr. McC. . .	18	2	History of severe influenza 6 months ago	1/300		
Mr. J. S. . .	32	3	Severe "influenza" 2 months previously	1/100		
Mr. D. R. . .	26	10	Canicola fever diagnosed 5 years ago	1/3,000	1/30	
Mr. R. R. . .	23	8	No record of illness	1/1,000	Negative	
Mr. K. . .	57	5	Canicola fever diagnosed 5 years ago	1/1,000	1/30	
Mr. C. . .	33	Intermittently	Canicola fever diagnosed December, 1955	1/3,000	1/100	

L. canicola to a significant degree. None of these animals revealed noticeable signs or symptoms of disease.

These findings strongly suggested the probability that infection had been transmitted from pig to man, but so far it had not been possible to isolate the leptospira from either pigs or man. Only one of the five human cases of confirmed canicola fever was ill during the course of the present investigation, and in his case blood cultures, dark-ground examination of the urine, and animal inoculation gave negative results, probably because he was not brought under notice at a sufficiently early stage of the disease. Specimens of urine from the bladders of a large number of pigs on Farm A showed no leptospire on dark-ground microscopy, and we failed to isolate the organism by inoculating hamsters with kidney tissue from "non-thriving" pigs with high antibody titres for *L. canicola*. It should be noted, however, that there was in the piggery at the time a concurrent infection of *Pasteurella septica* which killed the hamsters rapidly and contaminated the culture media inoculated at necropsy.

Because of the failure to demonstrate leptospire by these methods, it was decided to carry out experimental work to determine whether pigs could be artificially infected with *L. canicola* and whether leptospire could then be isolated from the urine of these pigs.

Experimental Investigations

1. Artificial Infection of Pigs with *L. canicola*

Six pigs aged 2-3 months whose sera failed to agglutinate *L. canicola* and *L. icterohaemorrhagiae* were inoculated with a culture of *L. canicola* (strain Aldgate) kindly supplied by Dr. J. C. Broom, of the Wellcome Laboratories of Tropical Medicine. This strain is highly virulent (a hamster inoculated with 0.3 ml. of the culture died on the fifth day). The pigs were inoculated by the following routes: (1) Subcutaneously through the soft skin of the groin (0.5 ml.). (2) By scarification of the skin behind the ear, one drop of culture being placed on the scarified area, covered with cotton-wool, and held firmly in place with medicated elastic adhesive bandage. (3) Intranasally by rubbing the inside of each nostril with a swab saturated in the culture. (4) Routes 1, 2, and 3 combined. (5) By mouth: 1 ml. of the culture was introduced into the back of the throat by means of a syringe. (6) Control.

Evidence of Disease Resulting from Inoculations.—Rectal temperatures of the pigs recorded before the experiment and each day afterwards showed no significant rise. No apparent symptoms of disease developed and the pigs continued to gain in weight.

Serology.—Ten days after inoculation, and periodically thereafter until the pigs were killed, blood was withdrawn from the ear veins and agglutination tests were carried out with the sera against *L. canicola*. The results are shown in Table VI. These results show that a marked serological

TABLE VI

Pig No.	Method of Inoculation	Titres of Agglutination of <i>L. canicola</i>			
		Before Inoculation	No. of Days After Inoculation		
			10	28	40
1	Subcutaneous ..	Negative	1/30,000	*	—
2	Scarification ..	"	1/10,000	1/10,000	—
3	Intranasal ..	"	Negative	Negative	Negative
4	Methods 1, 2, and 3	"	1/10,000	*	"
5	By mouth ..	"	Negative	1/300	1/3,000
6	Control ..	"	"	Negative	Negative

* Pigs 1 and 4 were killed on the 18th and the 12th day respectively.

response followed inoculation of the culture by all routes except the intranasal one. Subcutaneous inoculation and inoculation through the scarified skin resulted in strongly positive agglutinating sera within 10 days. On the other hand, antibody production in the pig inoculated by mouth was delayed and titre had reached only 1 in 100 by the 28th day, continuing to increase to 1 in 3,000 by the 40th day. It is possible in this case that the actual infection may have

been acquired through contact with the pigs already infected by the other methods, although it is noteworthy that pigs 3 and 6 failed to show any evidence of infection 47 days after the beginning of the experiment. The result in the pig infected through scarified skin (No. 2) is particularly interesting, since it not only indicates that the serological response must have resulted from invasion of the tissues by the leptospire but also that it is possible for natural infection to follow leptospiral contamination of wounds, so often inflicted when pigs fight with one another.

Attempts to recover infecting organisms were unsuccessful. Dark-ground examination of blood from the infected pigs taken 10 days after inoculation and urine specimens taken periodically thereafter failed to show leptospire.

Pig 4 was killed on the 12th day, pig 1 on the 18th day, and pigs 2 and 5 on the 40th day after inoculation. At necropsy no lesions were seen in any of the organs, and we were unable to recover leptospire from the kidney and liver of these four pigs either by cultural methods or by inoculation of hamsters.

2. Introduction of Non-infected Pigs into the Infected Piggery

In order to observe the effect of introducing non-infected pigs into an infected piggery the following investigation was carried out at Farm A.

Two pens of 20 pigs were chosen for this study. The pigs in the first pen—pen 1—had been introduced into it direct from the local market three weeks previously; those in the second pen—pen 2—one week previously. Both pens had housed pigs which on serological evidence were infected with leptospire, but after these had been removed for slaughter the pens had been given their customary cleaning by hosing and left vacant for 24 hours prior to the introduction of the fresh pigs. Three pigs from each pen were chosen, and blood specimens from the ear veins of the six were found to contain no leptospiral antibodies. Subsequent specimens of blood were taken from the six at intervals and tested against *L. canicola* and *L. icterohaemorrhagiae*. The results are shown in Table VII.

TABLE VII

Pig No.	Length of Time in Piggery							
	1 Week		3 Weeks		5 Weeks		8 Weeks	
	<i>L. can.</i>	<i>L. ictero.</i>	<i>L. can.</i>	<i>L. ictero.</i>	<i>L. can.</i>	<i>L. ictero.</i>	<i>L. can.</i>	<i>L. ictero.</i>
Pen 1 {	1	—	Neg.	Neg.	Neg.	Neg.	1/1,000	1/300
	2	—	"	"	"	"	1/10,000	1/1,000
	3	—	"	"	"	"	1/10,000	1/1,000
.. 2 {	4	Neg.	1/300	1/100	1/300	1/100	1/300	1/100
	5	"	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.
	6	"	"	"	"	"	"	"

From the serological results shown in this Table it appears that the three pigs in pen 1 became infected within six to eight weeks of their introduction into the piggery. In pen 2 the blood of one of the pigs agglutinated leptospire weakly to a titre of 1 in 300 after three weeks, but the titre failed to rise during the subsequent weeks and its significance is therefore doubtful. The other two pigs continued to be serologically negative.

Isolation of *L. canicola* from Urine.—A specimen of urine taken from the floor of pen 1 during the eighth week was examined by dark-ground microscopy and found to contain numerous leptospire (approximately one per field of uncentrifuged urine). The following day a pooled specimen of urine collected in a sterile long-handled pan from 12 pigs in this pen was examined, and again numerous active leptospire were seen (up to four per field). Separate specimens were then obtained in sterile containers from individual pigs in the pen and five out of six were found to be positive. On the other hand, eight specimens of urine taken from individual pigs in pen 2 were examined by dark-ground microscopy but no leptospire were seen. This accords with the negative serological findings for this pen.

A pooled specimen of urine from the pigs in pen 1 was inoculated into two hamsters: one of these died on the sixth and the other on the eighth day after inoculation. At necropsy, apart from some congestion of the blood vessels of the peritoneum, there were no obvious lesions. Dark-ground examination of heart blood failed to show leptospire, but six drops inoculated into Stuart's medium produced growth after 14 days' incubation. The culture was sent to Dr. Broom at the Wellcome Research Laboratories, and was identified as a strain of *L. canicola*.

3. Experimental Infection of Pigs with Infected Urine

Two of the six pigs used in experiment 1—namely, the one inoculated intranasally and the control animal—continued to show no serological evidence of infection. No leptospiral antibodies were present in either of these animals 47 days after the beginning of experiment 1. The following day they were inoculated with infected urine collected from 10 pigs in Farm A (pen 1). (The presence of leptospire was confirmed by dark-ground microscopy.) Pig 3 was inoculated subcutaneously with 3 ml. of untreated urine, while in the case of pig 6 a piece of cotton-wool soaked in urine was placed on an artificially scarified area behind the ear and held in place with medicated elastic adhesive bandage.

Symptoms of Disease Following Inoculation with Infected Urine.—Rectal temperatures were taken before the inoculations were made and daily thereafter. In both pigs a rise of several degrees was noted, from 102.5 to 106° F. (39.2 to 41.1° C.) on the sixth day in the case of pig 3, and from 102.8 to 104.6° F. (39.3 to 40.3° C.) in pig 6 on the 10th day. No other obvious symptoms developed. Blood cultures from a subcutaneous vein on the fifth day failed to produce a growth of leptospire. Blood-agar plates inoculated with the blood and incubated aerobically and anaerobically remained sterile, showing absence of concurrent septicaemia. Dark-ground examinations of urine taken on the 15th, 19th, and 20th days failed to reveal leptospire. Agglutination tests carried out with blood taken at intervals resulted in the titres with *L. canicola* and *L. icterohaemorrhagiae* shown in

TABLE VIII

Pig No.	Inoculated	Days After Inoculation					
		5		11		21	
		<i>L. can.</i>	<i>L. ictero.</i>	<i>L. can.</i>	<i>L. ictero.</i>	<i>L. can.</i>	<i>L. ictero.</i>
3	Subcutaneous	Neg.	Neg.	1/3,000	1/30	1/30,000	1/300
6	By scarification	..	..	1/10,000	1/1,000	1/30,000	1/1,000

Table VIII. It will be seen that inoculation of the infected urine by both routes was followed by a high antibody level by the 11th day.

Necropsy.—The two pigs were killed 22 days after inoculation. The post-mortem examination revealed no abnormalities. Bottles of Stuart's medium were inoculated with kidney and liver tissue from both pigs. Leptospire grew in one of the bottles inoculated with kidney from pig 6. The growth was slight after 12 days, but by the 18th day numerous leptospire were present. One of two hamsters inoculated with emulsified kidney from pig 6 died 14 days later, showing epistaxis and a post-mortem picture characteristic of a leptospiral infection with pronounced haemorrhages in the lungs. A blood culture from this animal gave a fair growth of leptospire by the 7th day and cultures of the kidney were positive one week later. A few drops of the heart blood introduced intraperitoneally into the second hamster resulted in its death 10 days later. A blood culture from this second animal resulted in growth of leptospire within one week. We failed to isolate leptospire from pig 3 either by culture or by animal inoculation, although two out of four hamsters inoculated with emulsified kidney died in 11 days with haemorrhagic lesions characteristic of leptospiral infection.

Discussion

The evidence submitted above has indicated that 19 out of 47 (40%) piggery workers engaged in 12 different farms in the environs of Edinburgh had been infected at some time with *L. canicola*. It seems probable that the infection resulted through contact with infected pigs, since in one farm 77% of the pigs tested, and in another 44%, had serum antibodies to *L. canicola* and the organism was shown to be excreted at times in large numbers in the urine. This high incidence of infection in humans is particularly striking, since in view of the small number of cases which result from man's contact with infected dogs (the only source of infection previously known to exist for man) it was thought that *L. canicola* had a low infectivity to man. When one takes into consideration the large number of dog-owners in the country and the fact that 25–40% of dogs show serological evidence of infection (Stuart, 1946; Broom and Macintyre, 1948) it is surprising that cases of human canicola fever do not occur more often. Broom (1951) found that persons most liable to become infected were those who had nursed a sick dog and cleaned up its dejects. On the other hand, McIntyre and Seiler (1953), investigating in Edinburgh the incidence of canicola fever among owners of dogs known to be infected with *L. canicola*, found that of 99 persons who had been in contact with sick animals and including 45 who were responsible for removal of the dejects, none were serologically positive to *L. canicola*.

It may be that in the case of piggery workers the conditions under which these men work predispose them to infection. It is known that they frequently suffer from open cuts and wounds in their hands which are apt to become contaminated when cleaning out the pens. In Farm A, where the rate of infection both in humans and in pigs was most striking, conditions in the pens may have been conducive to maintaining the infection. This piggery usually houses a herd of 400 pigs, which are all swill fed. No breeding is done and replacements are made as required from the local markets at ages of 2–3 months. Little bedding is used and the pens are hosed daily, so that the floors, other than the sleeping quarters, are rarely dry and often very wet. The pigs are crowded together from 20–30 in a pen, a practice adopted to maintain a high temperature in the piggery. It seems possible that the leptospire may remain viable for a fairly long time on the moisture-laden floors. It is not known how the pigs were originally infected, but it seems likely that the farm dogs which have access to the piggery may have introduced it and, once established in the herd, the infection has passed from pig to pig through infected urine contaminating skin abrasions or the mucous membranes of the mouth and throat.

While canicola fever in man is not as a rule a killing disease, two fatal cases have been reported (Weetch *et al.*, 1949; Wolff *et al.*, 1951). Furthermore, clinical infection with *L. canicola* gives rise to a sharp illness with meningeal symptoms alarming to the patient and his relatives and incapacitating the victim for some weeks. It is clear, therefore, that all possible steps should be taken to prevent the disease.

Up to the present the main emphasis has been placed on the possibility of spread of infection from dogs, but the results described in this paper indicate that infected pigs are a more important source. This fact should be made widely known to pig owners and their employees so that they may be aware of the danger and the necessity for employing a high standard of hygiene in the piggery. After the animal pens have been thoroughly cleaned by hosing it is recommended that they be treated with a hypochlorite solution* and allowed to dry. So far as it is possible, dogs should not be allowed to come into contact with the swine; the workers should be encouraged to wash and dry their hands and equipment after cleaning out the pens, and to cover immediately any cuts and abrasions with adequate protective dressings.

*Davidson and Smith (1936) found that "chlorox" diluted 1 in 64 was effective in killing leptospire in premises contaminated with the urine of rats.

Summary

Five cases of canicola fever, diagnosed on clinical and serological evidence, occurred during a period of five years among piggery workers engaged in farms in the environs of Edinburgh.

A survey of 47 piggery workers in 12 Edinburgh farms showed from the results of serological examinations that 19 (40%) had at some time been infected with *L. canicola*. In addition to the five known cases this figure includes five others with histories of illness suggestive of canicola fever.

Specimens of blood from pigs from the two farms in which most of the cases occurred were found to contain antibodies to *L. canicola* in titres high enough to indicate a leptospiral infection. In one farm 46 out of 75 (61%) of the pigs were positive and in the other 40 out of 98 (40%).

Four out of six pigs newly introduced into one of the infected piggeries developed antibodies to *L. canicola* within three to eight weeks. On the 47th day after admission leptospores were being excreted in large numbers in their urine.

A hamster inoculated with the infected urine died after six days and leptospores were grown in culture from the heart blood. They were identified as *L. canicola*.

Six pigs were inoculated each by a different route with a virulent culture of *L. canicola*. Those which were inoculated subcutaneously and through a scarified area of skin developed antibodies to titres of at least 1 in 10,000 within 10 days. No obvious symptoms of disease followed the administration of the culture by any of the routes employed.

Pigs which were inoculated with urine from infected pigs subcutaneously and by scarification developed antibodies to *L. canicola* within 13 days. No symptoms other than a slight febrile reaction and a tendency to be less vigorous followed the inoculations.

The above evidence indicates that pigs may harbour *L. canicola* without showing any noticeable symptoms of disease. The organisms are excreted in the urine, and infection is passed from pig to pig. Human infection may result through contact with infected pigs.

The incidence of canicola fever in piggery workers is high, and this is in contrast to the recognized low infectivity rate among dog owners.

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NORADRENALINE IN SHOCK DUE TO
VISCERAL PERFORATION

BY

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In states of shock survival of the patient ultimately depends on removing the cause of the shock. Some temporary measure to tide the patient over the hypotensive crisis is, however, often necessary to prevent the vicious circle of progressive irreversible shock, and may be absolutely essential if the patient is to survive a major surgical procedure.

The following three cases of shock associated with visceral perforation all responded only temporarily to the infusion of moderate amounts of blood and dextran, and the early use of a continuous noradrenaline infusion over a period of days appeared to play a necessary part in maintaining an adequate blood pressure and in ensuring the recovery of the patients from the condition of circulatory failure. The cases described are three consecutive cases of this type that were admitted to the Central Middlesex Hospital.

Case 1

A woman aged 66 collapsed at noon on December 22, 1955, with very severe pain in the left iliac fossa, the pain soon radiating across the whole abdomen. When seen she was grey and very ill. Her blood pressure was 95/70 and her pulse volume was poor.

An intravenous infusion was set up and 1 pint (570 ml.) of dextran was given. Her general condition improved, and immediately prior to operation (six hours after the onset of symptoms) her systolic blood pressure was 125.

Anaesthetic induction and maintenance was with nitrous oxide, trichlorethylene, and oxygen. Orotracheal intubation with a cuffed tube was performed under suxamethonium relaxation. Gallamine, 40 mg., was given, and later a suxamethonium drip was set up. Operation revealed faecal fluid and also solid faeces in the peritoneal cavity, due to a rupture of the sigmoid colon. Distal to the rupture there was an annular thickening of the wall of the bowel, this almost certainly being neoplastic in nature. The peritoneum was cleaned of faeces so far as possible and the perforated gut was delivered as a loop colostomy. After operation intensive antibiotic therapy with penicillin, streptomycin, and oxytetracycline was instituted.

After induction the systolic blood pressure rose to 130, but thence gradually fell during the course of the operation even though a further $\frac{1}{2}$ pint (284 ml.) of dextran was infused. The pulse volume became very poor and eventually the systolic pressure was barely 80. The patient was cold and very pale. Intravenous injection of 14 mg. of methylamphetamine hydrochloride ("methedrine") in two divided doses produced only a slight and very transient improvement in the blood pressure. A blood infusion was then started, but no immediate improvement followed.

In order to raise the blood pressure intravenous noradrenaline was given at the conclusion of the operation. A strength of 4 mg. of the bitartrate in 1,000 ml. of dextrose-saline was used, and at 60 drops a minute the systolic blood pressure rose from 80 to 125 within a matter of minutes (Fig. 1).

Back in the ward the intravenous noradrenaline was temporarily discontinued, one hour after its commencement, to see if the blood pressure would be maintained. At this time the patient had had a total of $1\frac{1}{2}$ pints (850 ml.) of