THE INFLUENCE OF ACUTE ALCOHOLISM ON THE
NORMAL VITAL RESISTANCE OF RABBITS TO
INFECTION.

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DURING the past six months a portion of the time at my disposal has been occupied with experiments the results of which I propose to embody in this contribution.

These studies were made in the Laboratory of Hygiene of the University of Pennsylvania under the auspices of the Committee of Fifty to Investigate the Alcohol Question, who generously placed at my disposal the funds necessary to defray the expenses of the work.

In the distribution of the several subdivisions of the general question relating to the influence of alcohol upon the physical and moral well-being of those who use it as a beverage, the committee has seen proper to assign to me for experimental solution one of the most interesting and important phases of the subject—viz., that concerning the influence of alcoholism, acute and chronic, upon the normal vital resistance of animals to various forms of infection.

In undertaking the work a general scheme of procedure was drawn up that seemed to meet most of the requirements of the problem, but as I now review it I find that it has been possible, in the time at my disposal, to cover only a limited portion of the ground included in this scheme.

The lines along which it was proposed to conduct these investigations are as follows:

1. Determine if the normal vital resistance of animals to infection by the common pathogenic bacteria is demonstrably influenced

by either acute or chronic alcoholism, induced through the use of known amounts of pure ethyl alcohol.

2. If any or no effect is observed, determine if the same holds good for animals under the influence of the commoner alcoholic beverages, as beer, wine, whisky, cordials, etc.

3. Determine if through either acute or chronic alcoholism the germicidal properties of the serum of the blood of animals is materially altered. If so, determine, if possible, the nature of this alteration.

Thus far the work has borne upon the question concerning the influence of acute alcoholism upon the resistance of rabbits to infection by the pyogenic cocci—i. e., the streptococcus pyogenes (erysipilatos) and the staphylococcus pyogenes aureus—and by the bacillus coli communis, and the results are in many ways sufficiently instructive to warrant their report at this time.

A difficulty that arose at the outset was in procuring cultures of pathogenic organisms of suitably diminished virulence without their being at the same time totally devoid of this property. As experience has taught us to expect certain deviations from the usual course of infection when normal animals are inoculated with attenuated cultures, such, for instance, as prolongation of the period of incubation and modification of the pathological lesions, the problem under consideration seemed to be in part most easy of solution through a comparison of results obtained by the use of such cultures on groups of alcoholized and non-alcoholized animals. Should such modifications occur in the normal animals, as would be anticipated, and an infection not differing from that produced by fully virulent cultures occur in the alcoholized animals, the difference could reasonably be referred to a reduction of vital resistance brought about by the alcohol administered.

To meet the requirements it would perhaps have been best to have employed cultures of organisms that were diminished in virulence to definite degrees of attenuation, such, for instance, as the bacillus anthracis attenuated to the degree of virulence represented by its primary and secondary vaccines. As such material was not at my disposal, however, cultures of another sort were used—namely,

those that were of a low degree of virulence without this degree being definitely determined.

Again, cultures of organisms were employed the pathogenic powers of which are usually irregular and uncertain, while in still other tests an effort was made to detect a difference between alcoholized and non-alcoholized animals when inoculated with virulent material but in very small doses, hoping in this way to demonstrate, by a difference in the period of incubation, a difference of resistance in the animals composing the two groups.

The experiments were made with cultures of streptococcus pyogenes of a low degree of virulence, with normal bacillus coli communis, and with virulent staphylococcus pyogenes aureus, and, as the results to be reported show, with very diverse consequences.

Another difficulty was encountered in regulating the dose of alcohol. The intention was to have the animals daily in a state of intoxication, but it is not easy to decide just when this stage is reached, as the only certain indication of it is inco-ordination of muscular movement. It frequently occurred that when alcohol was given to this stage the direct effect of the drug was such as to gravely imperil the life of the animal, and in a certain number of instances the animals did not rally from even so few as one or two such administrations. If the dose were diminished, then one could often not be sure that the rabbit was intoxicated.

On the other hand, one encounters occasionally an individual on which alcoholism to intoxication has apparently no effect upon the general health, and may be prolonged over relatively long periods. One of my animals, for instance, received daily doses of alcohol ranging from 5 to 15 cubic centimetres for one hundred and fourteen days. Its weight at the beginning was 1,330 grammes, and at the end 1,350 grammes, while during the interval its weight had been as high as 1,520 grammes and as low as 1,090 grammes. It died under the administration of 15 grammes daily with macroscopic lesions of only the gastric mucous membrane. I believe that the studies upon the effects of smaller, non-intoxicating doses of alcohol will demonstrate the possibility of continuing the administration of the drug over prac-

tically an indefinite period, quite to the stage of chronic alcoholism, in a fair proportion of the animals treated in this way.

The individual susceptibility of different animals to the physiological action of alcohol differed in such a way as to require at the beginning a special dose for each individual. It is impossible to maintain throughout a constant relation between body weight and dose necessary to produce the desired effects. For instance, it can not be said if 5 cubic centimetres of alcohol produces intoxication in a rabbit of 1,000 grammes weight, that necessarily 10 cubic centimetres will have the like effect in the next rabbit of 2,000 grammes weight. The dose can only be determined by experiment.

It frequently occurred that, when the necessary dose had been determined, its continuous administration over several or more days resulted in very rapid and marked loss in body weight, an indication of the greatest importance, meaning, that if the alcohol be continued the animal is practically certain to die. Under these circumstances it becomes necessary to either diminish the dose or cease the administration entirely for a time, until the lost weight is partially or completely recovered. During the interval of rest, as it may be called, the animal is of course not daily intoxicated, and while the records of these experiments refer to animals "daily under the influence of alcohol to the stage of intoxication," it will be borne in mind that with many of these animals such periods of rest, varying in duration, were more or less frequently necessary.

As it was impossible to induce the rabbits to take alcohol voluntarily, either with the food or otherwise, it became necessary to administer it through a soft-rubber catheter passed down the œsophagus into the stomach, and though this was done as gently as possible, the irritation resulting from the repeated passage of the catheter, together with the depressing influence of the drug, was accompanied in a number of instances by intercurrent infections which, from their character and location, I think can be reasonably traced to insignificant wounds of the mucous surface of the œsophagus made when the alcohol was administered.

In only two instances was death positively the result of inspira-

tion of alcohol into the air passages at the time of operation. When such an accident occurs death is practically instantaneous.

The most common macroscopic effect of the direct action of the alcohol was erosion and inflammation of the mucous membrane of the stomach, a condition that was unfortunately present in quite a number of my animals, and which complicated matters in such a way as to vitiate considerably the results of the experiments.

When the necessary dose of alcohol was determined, it was always given mixed with an equal quantity of distilled water.

The dose necessary to positively produce intoxication ranged from 5 cubic centimetres to 15 cubic centimetres of pure ethyl alcohol, though the usual dose in rabbits of from 1,500 to 1,800 grammes weight was from 7.5 cubic centimetres to 10 cubic centimetres, doses which if taken by a man of one hundred and fifty pounds weight would be roughly equivalent to from two thirds to five sixths of a pint of absolute alcohol. Notwithstanding this apparently very large amount, animals have repeatedly been encountered on which from 10 to 12, and even 15 cubic centimetres had no visible influence, though the continuance of these doses in many instances was followed by death associated with grave lesions of the gastric mucous membrane.

While rabbits offer conditions in a way favourable to experiments of this character, they are so liable to intercurrent bacterial and protozoal infections as to lead to many irregularities when large numbers of them are used. In the course of this work a number of experiments have been seriously vitiated by reason of such complications. The general plan followed in these experiments was to employ groups of equal numbers of animals. All were inoculated in the same way, then to one group alcohol was given, while to the other no alcohol was administered. They were all then kept under the same conditions of food, etc. Each animal was weighed in the morning before it was fed. In one or two cases the number of "controls" was fewer than that of the alcohol group. Control animals receiving only alcohol were not introduced into each experiment, as the necessary data on this point could always be had by reference to the records of

preceding experiments in which the different effects of the drug on different animals was recorded.

Without going further into the particulars, it will suffice to tabulate the details and briefly summarize the results of each experiment as follows:

EXPERIMENT I.

Summary of the results of the intravenous inoculation of rabbits receiving daily doses of alcohol to the stage of intoxication, with bouillon cultures of streptococcus pyogenes obtained from a phlegmonous inflammation in man:

Of eleven rabbits inoculated intravenously with varying amounts of streptococcus pyogenes, six received daily doses of alcohol for different lengths of time. The remaining five of this group received no alcohol. In addition, two rabbits received only daily doses of alcohol. Of the six inoculated animals that received alcohol, all died after marked loss of weight and all exhibited lesions referable to the inoculation. One revealed a condition of the liver probably the result of the action of the alcohol.

Of the five inoculated animals to which no alcohol was given, one died, one was killed, and three recovered.

The one that died presented no lesions referable to the inoculation. Cultures revealed the presence of streptococci in the liver mixed with another organism, while the other internal organs were sterile.

The animal that was killed presented no lesions of importance, and its blood and internal organs were found by culture test to be sterile.

Each of the three remaining animals suffered from temporary erysipelas of the ear at the site of needle puncture. They recovered from this, and at the end of one hundred and twenty days were apparently in good condition, one having gained 330 grammes, the other 110 grammes, and the other 270 grammes in weight.

Of the two animals that were not inoculated, but which received alcohol daily, one died after one hundred and fourteen days with a condition of the gastric mucous membrane referable to the alcohol, the other after thirty-four days with no macroscopic lesions to account for death.

EXPERIMENT II.

Summary of the results of intravenous inoculation of rabbits, receiving intoxicating doses of alcohol daily, with suspensions of streptococcus pyogenes:

The eighteen animals employed in this experiment were divided into four groups and treated as follows:

Four received intoxicating doses of ethyl alcohol for five days and were then inoculated intravenously with 0.5 cubic centimetre of a suspension of streptococcus pyogenes.

Five received intoxicating doses of methyl alcohol for five days and were then similarly inoculated.

The alcohol was continued in both groups after inoculation until death.

Five received, in addition to the inoculation, daily doses of distilled water, injected into the stomach in the same manner as was the alcohol in the other animals, for fifteen days. After this alcohol was given to two of them—to one for two days, to the other for six days—while the remaining three got nothing from the fifteenth day.

Four were simply inoculated. One of this group received a single dose of alcohol.

The nine latter animals served as controls.

RESULTS.—Of nine inoculated animals to which alcohol was given, seven died with suppurative lesions.

Of nine inoculated animals that received no alcohol until after the fifteenth day, when alcohol was given to two, five died, three were killed, and one was observed for fifty-two days. In only three of the nine were suppurative lesions detected at autopsy.

Of the seven alcohol animals that died, five presented lesions at autopsy that could be attributed to the action of the alcohol.

EXPERIMENT III.

Summary of the results of intravenous inoculation of rabbits receiving alcohol daily to the stage of intoxication, with suspensions of bacillus coli communis from human faeces:

Of five rabbits, each of which was inoculated with 1 cubic centimetre of a suspension in bouillon of bacillus coli communis, and all of which had

been receiving alcohol to the stage of intoxication daily for five days, four died in from eighteen to twenty hours and one in eighteen days after inoculation.

None presented lesions referable to the inoculation. One revealed a condition of the gastric mucous membrane that evidently resulted from the direct action of the alcohol. *Bacillus coli communis* was obtained in cultures from the internal organs of all.

Five rabbits, each of which had been receiving alcohol in doses ranging from 2.5 to 15 cubic centimetres daily for thirty-one days, were inoculated intravenously with the same material in the same amount that was employed in the preceding group.

One died within twenty-four hours after the inoculation.

Four died in from forty-three to fifty-five days after the inoculation.

Three presented at autopsy lesions referable to the inoculation—viz., the condition of the liver, gall bladder, and bile described by Blachstein.*

Two presented no lesions attributable to the inoculation.

Two showed a condition of the liver that may possibly have resulted from the prolonged action of the alcohol, while in the remaining three no results of the alcohol were evident.

Two control animals that were inoculated in the same manner with the same material, but which received no alcohol, were alive on the seventy-ninth day after inoculation. By the sixtieth day one had gained 230 grammes in weight, while the other, though apparently well, had lost 200 grammes in weight.

EXPERIMENT IV.

Summary of the results of inoculation of alcoholized animals with suspensions of *bacillus coli communis*:

Three animals received intravenous inoculation of 0.5 cubic centimetre of a suspension of *bacillus coli*. Immediately afterward the administration of alcohol was begun. One died during the night and one on the day following the inoculation. *Bacillus coli* was found by cultures in the internal organs of both. The third died eight days after inoculation with no characteristic lesions and no colon bacilli in the internal organs.

* Blachstein. Intravenous Inoculation of Rabbits with the *Bacillus Coli Communis* and the *Bacillus Typhi Abdominalis*. *Bulletin of the Johns Hopkins Hospital*, vol. ii, No. 14, July, 1891.

The mucous membrane of the stomach was eroded and there was a fibrino-purulent pericarditis and pleuritis, evidently the result of an intercurrent infection, probably induced by the repeated passage of the catheter along the œsophagus.

Three other rabbits that had been getting alcohol for four days were inoculated in the same manner as the preceding. Two died on the ninth day and one on the eighteenth day following inoculation.

In one, dead on the ninth day, were the characteristic lesions described by Blachstein. There was also present a condition of the stomach that was manifestly the result of the action of the alcohol.

Of the remaining two, in one death ensued from an intercurrent infection, while in the other death was the result of an intestinal intussusception. This latter animal presented erosion of the gastric mucous membrane that was evidently the result of the action of the alcohol.

In both animals that died on the ninth day colon bacilli were present in cultures from the internal organs, while in the one dead on the eighteenth day the blood and internal organs were sterile.

Three control animals were alive and apparently well on the forty-sixth day. One had gained 50 grammes, the other 280 grammes, while the third had lost 120 grammes in weight.

In short, of six alcoholized rabbits inoculated with colon bacilli, all died. One presented characteristic lesions at autopsy. Of three non-alcoholized, control animals, none died.

EXPERIMENT V.

Results of intravenous inoculation of rabbits receiving alcohol, with cultures of *staphylococcus pyogenes aureus*:

In this experiment the first inoculation was without effect, and the animals were inoculated a second time after an interval of seven days. Four animals were employed—viz., two alcoholized and two controls. The alcoholized animals died in fourteen and two days, respectively, after the inoculation. Both presented lesions referable to the inoculation and neither showed conditions due to the direct action of the alcohol. One control animal died in four days after the first inoculation, while the second died in six days after the second inoculation. To this latter animal alcohol was administered from the time of the second inoculation. Both presented lesions referable to the inoculation, and the one that got alcohol presented also conditions due to the direct action of the alcohol.

This experiment does not demonstrate any material difference between the alcoholized and the non-alcoholized animals as regards their susceptibility to this form of infection.

EXPERIMENT VI.

Subcutaneous inoculation of alcoholized animals with cultures of *staphylococcus pyogenes aureus*:

There were four animals in this group, two alcoholized and two controls. In all except one, an alcoholized rabbit, the subcutaneous inoculation was without effect up to the seventh day. On the seventh day the three remaining animals were inoculated again, but this time intravenously.

RESULTS.—One alcoholized animal died in three days after the subcutaneous inoculation. Death was due to pseudo-tuberculosis of the lungs. There was only a trifling area of suppuration at the seat of inoculation. The other alcoholized rabbit died four days after the intravenous inoculation and presented the usual condition of widespread miliary-abscess formation. Both control animals died after the intravenous inoculation—the one in seven days, the other in twenty-four hours. The former presented lesions characteristic of the inoculation, while the latter presented no macroscopic lesions at all at autopsy. The former control animal had been given alcohol since the date of its second intravenous inoculation. At autopsy it presented lesions referable to the direct action of the alcohol.

EXPERIMENT VII.

Intraperitoneal inoculation of alcoholized animals with cultures of *staphylococcus pyogenes aureus*:

Four animals were employed; two received alcohol and two served as controls.

The animals that exhibited no effects of the intraperitoneal inoculation at the end of a week were reinoculated with the same material, but this time the inoculation was intravenous.

One alcoholized animal died the day following the intraperitoneal inoculation, the other two days after the intravenous inoculation.

In neither were lesions detected that could account for death, or be positively referred to either the inoculation or the alcohol.

Both control animals recovered from the intraperitoneal inoculation and at the end of a week were inoculated intravenously.

One died two days after this latter inoculation and presented neither mycotic nor alcoholic lesions, death being due to rupture of the gravid uterus, while the other died nine days after intravenous inoculation with abscesses in myocardium and kidneys.

EXPERIMENT VIII.

Intravenous inoculation of alcoholized rabbits with bouillon cultures of *staphylococcus pyogenes aureus*:

Of the six inoculated animals to which alcohol was given, three died in less than twenty-four hours and three in from forty-eight to seventy-two hours after inoculation. In three, lesions were present that could positively be referred to the inoculation, and in one the condition was doubtful. In two no such lesions could be found.

In five of the six animals a condition of the mucous membrane of the stomach was found that was evidently the result of the direct action of the alcohol.

Of the six inoculated animals that did not get alcohol three died in less than twenty-four hours, two after five and twelve days, respectively, while the remaining animal was apparently well at the end of forty-three days.

Three of these animals presented lesions that resulted from the inoculation, in one the lesion was doubtful, in one no lesions were detected, and the sixth is still alive.

This experiment demonstrates a slight, though not very important or striking, difference between the course of infection in the two groups.

EXPERIMENT IX.

Subcutaneous inoculation of alcoholized rabbits with cultures of *staphylococcus pyogenes aureus*:

Of the six inoculated animals to which alcohol was given, one died during the night following the inoculation; the remaining five died in from five to fifteen days later.

Two of these animals presented no lesions referable to the inoculation, one presented an extensive local lesion, and three presented a lesion of the pleuræ and pericardium of doubtful significance. This condi-

tion was identical in the three animals and consisted of a fibrino-purulent inflammation of practically all the serous surfaces within the thoracic cavity. Cultures from this lesion revealed the presence of a staphylococcus that grew feebly, producing but a very faint, barely perceptible, cream colour, and in general gave the impression that it might be an attenuated or enfeebled culture of staphylococcus aureus. It was not studied in detail.

The animals in which this lesion was found died in five, fifteen, and fifteen days, respectively.

The three control animals used in this experiment manifested no ill effects of the treatment. They were alive and well at the end of forty-six days after inoculation.

In none of the six animals that received alcohol was there any macroscopic evidence of the action of the alcohol on the tissues.

EXPERIMENT X.

Intravenous inoculation of alcoholized rabbits with staphylococcus pyogenes aureus attenuated (?) by exposure to chloroform:

Four animals were used in this experiment.

Of the two inoculated animals to which alcohol was given one died on the fifth, the other on the second day following the inoculation. One presented a lesion of the kidney positively referable to the inoculation, the other a condition of the peritonæum that probably, though not certainly, resulted from the treatment to which the animal had been subjected.

Both of these animals presented extensive erosions of the gastric mucous membrane that was manifestly the result of the direct action of the alcohol.

Neither of the two control animals evinced any ill effects from the inoculation; both gained in weight, and at the end of twenty-eight days were eliminated from the experiment as not likely to manifest evidences of infection.

CONCLUSIONS.

The deductions that may be drawn from the results of these experiments are as follows:

That the normal vital resistance of rabbits to infection by streptococcus pyogenes (erysipelatos) is markedly diminished through the

influence of alcohol when given daily to the stage of acute intoxication. That a similar, though by no means so conspicuous, diminution of resistance to infection and intoxication by the bacillus coli communis also occurs in rabbits subjected to the same influences.

And that, while in alcoholized rabbits inoculated in various ways with staphylococcus pyogenes aureus, individual instances of lowered resistance are observed, still it is impossible to say from these experiments that in general a marked difference is noticed between alcoholized and non-alcoholized animals as regards infection by this particular organism.

It is interesting to note that the results of inoculation of alcoholized rabbits with the erysipelas coccus correspond in a way with clinical observations on human beings addicted to the excessive use of alcohol when infected by this organism.

In the course of the work an effort was made to determine if, through the oxidation of alcohol in the tissues to acids of the corresponding chemical group, the increase of susceptibility could be referred to a diminution in the alkalinity of the blood as a result of the presence of such acids. The number of experiments thus far made on this point is too small to justify dogmatic statements, but from what we have gathered there is but little evidence in support of this view.

Throughout these experiments, with few exceptions, it will be seen that the alcoholized animals not only showed the effects of the inoculations earlier than did the non-alcoholized rabbits, but in the case of the streptococcus inoculations the lesions produced (formation of miliary abscesses) were much more pronounced than are those that usually follow inoculation with this organism.

With regard to the predisposing influence of the alcohol, one is constrained to believe that it is in most cases the result of structural alterations consequent upon its direct action on the tissues, though in a number of the animals no such alteration could be made out by macroscopic examination. I am inclined, however, to the belief, in the light of the work of Berkley and of Friedenwald, done under the direction of Prof. Welch, in the Pathological Laboratory of the

Johns Hopkins University, that a closer study of the tissues of these animals would have revealed in all of them structural changes of such a nature as to indicate disturbances of important vital functions of sufficient gravity to fully account for the loss of normal resistance.

The conspicuous influence of the alcohol on the gastric mucous membrane in many of these animals, with the consequent disturbance of nutrition, is undoubtedly the explanation of the marked loss in body weight that was observed in many of the animals employed in these experiments. In this light the susceptibility induced by alcohol to excess is somewhat analogous to that induced by starvation, where we see the resistance of animals to particular forms of infection very markedly diminished.

TABULATED DETAILS OF FOREGOING EXPERIMENTS.

EXPERIMENT I.

Table showing the Results of Intravenous Inoculations of Rabbits that were receiving Daily Doses of Ethyl Alcohol to the Stage of Intoxication with Bouillon Cultures of the *Streptococcus Pyogenes*, obtained from a Phlegmonous Inflammation of the Foot of a Man.

Rab- bits.	No. of days ob- served.	Total amount of alcohol received.	Daily dose of alcohol.	Interval between the beginning of alcohol and time of inoculation.	WEIGHT IN GRAMMES.		Lesions ref- erable to inoculations. + = present. O = absent.	Lesions ref- erable to the alcohol. + = present. O = absent.	Results and remarks.
					Begin- ning.	End.			
1	41	250 c. c.	5 to 10 c. c.	36 days. Was then inoculated with 1 c. c. of bouillon culture of strep- tococcus intra- venously.	1,190	910	+	+	Died six days after inoculation. Liver very yellow and friable; contained large numbers of streptococci; many of the capillaries quite filled with them. Streptococci also present in pure culture in blood, kidney, and bone marrow. No abscesses detected.
2	40	240 c. c.	5 to 7.5 c. c.	35 days. Inocula- tion same as that of No. 1.	1,210	880	+	0	Died on sixth day after inoculation. Numerous miliary abscesses in muscles along the spine. No abscesses in myocardium or kidneys.
3	49	297.5 c. c.	5 to 7.5 c. c.	45 days. Intrave- nous inoculation of bouillon cul- ture of strepto- coccus 24 hours old.	1,280	960	+	0	Cultures.—Streptococci in pure culture in muscle abscesses, blood, liver, kidney, and spleen. Died on fifth day after inoculation. Miliary abscesses throughout the voluntary musculature. Abscesses in myocardium. Pale areas, but no abscesses in kidneys. Spleen dark and congested.
4	47	282.5 c. c.	5 to 7.5 c. c.	45 days. Inocula- tion same as that of No. 3.	1,200	1,040	+	0	Cultures.—Streptococci in pure culture from pale points in heart, from blood, liver, spleen, kidney, and peritoneal cavity. Died on third day after inoculation. No abscesses in muscles. Several pale points in myocardium; these contained streptococci in large numbers on microscopic examination.

Rab- bits.	No. of days ob- served.	Total amount of alcohol received.	Daily dose of alcohol.	Interval between the beginning of alcohol and time of inoculation.	WEIGHT IN GRAMMES.		Lesions ref- erable to in- oculations. +=present O=absent	Lesions ref- erable to in- the alcohol +=present O=absent.	Results and remarks.
					Begin- ning.	End.			
5	16	145 c. c.	7.5 to 10 c. c.	Inoculated 3 times. Intervals: First, 2 days; second, 4 days; third, 7 days. Last in- oculation (fatal) was 0.8 c. c. of a bouillon culture of streptococcus intravenously.	1,740	1,290	+	0	Animal had two subcutaneous inoculations, first two days and second four days after beginning of alcohol. Seven days after beginning of alcohol it received an intravenous injection of 0.8 c. c. of a bouillon culture of streptococcus pyogenes. Died nine days after last inoculation. Sites of subcutaneous inoculations sterile. As result of intravenous inoculation the voluntary muscles were everywhere studded with miliary abscesses. Similar abscesses in diaphragm; none in internal organs. <i>Cultures</i> from abscesses in muscles and from blood show streptococci in pure culture.
6	3	30 c. c.	10 c. c.	Both given at same time. Same in- oculations as those for No. 5.	1,910	1,740	+	0	Miliary abscesses throughout voluntary muscles, especially those of thorax. Spleen very large, almost black in colour; measured 6.5 cm. long, 2 cm. wide, and 1.5 cm. thick. Numerous abscesses in myocardium. Cultures and cover slips revealed streptococci in muscle abscesses, liver, spleen, blood, and kidney.

Control Animals, received Alcohol, not inoculated.

A	114	845 c. c.	5 to 15 c. c.	Not inoculated.	1,330	1,350		+	The daily dose of 15 c. c. was begun eight days before death, after the animal had been getting 10 c. c. daily for the thirty-seven preceding days. Autopsy revealed macroscopic lesions only in the stomach. The walls were thickened and edematous, in some places thin. There was widespread erosion and necrosis of the mucous membrane. The animal was markedly susceptible to alcohol. At autopsy, no macroscopic lesions to account for death were found.
B	34	147.5 c. c.	5 to 10 c. c.	Not inoculated.	1,030	600		0	

Control Animals inoculated, but received no Alcohol.

C Control for No. 1.	120	No alcohol.		No alcohol. Inoculated at same time as No. 1, and in same way.			+ Erysipelas of ear about site of operation.		In three weeks after inoculation this animal was well, having had a local erysipelas of ear at point of puncture of needle. After four months it had gained 330 grammes in weight, and was not observed further.
D Control for No. 2 and No. 6.	120	Do.		No alcohol. Inoculated at same time and in same way as No. 2.			+ Temporary erysipelas of ear at site of operation.		After about three weeks the animal was well of its local erysipelas in ear. It had recovered its lost weight, and was apparently in good condition. At end of four months it had gained 110 grammes in weight. Observation discontinued.
E Control for No. 3.	120	Do.		No alcohol. Inoculated at same time and in same way as No. 3.			+ Temporary erysipelas of ear.		Temporary redness and swelling of ear at site of operation. At end of four months had gained 270 grammes. Observation discontinued.
F Control for No. 4.	16	Do.		No alcohol. Inoculated at same time and in same way as No. 4.	1,220	800	+		Died after sixteen days. For some time had had profuse watery discharge from nostrils and mouth. This began on fourth day after inoculation. No lesions of importance found at autopsy. <i>Cultures</i> .—Blood: pure culture of streptococci. Liver: streptococci, with a large micrococcus. Lung, kidney, and spleen sterile.
G Control for No. 5.	15	Do.		No alcohol. Inoculated at same times and in same way as No. 5.	1,410	1,590	+ Circumscribed pus formations at sites of subcutaneous inoculations.		Animal killed on fifteenth day— <i>i. e.</i> , nine days after its last (intravenous) inoculation. No miliary abscesses in muscles and no lesions of internal organs found at autopsy. Circumscribed pus formations in stages of healing at both sites of subcutaneous inoculation. <i>Cultures</i> from sites of subcutaneous inoculation and internal organs showed them to be sterile.

EXPERIMENT II.

Table showing the Results of Intravenous Inoculation of Rabbits that were receiving Daily Doses of Alcohol to the Stage of Intoxication, with Suspensions of *Streptococcus Pyogenes*.
Ethyl Alcohol.

Rab- bits.	No. of days ob- served.	Total amount of alcohol received.	Daily dose of alcohol.	Interval between the beginning of alcohol and time of inoculation.	WEIGHT IN GRAMMES.		Lesions ref- erable to in- oculations. +=present. O=absent.	Lesions ref- erable to in- oculations. +=present. O=absent.	Results and remarks.
					Begin- ning.	End.			
7	13	142.5 c. c.	7.5 to 15 c. c.	5 days. Intra- venous injection of 0.5 c. c. of a sus- pension of strep- tococcus pyo- genes. Do.	2,010	1,650	O	O	Died eight days after inoculation. <i>Autopsy</i> .—No lesions anywhere to be detected. No streptococci in cultures. Evidently an intercurrent infection.
8	12	142.5 c. c.	7.5 to 15 c. c.	Do.	1,600	1,350	+ Muscle abscesses.	+ (Stomach.)	Died seven days after inoculation. Abscesses in muscles of both thighs; none in heart or kidneys. Mucous membrane of stomach very much eroded. <i>Cultures</i> .—Streptococci in large numbers and in pure culture from blood, liver, kidney, and muscle abscess.
9	10	90 c. c.	7.5 to 10 c. c.	Do.	1,020	940	+ Strepto- cocci in blood.	O	Died fourth day after inoculation. <i>Autopsy</i> .—No abscesses anywhere in voluntary muscles. Several diffuse pale areas in heart; numerous necrotic areas in liver. <i>Cultures</i> demonstrate a mixed infection; those from blood and kidney contain streptococci, those from the other organs contain a short oval bacillus.
10	12	132.5 c. c.	7.5 to 15 c. c.	Do.	1,860	1,530	O	+ (Stomach.)	Died seven days after inoculation. <i>Autopsy</i> .—Muscle abscesses not detected. Liver contained coecidia nodules. Kidneys presented several small cortical hemorrhages. Mucous membrane of stomach inflamed and eroded. <i>Cultures</i> .—No streptococci in cultures from blood, liver, spleen, kidneys, or peritoneal cavity. In all these tubes was a short oval bacillus.
11									Died on fourth day as result of alcohol. Had not been inoculated.

Animals receiving Commercial (Pure) Methyl Alcohol.

12	11	109 c. c.	3 to 15 c. c.	5 days. Inocula- tion same as in preceding ani- mals of this ex- periment.	1,520	1,260	+	+	Died six days after inoculation. <i>Autopsy</i> .—No muscle abscesses detected. Liver studded with minute yellow points. Mucous men- brane of stomach very much reddened and eroded. <i>Cultures</i> .—Streptococci in pure culture and in large numbers from blood, liver, and spleen. Died on day after the inoculation.
15	7	54 c. c.	3 to 10 c. c.	Do.	1,200	1,110	+	0	<i>Autopsy</i> .—Liver contained psorosperm nodules, in which streptococci in large numbers were found along with the characteristic parasite. Kidneys pale; presented numerous minute cysts (?) over entire cortex. No abscesses anywhere. <i>Cultures</i> .—Streptococci in pure culture and in large numbers from blood, liver, spleen, kidney, and peritoneal cavity. Died on seventh day after inoculation.
14	12	109 c. c.	3 to 15 c. c.	Do.	1,000	1,040	+	+	<i>Autopsy</i> .—A single abscess in muscle of the thigh was detected. Slight excess of moisture in peri- toneal cavity. No abscesses in myocardium or kidneys. A widespread area of erosion and in- flammation of the mucous membrane of the stomach. <i>Cultures</i> .—Streptococci in pure culture from spleen, liver, blood, kidney, and peritoneal cavity. They were present in only small numbers. Died on eighth day after inoculation.
15	13	124 c. c.	3 to 15 c. c.	Do.	1,440	1,420	+	+	<i>Autopsy</i> .—On right leg, near axilla, between skin and muscles, was a circumscribed collection of pus of about the size of an almond. No miliary abscesses detected. Several necrotic areas in liver. Mucous membrane of stomach very red and eroded. This animal had a very acute and painful erysipelas of the ear for several days after inoculation. <i>Cultures</i> .—Streptococci from blood, liver, and large abscess on leg. Died on second day after inoculation.
16	8	46.5 c. c.	3 to 10 c. c.	Do.	1,240	1,140	+	0	<i>Autopsy</i> .—Muscle abscesses in left thigh and in abdominal muscles. Several abscesses in myo- cardium. <i>Cultures</i> .—Streptococci from blood, liver, kidney, and muscle abscesses.

Control Animals for this Experiment. These Animals were inoculated with the Same Material, at the Same Time, and in the Same Way as the Ten Preceding Animals. For Fifteen Days Each received 20 c. c. of Distilled Water daily, injected into the Stomach through a Soft-rubber Catheter.

Rab- bits.	No. of days ob- serv- ed.	Total amount of alcohol received.	Daily dose of alcohol.	Interval between the beginning of alcohol and time of inoculation.	WEIGHT IN GRAMMES.		Lesions ref- erable to in- oculations. + = present. O = absent.	Lesions ref- erable to the alcohol. + = present. O = absent.	Results and remarks.
					Begin- ning.	End.			
17	21	20 c. c. of water daily for 15 days. Alcohol 8 days, nothing begun. In 6 days 30 c. c. of alcohol given.	Water, 20 c. c. Alcohol, 10 c. c. 8 days, nothing.	5 days from the beginning of wa- ter. Inoculation same as preced- ing animals.	1,010	860	O (?) Condition of the ear of this rab- bit was evi- dently ery- sipelatos. Unfortu- nately it was not examined at autopsy.	O	Died on fifteenth day after inoculation and on fifth day after alcohol was begun. <i>Autopsy.</i> —For five days before death this animal has had very sore ear. It was thick, painful, and dependent. Beyond a slight diminution in colour, internal organs were normal. No lesions of muscles. <i>Cultures.</i> —Blood, liver, and kidneys sterile.
18	18	Water as in No. 17. One day, nothing; then got 10 c. c. alcohol on each of 2 days.	Water, 20 c. c. Alcohol, 10 c. c.	5 days from begin- ning of water. Inoculation as above.	1,130	1,020	O	O	Died after second dose of alcohol—i. e., thirteen days after inoculation. <i>Autopsy.</i> —Neither recent nor remote suppurative lesions anywhere. Small area of consolidation in left lung (inspiration pneumonia (?)); no bac- teria found in cover slips from this. <i>Cultures.</i> —Blood, liver, and kidneys sterile.
19	52	No alco- hol, 20 c. c. water daily for 15 days. Then got nothing for 37 days.	None.	5 days from begin- ning of water.	1,650	1,500	O		The weight of the animal ran up as high as 1,710 and down as low as 1,450 grammes while in the experiment. At end of fifty-two days it was apparently well. Observation was discontinued. Showed no signs of sickness at any time.

20	16	Do.	"	Do.	1,120	1,130	0		The weight of the animal went up to 1,200 grammes in course of the experiment. It was killed on sixteenth day. <i>Autopsy</i> .—Neither recent nor remote lesions anywhere. Viscera apparently normal. <i>Cultures</i> .—Blood, liver, spleen, and kidney sterile. Weight was up to 1,080 grammes at one time. Killed on sixteenth day. <i>Autopsy</i> .—No lesions of any kind anywhere. Animal apparently normal. <i>Cultures</i> .—Blood, liver, spleen, and kidney sterile.
21	16	Do.	"	Do.	1,010	1,030	0		
<i>Control Animals getting Nothing but the Inoculation.</i>									
22	11	No alcohol. Inoculated on same date and in same way as preceding animals.			920	960	+ Abscesses. Streptococcus septicæmia.		Weight was up to 1,030 during experiment. Died five days after inoculation. <i>Autopsy</i> .—Abscesses in voluntary muscles, in myocardium, and in right kidney; none in left kidney. <i>Cultures</i> .—Streptococci in pure culture for blood, liver, spleen, kidney, and peritoneal cavity. Intercurrent infection before it was inoculated. Excluded from the experiment.
23									Died on twenty-fifth day. For some days before death there was profuse watery discharge from mouth and nose. <i>Autopsy</i> .—A small caseous gland in right axilla. Did not contain streptococci on microscopic examination. No other lesions noted beyond numerous minute petechiae over cortex of kidneys. <i>Cultures</i> .—Blood, liver, kidney, and peritoneal cavity sterile.
24	25	Do.			1,320	1,040	+ (?) Caseous gland in axilla.		Died on second day after its dose of alcohol—i. e., on twelfth day after inoculation. <i>Autopsy</i> .—Evidence of healed peritonitis. Two large abscesses in left pectoral muscle; no abscesses in myocardium or kidneys. The muscle abscesses were apparently of long standing. <i>Cultures</i> .—Streptococci from muscle abscesses. Blood and kidney sterile.
25	17	None until 16th day, when 1 dose of 10 c. c. was given.		Do.	1,480	1,250	+ Abscesses in muscle.		

Rab- bits.	No. of days ob- served.	Total amount of alcohol received.	Daily dose of alcohol.	Interval between the beginning of alcohol and time of inoculation.	WEIGHT IN GRAMMES.		Lesions ref- erable to in- oculations. + = present. O = absent.	Lesions ref- erable to in- the alcohol. + = present. O = absent.	Results and remarks.
					Begin- ning.	End.			
26	16	No alco- hol.		Do.	1,490	1,090	O		Killed on sixteenth day after experiment was be- gun— <i>i. e.</i> , eleventh day after inoculation. <i>Autopsy</i> .—Suppurative lesions, neither recent nor remote, were anywhere to be detected. <i>Cultures</i> .—No streptococci in either the blood or the internal organs.

EXPERIMENT III.

Table showing the Results of Intravenous Inoculation of Rabbits receiving Daily Doses of Ethyl Alcohol to the Stage of Intoxication, with Suspensions of *Bacillus Coli Communis* from Human Faeces.

27	6	55 c. c.	7.5 to 10 c. c.	5 days. Intra- venous injection of 1 c. c. of opaque suspension of <i>b.</i> <i>coli</i> 52 hours old.	1,990	1,970	O	+	Died about five hours after inoculation. <i>Autopsy</i> .—Mucous membrane of stomach red; slight congestion of spleen and kidneys. <i>Cultures</i> .—A few colonies of bacillus coli from liver. Blood sterile.
28	6	55 c. c.	7.5 to 10 c. c.	Do.	1,890	1,800	O	O	Found dead on morning following the injection. <i>Autopsy</i> .—About 3 c. c. of reddish fluid in peri- tonaeum. One or two dark areas in lungs. No other lesions. <i>Cultures</i> .—Liver, blood, and peritoneal cavity gave bacillus coli in pure culture.
29	23	240 c. c.	7.5 to 10 c. c.	Do.	1,400	920	O	O	Died on twenty-third day— <i>i. e.</i> , eighteen days after inoculation. <i>Autopsy</i> .—Pseudo-tuberculosis of apex of left lung. Liver pale and tough. Gall bladder distended with dark-green bile.
30	6	55 c. c.	7.5 to 10 c. c.	Do.	1,690	1,770	O	O	<i>Cultures</i> .—Peritoneal cavity, five colonies, and bile, one colony; all were of bacillus coli. Found dead on morning following the inoculation; had evidently been dead some time, as post-mor- tem changes were in progress in all the organs. <i>Cultures</i> .—Bacillus coli in pure culture from spleen, kidney, liver, and blood.

31	6	55 c. c.	7.5 to 10 c. c.	Do.	1,710	1,470	0	0	Found dead on morning following the inoculation. Post-mortem decomposition more or less advanced in all the viscera. No lesions discernible to naked eye. Pure cultures of bacillus coli obtained from blood, liver, spleen, kidney, and peritoneum.
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The Following Animals were inoculated at the Same Time as the Preceding, with the Same Amount of the Same Material. They differed from the Preceding in having received Alcohol daily for a much Longer Time before the Inoculation.

32	32	112.5 c. c.	2.5 to 7.5 c. c.	31 days. Same inoculation as above.	1,130	1,070	0	+	(?) (Liver.)	This animal was so susceptible to alcohol that it could not be given regularly. Found dead on morning following the inoculation. The only lesions found at autopsy were very pale liver and a circumscribed oedematous patch in the lung. Colon bacilli in pure culture from blood, liver, spleen, and kidney.
33	75	440 c. c.	2.5 to 10 c. c.	33 days. Inoculated as above.	2,000	1,310	+	0	(Bile.)	Died on seventy-fifth day—i. e., forty-three days after inoculation. <i>Autopsy</i> .—Moderate emaciation. Liver so thickly studded with coccidia that nothing could be detected as to presence of other lesions. Gall bladder very much distended with clear, pale bile in which floated amorphous flakes that could be seen through the walls of the organ. These consisted of leucocytes, epithelium, blood corpuscles, and bacteria. <i>Cultures</i> .—Pure cultures of bacillus coli from bile and blood. Cultures from liver contained colon bacilli with another bacillus (bacillus pyrogenes). Died on eighty-eighth day—i. e., fifty-five days after inoculation.
34	88	580 c. c.	5 to 15 c. c.	Do.	1,560	1,330	+	0	(Liver and bile.)	<i>Autopsy</i> .—Slight emaciation. Several irregular necroses in liver. Very great distention of gall bladder with clear, pale-greenish bile, in which was an amorphous sediment. <i>Cultures</i> .—Colon bacilli in pure culture from the bile. Liver and blood sterile.

Rab- bits.	No. of days ob- served.	Total amount of alcohol received.	Daily dose of alcohol.	Interval between the beginning of alcohol and time of inoculation.	WEIGHT IN GRAMMES.		Lesions ref- erable to in- oculations. +=present, O=absent.	Lesions ref- erable to the alcohol. +=present, O=absent.	Results and remarks.
					Begin- ning.	End.			
35	87	560 c. c.	2.5 to 15 c. c.	Do.	1,620	1,220	O	+ (?) (Liver.)	Found dead on eighty-seventh day— <i>i. e.</i> , fifty-four days after inoculation. <i>Autopsy.</i> —Liver large, tough, rough on its surface. On section, the open mouths of vessels are very conspicuous. Gall bladder filled with normal dark-green bile. <i>Cultures</i> demonstrated the blood, liver, and bile to be sterile. Found dead on eighty-fourth day— <i>i. e.</i> , fifty-one days after inoculation. <i>Autopsy.</i> —Both lungs in part affected with pseudo- tuberculosis. Liver presented several irregular parts of yellowish superficial necroses. <i>Gall</i> <i>bladder</i> very large, distended with pale, clear bile, in which floated flakes of amorphous mate- rial; these could be seen through the walls of the distended organ. <i>Cultures.</i> — <i>Bacillus coli</i> was obtained only from the bile. It was here in pure culture. From lungs <i>bacillus pyogenes</i> (?) was obtained in pure culture.
36	84	537.5 c. c.	2.5 to 10 c. c.	Do.	1,570	1,070	+	O	
							(Liver and bile.)		

Controls. Injected at Same Time as the Others, but received no Alcohol.

37	79			Injected as above.	1,290				Seventy-nine days after inoculation this animal is still alive. Had gained by sixtieth day 230 grammes. Observation discontinued.
38	79			"	1,820				Seventy-nine days after inoculation the animal is alive, is apparently well though it had lost 200 grammes in weight by sixtieth day.

EXPERIMENT IV.

Table giving the Results of Intravenous Inoculation of Rabbits that were receiving Daily Doses of Ethyl Alcohol to the Stage of Intoxication, with Suspensions of *Bacillus Coli Communis* from Human Feces.

	11	90 c. c.	10 c. c.	Simultaneous, Inoculated with 0.5 c. c. of a suspension of bacillus coli from agar culture 24 hours old.	1,540	1,180	0	+	
39								(Stomach.)	Died eight days after inoculation. Had been under observation for two days before any treatment was begun.
40	2	20 c. c.	10 c. c.	Do.	1,330	1,190	0	0	<i>Autopsy</i> .—Acute fibrino-purulent pleuritis and pericarditis, due to intercurrent infection. Mucous membrane of stomach slightly eroded. No colon bacilli found in the cultures from blood and internal organs.
41	1	10 c. c.	10 c. c.	Do.	1,760		0	0	Died on the day following inoculation. <i>Autopsy</i> .—The only lesion found was an intussusception of the colon involving about 12 cm. of the length. It was very acutely congested, and evidently recent. <i>Cultures</i> .—Blood sterile. Liver: a few colonies of bacillus coli.
42	9	47.5 c. c.	5 to 7.5 c. c.	4 days. Inoculated as above.	1,180	950	0	+	Died during night of the day on which it was inoculated. <i>Autopsy</i> .—No macroscopic lesions. <i>Cultures</i> .—Blood and liver contained large numbers of bacillus coli.
43	18	177.5 c. c.	7.5 to 10 c. c.	Do.	2,110	1,780	0	0	Died on ninth day—i. e., five days after inoculation. <i>Autopsy</i> .—Liver presented several areas of superficial necrosis. Gall bladder filled with normal bile. A recent volvulus, with intussusception of small intestine. Lymphatic apparatus of intestine enlarged, but not congested. Mucous membrane of stomach eroded. <i>Cultures</i> .—Colon bacilli in small numbers were obtained from liver, blood, bile, and spleen. Died on eighteenth day—i. e., fourteen days after inoculation. <i>Autopsy</i> .—Death ensued from intercurrent infection. No colon bacilli found in cultures.

Rab- bits.	No. of days ob- served.	Total amount of alcohol received.	Daily dose of alcohol.	Interval between the beginning of alcohol and time of inoculation.	WEIGHT IN GRAMMES.		Lesions ref- erable to in- oculations, + = present, O = absent.	Lesions ref- erable to the alcohol. + = present, O = absent.	Results and remarks.
					Begin- ning.	End.			
44	9	87.5 c. c.	7.5 to 10 c. c.	Do.	1,520	1,180	+	+	Died on ninth day— <i>i. e.</i> , five days after inoculation. <i>Autopsy</i> .—Moderate emaciation. Several irregular necroses in liver. Gall bladder distended with pale bile, in which amorphous flakes could be seen through the wall of the distended organ. Amorphous matter consisted of leucocytes, blood corpuscles, and bacteria. Mucous membrane of stomach red and eroded. <i>Cultures</i> .— <i>Bacillus coli</i> in blood, liver, bile, and spleen.

Controls; inoculated in the Same Way but with a Larger Dose of the Same Material as the Preceding Animals, but received no Alcohol.

45				No alcohol. Intra- venous inocula- tion of 0.8 c. c.	1,560				After forty-six days animal apparently well. Weight, 1,610 grammes.
46					1,960				After forty-six days animal apparently well. Weight, 1,840 grammes.
47					1,510				After forty-six days animal apparently well. Weight, 1,790 grammes.

EXPERIMENT V.

Table showing the Results of Intravenous Inoculation of Rabbits receiving Daily Doses of Ethyl Alcohol to the Stage of Intoxication, with Bouillon Cultures of *Staphylococcus Pyogenes Aureus*.

48	24	200 c. c.	10 to 15 c. c.	3 days. Intravenous inoculation of 0.3 c. c. of 24-hour bouillon culture of <i>S. aureus</i> . After 7 days, similar injection of 0.5 c. c.	1,900	1,250	+	0	Died on twenty-fourth day— <i>i. e.</i> , twenty-one days after first and fourteen days after second inoculation. <i>Autopsy</i> .—Several old abscesses in the kidneys; gave appearance of being encapsulated; none in myocardium or voluntary muscles. Widespread pseudo-tuberculosis of right lung. This is evidently the cause of death. <i>Cultures</i> .— <i>Staphylococcus aureus</i> from kidney. Blood, liver, and bile sterile. A long, slender bacillus growing in felt-like, tenacious colonies from the diseased lung. Died on twelfth day— <i>i. e.</i> , nine days after first and two days after second inoculation. <i>Autopsy</i> .—One small abscess in voluntary muscles. Numerous small abscesses in kidneys. None in myocardium. <i>Cultures</i> .— <i>Staphylococcus aureus</i> in very small numbers from blood and kidney. Peritoneum sterile.
49	12	110 c. c.	10 c. c.	Do.	1,360	1,160	+	0	
Controls.									
50	13	None until 7th day of experiment, then alcohol was begun. Total amount, 50 c. c.	10 c. c.	Alcohol given simultaneously with the second inoculation; first inoculation as above; second inoculation on seventh day consisted of 0.5 c. c. of a bouillon culture of <i>S. aureus</i> intravenously.	2,430	2,250	+	+	Died on thirteenth day— <i>i. e.</i> , ten days after first and six days after second inoculation. <i>Autopsy</i> .—Mucous membrane of stomach very much inflamed and eroded. Several conglomerate abscesses in kidneys, none in myocardium or in voluntary muscles. <i>Cultures</i> .— <i>Staphylococcus aureus</i> from kidney. Blood and liver sterile.

Rab- bits.	No. of days ob- served.	Total amount of alcohol received.	Daily dose of alcohol.	Interval between the beginning of alcohol and time of inoculation.	WEIGHT IN GRAMMES.		Lesions ref- erable to in- oculations. + = present. O = absent.	Lesions ref- erable to in- the alcohol. + = present. O = absent.	Results and remarks.
					Begin- ning.	End.			
51	4	None.		One inoculation of 0.3 c. c. of bou- illon culture of <i>S.</i> <i>aureus</i> intrave- nously. No alco- hol.	1,170	920	+	O	Died four days after inoculation. <i>Autopsy</i> .—Abscesses in myocardium and kidneys. None in voluntary muscles. No cultures.

EXPERIMENT VI.

Table showing Results of Subcutaneous Inoculation of Rabbits receiving Daily Doses of Ethyl Alcohol to the Stage of Intoxication, with Cultures of Staphylococcus Pyogenes Aureus.

52	14	125 c. c.	10 to 15 c. c.	3 days. Subcutane- ous inoculation of 1 c. c. of a 24-hour bouillon culture of <i>S.</i> <i>aureus</i> ; 7 days later intravenous inoculation of 0.5 c. c. of simi- lar culture.	1,350	930	+	O	Died on fourteenth day—i. e., eleven days after first and four days after second inoculation. <i>Autopsy</i> .—Typical disseminated miliary abscess formations in muscles and internal viscera. No cultures.
53	6	55 c. c.	7.5 to 10 c. c.	3 days. One sub- cutaneous inocu- lation as above.	1,380	1,080	+	O	Died on sixth day—i. e., three days after inocula- tion. <i>Autopsy</i> .—Small purulent mass at site of inocula- tion. No abscesses anywhere. Large part of both lungs affected with pseudo-tuberculosis. <i>Cultures</i> .— <i>Staphylococcus aureus</i> from site of in- oculation. The slender bacillus referred to in protocol of Rabbit 48 obtained from lung.

Controls.

54	14	60 c. c. Alcohol was begun 7 days after first inoculation— <i>i. e.</i> , with the second inoculation.	10 c. c. for 6 days after second inoculation.	7 days after first inoculation; first inoculation was 1 c. c. of a bouillon culture of <i>S. aureus</i> subcutaneously; second was 0.5 c. c. of similar cultures intravenously.	2,390	2,080	+	+	(Abscesses in kidneys.)	(Stomach)	Died on fourteenth day— <i>i. e.</i> , seven days after second inoculation. <i>Autopsy</i> .—Post-mortem decomposition advanced. Straw-coloured fluid containing fibrin-like strands in pleural cavity. Abscesses in kidneys. Stomach injected. <i>Cultures</i> .— <i>Staphylococcus aureus</i> from kidney, liver, and pleural cavity. Bile, spleen, and peritoneum sterile.
55	8	No alcohol.		First inoculation as above; second as above. No alcohol.	1,940	1,890	0	0			Died on day following last (second) inoculation. <i>Autopsy</i> .—Beyond a slight distention of the pericardial sac with fluid, there were no lesions anywhere to be detected by the naked eye. No abscesses anywhere. <i>Cultures</i> .— <i>Staphylococcus aureus</i> in moderate numbers from blood and kidney. Pericardial sac sterile.

EXPERIMENT VII.

Table showing Results of Intraperitoneal Inoculation of Rabbits receiving Daily Doses of Ethyl Alcohol, with Cultures of *Staphylococcus Pyogenes Aureus*.

56	4	40 c. c.	70 c. c.	3 days. Inoculated into peritoneum with 0.5 c. c. of 24-hour bouillon cultures of <i>S. aureus</i> .	1,050	880	0	0	Died on day following inoculation. <i>Autopsy</i> .—Beyond a few c. c. of reddish fluid in peritoneum, there was no evidence of peritonitis. No other lesions. <i>Cultures</i> .— <i>Staphylococcus aureus</i> in pure culture from peritoneum. Blood and liver sterile.
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Rab- bits.	No. of days ob- served.	Total amount of alcohol received.	Daily dose of alcohol.	Interval between the beginning of alcohol and time of inoculation.	WEIGHT IN GRAMMES.		Lesions ref- erable to in- oculations. + = present. O = absent.	Lesions ref- erable to in- oculations. + = present. O = absent.	Results and remarks.
					Begin- ning.	End.			
57	12	110 c. c.	10 c. c.	3 days. First inocu- lation as in No. 56, second inocu- lation on seventh day. Intravenous injection of 0.5 c. c. of bouillon culture of <i>S.</i> <i>aureus</i> .	1,590	1,430	O	O	Died two days after second inoculation. <i>Autopsy</i> .—Small purulent nodule at point of punc- ture of first (intraperitoneal) inoculation. No peritonitis. Pericardium roughened, but con- tained no bacteria microscopically. It had not the appearance of recent inflammation. Minute red points over the surface of kidneys. No ab- scesses detected anywhere. <i>Cultures</i> .—A few colonies of <i>staphylococcus aureus</i> from blood and liver.

Controls.

58	3			No alcohol. Inocu- lated as No. 56.			O	O	Died on second day after inoculation. <i>Autopsy</i> .—Ruptured uterus, with three dead fetuses lying in abdominal cavity. <i>Cultures</i> .—Blood sterile. <i>Staphylococcus aureus</i> and short bacilli in peritoneal cavity.
59	16			No alcohol. 7 days after the intra- peritoneal inocu- lation an intra- venous inocula- tion of 0.5 c. c. of bouillon cul- ture of <i>S. aureus</i> was given.	1,000	870	+	O	Died nine days after second inoculation— <i>i. e.</i> , the intravenous injection. <i>Autopsy</i> .—Kidneys and myocardium studded with abscesses. Lung presented several caseous or suppurating nodules that contained cocci. <i>Cultures</i> .— <i>Staphylococcus aureus</i> in liver, kidney, and bile.

Table showing Results of Intravenous Inoculation of Rabbits receiving Alcohol daily to the Stage of Intoxication, with Bouillon Cultures of Staphylococcus Pyogenes Aureus.

60	2	12·5 c. c.	12·5 c. c.	Simultaneous. Intravenous inoculation with 0·4 c. c. of a 24-hour bouillon culture of S. aureus.		(Heart and kidneys.)	+	(Stomach.)	Died on second day. <i>Autopsy</i> .—Very delicate network of lymph over surface of heart. Numerous very minute yellow points in kidneys. Mucous membrane of stomach red and eroded. <i>Cultures</i> .— <i>Staphylococcus aureus</i> in small numbers from blood, in very large numbers from kidney. Died on third day.
61	3	22·5 c. c.	10 to 12·5 c. c.	Do.	1,990 1,860	(Myocardium, kidneys.)	+	(Stomach.)	<i>Autopsy</i> .—Animal died as result of an accident. A small amount of alcohol was inspired into lungs. Death followed at once. Several yellow points in myocardium, and numerous similar points in kidneys. None seen in voluntary muscles. Mucous membrane of stomach very red and eroded over large part of its surface. <i>Cultures</i> .—Blood sterile. Kidneys gave staphylococcus aureus in very large numbers. Died fifteen hours after inoculation.
62	1	12·5 c. c.		Do.	2,000	0	+	(Stomach.)	<i>Autopsy</i> .—Entire cardiac two thirds of stomach intensely reddened and mucous membrane eroded. <i>Cultures</i> .—Blood sterile. Kidney, four colonies of staphylococcus aureus. Died forty-eight hours after inoculation.
63	2	22·5 c. c.	10 to 12·5 c. c.	Do.	2,060	(Kidneys.)	+	(Stomach.)	<i>Autopsy</i> .—Conglomerate and single miliary abscesses in both kidneys. Walls of stomach very much thickened, edematous, and acutely reddened over about half its surface. Stomach contained small amount of dark grumous material. <i>Cultures</i> .—Blood sterile. Kidney contained staphylococcus aureus.
64	1	12·5 c. c.		Do.	1,390	+ (?) (Pericardium.)	0		Found dead fifteen hours after inoculation. <i>Autopsy</i> .—Pericardium filled with bloody serum. Small amount of fluid in peritoneum. <i>Cultures</i> .—Blood, twenty-one colonies. Kidney, one colony of staphylococcus aureus.

Rab- bits.	No. of days ob- served.	Total amount of alcohol received.	Daily dose of alcohol.	Interval between the beginning of alcohol and time of inoculation.	WEIGHT IN GRAMMES.		Lesions ref- erable to in- oculations, + = present, O = absent.	Lesions ref- erable to in- the alcohol. + = present, O = absent.	Results and remarks
					Begin- ning.	End.			
65	1	12.5 c. c.		Do.	1,790		O	+	Found dead fifteen hours after inoculation. <i>Autopsy</i> .—Small amount of fluid in peritoneum. No peritonitis. Mucous membrane of stomach red and eroded. <i>Cultures</i> .—Staphylococcus aureus in blood and kidneys.
<i>Controls— inoculated, but received no Alcohol.</i>									
66	11			No alcohol. Inocu- lated as above.	2,150	1,530	+		Died on twelfth day after inoculation. <i>Autopsy</i> .—Numerous old abscesses in muscles, many almost as large as a pea. Purulent suppuration about the joint of right hock. Numerous old abscesses in kidneys. None in heart. <i>Cultures</i> .—Staphylococcus aureus from kidney and suppurating joint. Blood sterile. Died twenty hours after inoculation. <i>Autopsy</i> .—Numerous extremely minute white points in myocardium. Several pale, circumscribed, and also diffuse points in kidneys. Mucous membrane of stomach normal. <i>Cultures</i> .—Blood and kidneys sterile. Died twenty-one hours after inoculation. <i>Autopsy</i> .—Pericardium distended with serum. Heart covered with a delicate network of fibrin. Myocardium studded with minute pale points. Voluntary muscles presented numerous small lens-shaped pale points. Kidneys presented nu- merous pale areas that dipped into the cortex in a wedge-shaped manner. <i>Cultures</i> .—Staphylococcus aureus from kidney. Blood sterile.
67	1			Do.	2,110		O		
68	1			Do.	1,720		+		

69	36		Do.	1,730				After forty-three days animal is apparently well. Weighs 1,560 grammes.
70	1		Do.	1,350				Died twenty hours after inoculation. <i>Autopsy</i> .—Pericardium filled with serum, in which was a colourless clot and a few strands of fibrin. Diffuse pale areas in cortex of kidneys. <i>Cultures</i> .—Blood, one colony of staphylococcus aureus. Kidney sterile.
71	4		Do.	1,970	1,780			Died on fifth day after inoculation. <i>Autopsy</i> .—On inner aspect of left thigh was a collection of pus about the size of a chestnut. Numerous abscesses in muscles. Several abscesses in myocardium. Numerous abscesses in both kidneys. Small area of peritonitis in left iliac region. <i>Cultures</i> .—Staphylococcus aureus from blood, kidney, and abscess in thigh.

EXPERIMENT IX.

Table showing the Results of Subcutaneous Inoculation of Rabbits receiving Alcohol to the Stage of Intoxication daily, with Cultures of *Staphylococcus Pyogenes Aureus*.

72	11	55 c. c.	5 c. c.	Simultaneous. Subcutaneous inoculation of 1 c. c. of a bouillon culture of <i>S. aureus</i> .	2,520	2,140				0	Died on twelfth day after inoculation. <i>Autopsy</i> .—At site of inoculation in the left groin the tissues were dissected apart, leaving a moderately large excavation. This contained neither serum nor pus. About the borders of this the tissues were very oedematous, the oedema extending up into the neck and into the thighs of both sides. Middle lobe of right lung consolidated. <i>Cultures</i> .—Staphylococcus aureus from blood, from site of inoculation in large numbers, and from kidney. Lung also contained them, but associated with a short bacillus.
73	14	75 c. c.	5 to 10 c. c.	Do.	1,690	1,460				0	Died on fifteenth day after inoculation. <i>Autopsy</i> .—A trace of suppuration only at site of inoculation. Fibrino-purulent pleuritis and pericarditis. Moderate amount of blood-stained purulent matter in pleural cavities. <i>Cultures</i> .—From pleural cavity a feebly growing staphylococcus was obtained. Can not say that it was or was not staphylococcus aureus.

Rab- bits.	No. of days ob- served.	Total amount of alcohol received.	Daily dose of alcohol.	Interval between the beginning of alcohol and time of inoculation.	WEIGHT IN GRAMMES.		Lesions ref- erence to in- oculations. + = present. O = absent.	Lesions ref- erence to the alcohol. + = present. O = absent.	Results and remarks.
					Begin- ning.	End.			
74	5	30 c. c.	5 to 10 c. c.	Do.	1,720	1,400	+ (?) (Pericar- ditis and pleuritis.)	O	Died on fifth day as direct result of last dose of alcohol, from under the influence of which it did not recover. Animal was very susceptible to alcohol. By mistake its last dose was 10 c. c. instead of 5 c. c., as had been the case. <i>Autopsy.</i> —Slight purulent reaction at site of inoculation. Purulent pericarditis and pleuritis. No abscesses. Slight peritonitis. <i>Cultures.</i> —Blood, left pleura, kidney, and spleen gave a feebly growing staphylococcus identical with that found in No. 73. Site of inoculation gave typical staphylococcus aureus. <i>Autopsy.</i> —No macroscopic lesions anywhere to account for death. Stomach normal and filled with partly digested food. <i>Cultures.</i> —Staphylococcus aureus from site of inoculation. Blood and kidney sterile. <i>Autopsy.</i> —At site of inoculation was circumscribed collection of cheesy pus of about size of an almond. Fibrino-purulent pericarditis and pleuritis. Both thoracic cavities filled with purulent matter. <i>Cultures.</i> —Staphylococcus aureus in large numbers from the site of inoculation. A few colonies of cocci from liver. Thoracic cavity gave large numbers of slowly growing micrococci that gave the impression of an enfeebled culture of staphylococcus aureus (see Nos. 73 and 74). Died on tenth day after inoculation. <i>Autopsy.</i> —Only slight reaction at site of inoculation. No lesions on macroscopic examination to account for death. <i>Cultures.</i> —Blood, liver, and kidney sterile.
75	1	10 c. c.		Do.	1,590		O	O	
76	14	140 c. c.	10 c. c.	Do.	2,420	2,050	+ (?) (Pericar- ditis and pleuritis.)	O	
77	9	90 c. c.	10 c. c.	Do.	1,660	1,260	O	O	

Controls.

78	46			2,130		0		Apparently well after forty-six days. Weighs 1,850 grammes.	Weights
79	46			1,560		0		Apparently well after forty-six days. Weighs 1,780 grammes.	Weights
80	46			1,490		0		Apparently well after forty-six days. Weighs 1,570 grammes.	Weights

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EXPERIMENT X.

Results of Intravenous Inoculation of Rabbits that were receiving Alcohol daily to the Stage of Intoxication, with a Culture of *Staphylococcus Pyogenes Aureus* attenuated (?) by Exposure to Chloroform.

81	7	45 c. c.	5 to 7.5 c. c.	1,200	1,050	+ (Pelvis of kidney, Thoracic cavity (?).)	+ (Stomach.)	Died on fifth day after inoculation. <i>Autopsy</i> .—Pleural cavities and pericardium filled with clear serum. Purulent inflammation of pel- vis of right kidney; no cortical lesions. Urine contained microscopically numerous micrococci. Mucous membrane of stomach eroded. <i>Cultures</i> .—Blood, left kidney, peritoneum, and liver sterile. Pelvis of right kidney and urine con- tained staphylococcus aureus in large numbers.
82	4	22.5 c. c.	5 to 7.5 c. c.	1,630	1,640	+ (?) (Peritoni- tis.)	+ (Stomach.)	Died on second day after inoculation. <i>Autopsy</i> .—General acute peritonitis, with deposit of lymph over coils of intestines. Mucous men- brane of stomach very red and eroded. <i>Cultures</i> .—Blood, kidney, and peritoneum all con- tained a pure culture of a staphylococcus that grew slowly and suggested an attenuated staphy- lococcus aureus.

Controls.

83	28			1,350	1,530			The observation was discontinued at twenty-eighth day. The animals had gained in weight, and had at no time shown effects of the treatment.
84	28			1,410	1,750			