Physiology. — *"On Adsorption of Poisons by Constituents of the Animal Body. I. The adsorbent power of serum and brain-substance for Cocain"*. By L. EERLAND and W. STORM VAN LEEUWEN. (Communicated by Prof. R. MAGNUS).

(Communicated at the meeting of January 31, 1920).

In a previous paper[1]) STORM VAN LEEUWEN has shown that in the serum and the tissues of rabbits there are substances capable of inactivating pilocarpin. At the same time he was able to demonstrate that this does not happen by destroying pilocarpin, but through a physical adsorption of pilocarpin by certain components of the serum, whose nature could not be determined thus far. From quantitative investigations it also became evident that this physical adsorption proceeds according to the same laws that hold for the adsorption of dyes by animal charcoal.

In the paper alluded to just now, STORM VAN LEEUWEN has already pointed out that the adsorption of pilocarpin by rabbit's serum is not the only case of the kind, since many facts, described in the literature, render it highly probable that many similar adsorptions appear in the animal body. We know, for instance, that many poisons such as digitalis, atropin, cocain, strychnin etc. may be rendered inactive by animal tissue. This inactivation is commonly conceived to be a decomposition of the poison; we, however, believe that in many of those cases adsorption comes into play. True, in numerous cases poisons in the body are inactivated chemically, but we believe that this chemical action is in many cases preceded by a physical adsorption. The reason why we attach great importance to the question whether poisons are rendered inactive along the chemical path, or through adsorption, is that the great difference in the sensitivity of various individuals to poisons that bring about *a very quick, acute poisoning process,* can be accounted for by an adsorption, not by a chemical process.

The following example may serve to illustrate this:

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[1]) W. STORM VAN LEEUWEN. Sur l'existence dans le corps des animaux de substances fixant les alcaloides Arch. Neerl. de Physiol. Tome 2 p. 650 1918.

It is well known that some people are less sensitive to the poisoning action of cocain than others. According to HATCHER and EGGLESTON [1]) cases are known in which 16 mgr. and 20 mgr. given subcutaneously were fatal, whereas in other cases 1.25 grms of cocain given subcutaneously had no effect whatever. HATCHER and EGGLESTON have proved conclusively that cocain, novocain and many other local anaesthetics become inactive very soon after being injected into an animal, while they have also demonstrated that various tissues, above all the liver, are able to decompose these poisons chemically. This, indeed was no novel experience, for BIER already found, when experimenting with rabbits, that cocain that has for some time been in contact with animal tissue, has thereby become less active, while SANO [2]) had come to the same conclusion for cocain with respect to brain-substance. BIER and SANO believed that this inactivation was caused by chemical decomposition.

HATCHER aud EGGLESTON's assertion that the liver can decompose cocain to a large extent, is incontestible. Still, this decomposing process cannot be so quick as to afford an explanation for the large differences in the sensitivity of different people. When after an injection of a few milligrammes of cocain the patient shows after a short time (a few minutes) serious symptoms of intoxication, the reason can *not* be that the cocain in his body is not decomposed quickly enough, for this decomposition cannot be so quick even with normal individuals. This, in fact, has also been pointed out by HATCHER and EGGLESTON themselves. Now it would seem to us that the abnormal sensitivity of some individuals to cocain might be explained as follows: When cocain is administered to a normal man or animal it will be used:

A in those places (i.a. the central and peripheral nervous system) where it exerts an influence.

B in other places (i.a. free chemoreceptors distributed in the blood). The sensitivity of a special individual to cocain will then be largely determined by the ratio between the number of the places of adsorption referred to under A and B. [3])

[1]) C. EGGLESTON and R. HATCHER. A further contribution to the pharmacology of the local anaesthetics. Journ. Pharm. and exp. Therap. vol. XIII. p. 433. 1919.

[2]) TORATA SANO. Ueber die Entgiftung von Strychnin und Kokain durch das Rückenmark. Ein Beitrag zur physiologischen Differenzierung der einzelnen Rückenmarks-abschnitte. Pflügers Arch. Bd. 120; p. 367. 1907.

TORATA SANO. Ueber das entgiftende Vermögen einzelner Gehirnabschnitte gegenüber dem Strychnin. Pflügers. Arch. Bd. 124, p. 369. 1908.

[3]) The places of adsorption sub *A* may be termed "*dominant* chemoreceptors", those sub *B* "*secondary* chemoreceptors."

In order to confirm this hypothesis it must first of all be ascertained whether the places mentioned sub B (i. e. the secondary chemoreceptors) really exist in the body.

In this paper we shall endeavour to settle this question with regard to cocain.

As already stated the researches of BIER, SANO, HATCHER and EGGLESTON, and others had already brought to light that cocain can be inactivated by animal tissue. It lay with us to show that this inactivation takes place through physical adsorption.

We had to proceed as follows:

1. We had to ascertain the action of a cocain solution of known strength on a special organ.

2. We had to show that the cocain solution became less active after the addition of animal tissue.

3. We had to demonstrate that the cocain was not decomposed in the less active mixture, so that all the active cocain could again be extracted from the mixture.

The effect of cocain upon the nervus Ischiadicus of the frog was taken as the index for cocain-action. We applied ZORN's [1]) method [2]), of which we give a brief description (see Fig. I).

The nerve of a nerve-muscle preparation is led through a small ebonite basin, which is to hold the cocain (and other liquids); on either side of the place where the nerve is in contact with the local anaesthetic, electrodes can be applied, which communicate with the secondary coil of an inductorium. By the aid of Pohl's commutator the nerve can be stimulated alternately by E′ and E″. First the position of the secondary coil is determined (to be read from S) at which the muscle can just be stimulated from E′ as well as from E″. Subsequently the liquid with the local anaesthetic is put in the basin, and after this we investigate how strong the solution must be in order to make the muscle after a certain time irresponsive to the stimulus from the electrode E′. The stimulus from E″ must retain its effect upon the muscle to make sure that during the experiment the excitability of the muscle itself is not diminished. We invariably experimented with a gastrocnemius-ischiadicus preparation of Rana esculenta. Due care was taken to keep the room-temperature constant. We made sure beforehand that the liquids used for

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[1]) ZORN. Beiträge zur Pharmacologie der Mischnarcose. II. Zeitschr. f. exp. Path. und Ther. Bd. 12, p. 529 1913.

[2]) Cf. W. STORM VAN LEEUWEN. Physiologische waardebepalingen van geneesmiddelen. Wolters, Groningen, 1919.

the cocain solution were in themselves indifferent to the nerve. This proved to be the case for 0.6 % Ringer, for 0.9 % Ringer, for serum as well as for an emulsion of brain-substance.

Experiment I. The liquid used was:

0.2 c.c. hydrochloras cocain (5 %) + 4 c.c. 0.9 % Ringer's fluid, i.e. a solution of $^1/_4$ % cocain in 0.9 % Ringer.

We found:

Accumulator 2 volts.

Stimulation at:	Reading taken of the inductorium with stimulation at (E')	Control (E'')	
3 00 h.	1.96	1.96	
3.02	1.96	1.96	
3.04	1.92	1.96	
3.06	1.92	1.96	
3.08	1.90	1.96	
3.10	1.90	1.96	
3.12	1.88	1.96	
3.14	1.86	1.96	
3.16	1.86	1.96	
3.18	1.86	1.96	
3.20	1.86	1.96	
3.24	1.82	1.96	
3.26	1.82	1.96	
3.28	1.80	1.96	
3 30	1.80	1.96	
3.32	1 78	1.96	
3.34	1.78	1.96	
3.36	1.74	1.96	
3.38	1.64	1.96	
3.40	1.40	1.96	
3.42	1.38	1.96	
3.44	1.34	1.96	
3.46	1 2	1.96	(muscle still responsive).

No contraction at the strongest current.

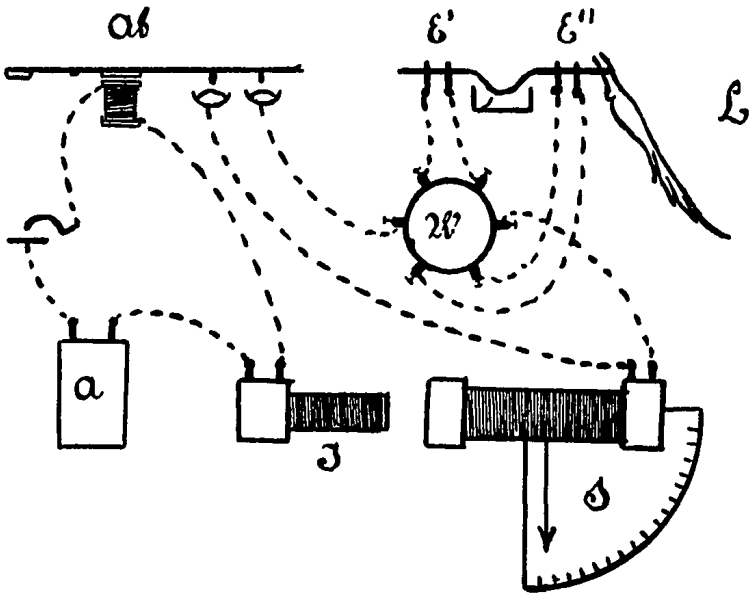

Fig. 1. Apparatus after ZORN (borrowed from a communication by ZORN).

So it appeared that the nerve had become irresponsive after 48 minutes by the effect of $^1/_4$ % cocain solution. The process of the experiment will be seen from the curve in Fig. 2.

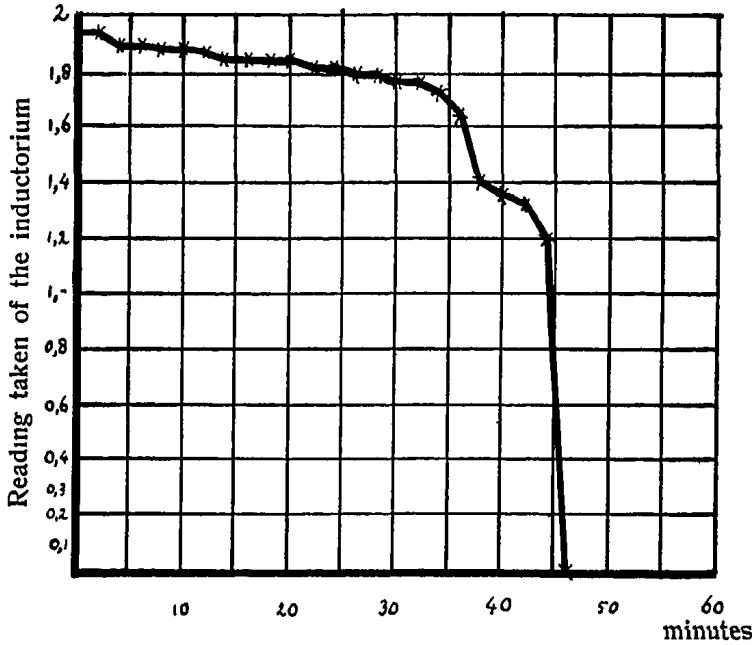

Fig. 2. Effect of $^1/_4$ % hydrochloras cocain upon the nervus ischiadicus of a muscle nerve preparation of Rana esculenta.

Abcissa: Time in minutes.

Ordinate: Stimulus required to make the muscle contract through indirect stimulation.

The same experiment was repeated several times to the following effect:

Exp.	2.	$^1/_4$ %	cocain	solution	nerve	irresponsive	after	43 min.
,,	3.	$^1/_4$ %	,,	,,	,,	,,	,,	42 ,,
,,	4.	$^1/_4$ %	,,	,,	,,	,,	,,	44 ,,
,,	5.	$^1/_4$ %	,,	,,	,,	,,	,,	43 ,,
,,	6.	$^1/_4$ %	,,	,,	,,	,,	,,	42 ,,
,,	7.	$^1/_4$ %	,,	,,	,,	,,	,,	45 ,,
,,	8.	$^1/_4$ %	,,	,,	,,	,,	,,	41 ,,
,,	9.	$^1/_4$ %	,,	,,	,,	,,	,,	42 ,,
,,	10.	$^1/_4$ %	,,	,,	,,	,,	,,	43 ,,

It follows, then, that on an average the nerve is irresponsive in $^1/_4$ % cocain solution in **43** minutes.

We now proceeded to ascertain the adsorbent power of human bloodserum.

Exp. 11. The liquid consisted of: 0,1 cc. 5 % cocain solution + 1,9 cc. of serum, i.e. a concentration of $^1/_4$ % *cocain in serum.*

In this case the muscle remained normally responsive for a whole hour, so that the effect of 5 mgr. cocain is eliminated by 2 cc. of human serum. The process of this experiment will be seen from the curve in Fig. 3.

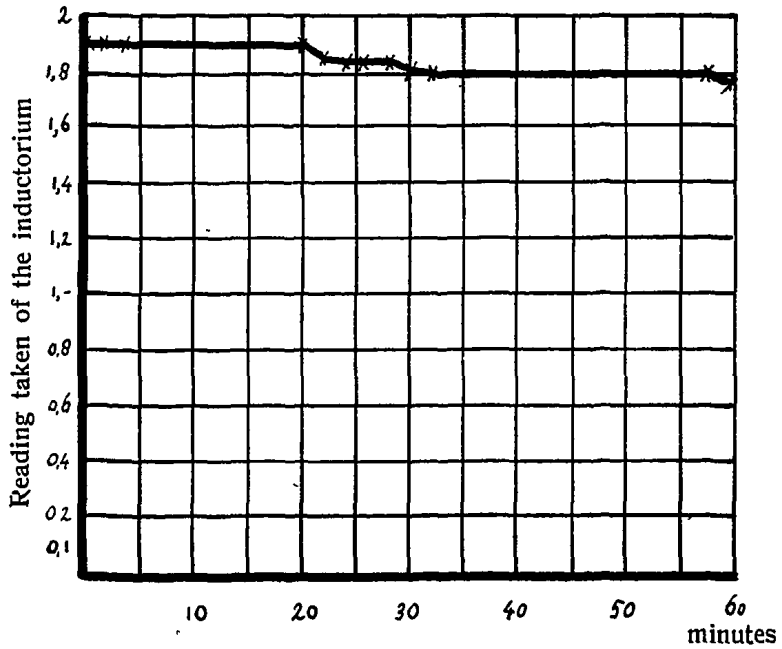

Fig. 3. Effect of $^1/_4$ % cocain in human serum on the nervus ischiadicus of a muscle nerve preparation of Rana esculenta.

After this Exp. 11 was repeated with dog's serum.

Exp. 12. The liquid used was 0.1 cc. 5 % cocain + 2 cc. of dog's serum, that is about $^1/_4$ % cocain in serum: (see table p. 837.

Here also the inhibiting influence of the serum can be seen distinctly.

A similar result was obtained in *exp.* 13 with cat's serum and in

exp. 14 with rabbit's serum. Hereafter we endeavoured to detach the cocain from the serum. To this end we used the liquid of exp. 12 and 13 to the following effect:

After 2 minutes' stimulation.	Reading taken of the inductorium (E')	Control (E'')
4	1.9	1.9
6	1.9	1.9
8	1.9	1.9
10	1.9	1.9
12	1.9	1.9
14	1.9	1.9
16	1.9	1.9
18	1.9	1.9
20	1.9	1.9
22	1.9	1.9
24	1.9	1.9
26	1.9	1.9
28	1.9	1.9
30	1.86	1.9
32	1.86	1.9
34	1.86	1.9
36	1.86	1.9
38	1.86	1.9
40	1.84	1.9
42	1.84	1.9
44	1.82	1.9
46	1.8	1.9
48	1.8	1.9
50	1.8	1.9
52	1.8	1.9
54	1.8	1.9
56	1.8	1.9
58	1.8	1.9
60	1.8	1.9

To 14 cc. of the liquid (serum + cocain) was added 1½ times the volume of alcohol 96 % + 2 drops of HCL. This was centrifugalized and filtered, the filtrate was turbid. The precipitate was subsequently washed with alcohol and part of the alcohol was evaporated down in vacuo. After this the solution was acidified and shaken out twice with ether. The ether extract was then acidulated with $^1/_{10}$ N. HCL to get an aqueous cocain solution. This solution was again neutralized with bicarbonas natricus. With this liquid the experiment was repeated.

Exp. 15. We used the liquid of exp. 12 after extracting it with alcohol, the amount of cocain was calculated at about $^1/_4$ %.

Stimulation after:	Reading taken of the induct. (E')	Control (E'')
2 min.	1.96	1.96
4	1.96	1.96
6	1.9	1.96
8	1.74	1.96
10	1.68	1.96
12	1.68	1.96
14	1.68	1.96
16	1.66	1.96
18	1.6	1.96
20	1.56	1.96
22	1.52	1.96
24	1.5	1.96
26	1.4	1.96
28	1.38	1.96
30	1.32	1 96
32	1.26	1.96
34	1.2	1.96
36	1.18	1 96
38	1.1	1.96
40	(no longer any contraction).	1.96

So after 40 minutes the nerve was anaesthetic, from which it

appears that through the treatment with acid and alcohol all the cocain adsorbed by the serum was detached. (Normal value for $^1/_4$ % cocain is 43 minutes).

Exp. 16. The liquid used is that of exp. 13 treated with alcohol and acid. Here also we found that after 40 minutes the muscle had lost its contractility, so that the result coincided with that of experiment 15.

In the following experiments we used a stronger solution of cocain, viz. $^1/_2$ % cocain.

Exp. 17. The liquid is 0.4 cc. 5 % cocain + 4 cc. Ringer 0.9 %, consequently $^1/_2$ % cocain hydrochloricum.

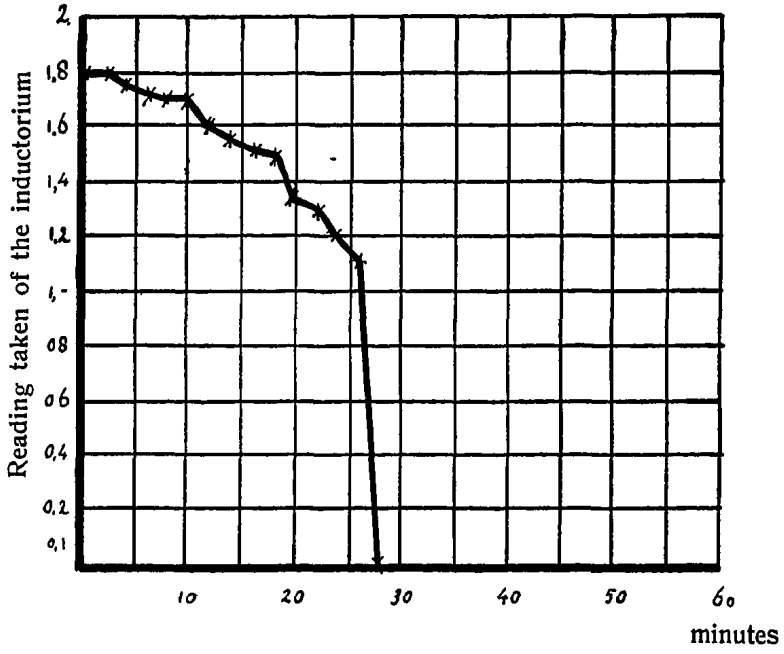

Fig. 4. Effect of $^1/_2$ % cocain hydrochloricum solution in Ringer's fluid (0 6 %) on the nervus ischiadicus of a muscle nerve preparation of Rana esculenta.

The result of this experiment is represented by the curve in Fig. 4. After 28 minutes the nerve was irresponsive, while it appeared that, through stimulation with electrode E'', the muscle itself had remained responsive. Two other experiments yielded the same results.

Exp. 18. Liquid $^1/_2$ % cocain; nerve irresponsive after 30 min.

Exp. 19. Liquid $^1/_2$ % cocain; nerve irresponsive after 30 minutes. Average time in which the nerve becomes irresponsive with $^1/_2$ %

cocain: 29½ min. When serum was added the adsorptive action revealed itself again distinctly.

Exp. 20. 0.4 cc. 5 % cocain + 4.5 cc. rabbit's serum, which is equal to ca. ½ % cocain hydrochloricum in serum.

Stimulation after:	Reading taken of the inductorium (E')	Control (E'')
2 min.	1.8	1.8
4	1.8	1.8
6	1.8	1.8
8	1.8	1.8
10	1.8	1.8
12	1.8	1.8
14	1.8	1.8
16	1.8	1.8
⋮	1.8	1.8
42	1.8	1.8
44	1.78	1.8
46	1.78	1.8
48	1.78	1.8
50	1.78	1.8
52	1.78	1.8
54	1.76	1.8
56	1.76	1.8
58	1.76	1.8
60	1.76	1.8

It wil be seen that we found distinct inhibition by serum also in this experiment, for after an hour the conductibility of the nerve had diminished only slightly.

This experiment was repeated (exp. 21), which again showed no anaesthesia of the nerve. Subsequently we inquired into the action of 1 % cocain.

Exp. 22. Liquid: 0.8 cc. 5 % cocain solution + 4.22 cc. Ringer 0.9 % equal to 1 % cocain hydrochloricum in Ringer's solution.

Stimulation after:	Reading taken of inductorium	Control
2 min.	1.9	1.9
4	1.9	1.9
6	1.88	1.9
8	1.84	1.9
10	1.8	1.9
12	1.7	1.9
14	1.6	1.9
16	1.4	1.9
18	1.3	1.9
20	1.2	1.9
22	(irresponsive)	1.9

Nerve does not respond any more after 22 min.

Exp. 23 1 % cocain irresponsive after 18 min.

Exp. 24 „ „ „ „ 22 „

Exp. 25 „ „ „ „ 20 „

From which we see that after about 20 minutes the conductibility of the nerve is eliminated by 1 % cocain hydrochloricum.

In experiment 26 and 27 we ascertained the influence of serum on the 1% cocain solution.

Exp. 26. Liquid: 1% cocain hydrochloricum in rabbit's serum:

Stimulation after:	Reading taken of inductorium E'	Control (E'')
2	1.8	1.8
4	1.8	1.8
6	1.78	1.8
8	1.78	1.8
10	1.74	1.8
12	1.74	1.8
14	1.74	1.8
16	1.72	1.8
18	1.66	1.8

(Table continued).

Stimulation after:	Reading taken of inductorium (E')	Control (E'')
20	1.64	1.8
22	1.6	1.8
24	1.56	1.8
26	1.5	1.8
28	1.46	1.8
30	1.4	1.8
32	1.2	1.8
34	1.16	1.8
36	1.1	1.8
38	—	1.8

After 38 minutes the nerve appears to be no longer responsive, so there must be distinct inhibition.

Exp. 27. Liquid: 0.8 cc. 5 % cocain solution + 4.2 cc. of cavia's serum i.e. to 1 % cocain hydrochloricum in cavia's serum.

Stimulation after:	Reading taken of inductorium (E')	Control (E'')
2	1.9	1.9
4	1.9	1.9
6	1.9	1.9
8	1.9	1.9
10	1.9	1.9
12	1.9	1.9
14	1.9	1.9
16	1.8	1.9
18	1.8	1.9
20	1.8	1.9
22	1.76	1.9
24	1.7	1.9

(Table continued).

Stimulating after:	Reading taken of inductorium (E')	Control (E'')
26	1.6	1.9
28	1.52	1.9
30	1.46	1.9
32	1.4	1.9
34	1.4	1.9
36	1.34	1.9
38	1.26	1.9
40	1.2	1 9
42	1	1.9
44	—	

The result of this exp. is similar to that of exp. 26, viz. only after 44 minutes irresponsiveness of the nerve.

The liquid of experiment 27 was treated with alcohol and acid as in experiment 15, and was used in *experiment* 28 (the cocain content was calculated at 1 %). After 22 minutes the nerve was no longer responsive from which it appeared that (compare the results of experiments 23, 24, 25) through extraction with alcohol the cocain had been detached.

We now considered the question whether the behaviour of brain-substance toward cocain is similar to that of serum. To 5 grms of rabbit's brains was added 10 cc. of a 2 % solution of cocain in Ringer 0.6 %. After standing for 30 minutes at room-temperature it was centrifugalized and the supernatant fluid was examined. A control experiment was made on 5 grammes of brains and 10 cc. of Ringer without cocain. The latter liquid proved to be indifferent to the nerve.

Exp. 29. Liquid: 5 grms of rabbit's brain-substance and 10 cc. 2 % cocain; contains 1,33 % cocain (see Table Exp. 27).

So it appears that after 50 min. the nerve has become anaesthetic. Since in the normal experiments with 1 % cocain anaesthesia appears after 20 minutes, we must conclude that also brain-substance inhibits cocain.

Exp. 30. Repetition of experiment 29 but with cat's brains.

Stimulation after:	Reading taken of inductorium	Control
2	1.9	1.9
4	1.9	1.9
6	1.9	1.9
8	1.9	1.9
10	1.9	1.9
12	1.9	1.9
14	1.9	1.9
16	1.8	1.9
18	1.7	1.9
20	1.7	1.9
22	1.7	1.9
24	1.7	1 9
26	1.7	1.9
28	1.7	1.9
30	1.7	1.9
32	1.7	1.9
34	1.7	1.9
36	1.6	1.9
38	1.5	1.9
40	1.5	1.9
42	1.5	1.9
44	1.4	1.9
46	1.26	1.9
48	1.2	1.9
50	—	1.9
52	—	1.9

Stimulation after:	Reading taken of inductorium	Control
2	1.8	1.8
4	1.8	1.8
6	1.8	1 8
8	1.8	1.8
10	1.8	1.8
12	1.8	1.8
14	1 8	1.8
16	1.8	1.8
18	1.8	1.8
20	1.8	1.8
22	1.7	1.8
24	1.6	1.8
26	1.5	1 8
28	1.5	1.8
30	1 5	1.8
32	1.4	1.8
34	1.3	1 8
36	1.3	1.8
38	1.3	1.8
40	1.3	1.8
42	1.3	1.8
44	1.3	1.8
46	1.3	1.8
48	1.3	1 8
50	1.3	1.8
52	1.2	1.8
54	1.1	1.8
55	—	1.8

From which we see that the nerve is irresponsive after 55 minutes. Here then there is also adsorption. In order to prove that the cocain is not decomposed, but adsorbed physically, brain-substance and cocain is treated with alcohol and acid as in experiment 15.

Exp. 31. Liquid: brain-substance + cocain after treatment with hydrochloric acid and alcohol, computed at 1 % cocain hydrochloricum.

Stimulation after:	Reading taken of inductorium	Control
2	1.8	1.8
4	1.8	1.8
6	1.7	1.8
8	1.68	1.8
10	1.6	1.8
12	1.5	1.8
14	1.44	1.8
16	1.4	1.8
18	1.4	1.8
20	1.3	1.8
22	1.1	1.8
24	—	1.8

Here, then, the cocain action manifests itself again, for the nerve is irresponsive after 24 minutes, so that no cocain has been decomposed by the brain-substance.

In order to show that from brain-substance, after extraction with hydrochloric acid and alcohol, no materials are abstracted which, of themselves, are deleterious to the nerve, so that thereby in experiment 31 the cocain action might have been intensified, we undertook a control exp. 32, in which a liquid was added to the nerve that was composed of 5 grms. of cat's brains and 10 c.c. RINGER 0.6 % and then extracted with hydrochloric acid and alcohol. This liquid again proved to be indifferent to the nerve, because within an hour the responsiveness had not diminished.

Exp. 33. This experiment is a repetition of exp. 31.

Liquid: Cat's brain-substance and cocain-solution equal to 1 % cocain hydrochloricum.

After 54 minutes the nerve is irresponsive, which again shows that the cocain action is inhibited by brain-substance.

Exp. 34. The liquid of exp. 33 was again treated with alcohol and hydrochloric acid.

Stimulation after:	Reading taken of inductorium	Control
2 min	1.9	1.9
4	1.8	1.9
6	1.7	1.9
8	1.68	1.9
10	1.66	1.9
12	1.64	1.9
14	1 64	1.9
16	1.62	1.9
18	1.6	1.9
20	1.56	1.9
22	1.4	1.9
24	1.2	1.9
26	1.1	1.9
28	—	1.9

We see from this that the cocain has again been detached. Of the cocain thus obtained. Dr. LE HEUX determined the melting point, which was 96,6° (uncorrected), which again proves that the cocain has not been decomposed (not even partially), but that only a physical adsorption has taken place. (Normal melting point of cocain hydrochl. 98°).

Since it had now become evident that brain-substance is capable of adsorbing cocain, we ascertained whether one of the familiar brain lipoids viz. lecithin[1]), could also exert this action.

Exp. 35. Liquid: 1 cc. 5 % lecithin solution + 1½ c.c. aqua distillata + 2½ c.c. RINGER (1.2 %) without cocain. In this experiment the responsiveness of the nerve had hardly changed, from which we see that lecithin of itself does not injure the nerve.

Exp. 36. 1 cc. 5% lecithin solution + ½ cc. aq. dest. + 1 cc. 5% cocain + 2½ cc. Ringer (1.2%), that is 1% cocain hydrochloricum in 1% lecithin.

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[1]) The lecithin was supplied by MERCK.

Stimulation after:	Reading taken of inductorium (E')	Control (E'')
2 min.	1.9	1.9
4	1.9	1.9
6	1.9	1.9
8	1.9	1.9
10	1.9	1.9
12	1.9	1.9
14	1.9	1.9
16	1.9	1.9
18	1.9	1.9
20	1.9	1.9
22	1.9	1.9
24	1.9	1.9
26	1.9	1.9
28	1.9	1.9
30	1.9	1.9
32	1.9	1.9
34	1.8	1.9
36	1.72	1.9
38	1.6	1.9
40	1.5	1.9
42	1.3	1.9
44	1.12	1.9
46	—	1.9

The nerve is irresponsive after 46 minutes.

Exp. 36. Liquid: 3 cc. 2% lecithin and 2 cc. Ringer (1.8%) and 1 cc. cocain solution 5% is equal to 0.83% cocain hydrochloricum in a 1% lecithin solution.

Result: After 62 minutes the nerve is still responsive.

From experiments 35 and 36 it appears then that 50 mgrs of lecithin can inhibit the action of 50 mgrms of cocain considerably.

Exp. 37. Here we examined the influence of an ether extract of dried cat's brains. Of itself this extract is indifferent to the nerve, which after 60 minutes is still normally responsive.

Exp. 38. Liquid: 0.8 cc. 5% cocain solution and 4.2 cc. extract of dried cat's brains, thus containing 1% cocain.

Stimulation after:	Reading taken of inductorium (E')	Control (E'')
2 min.	1.8	1.8
4	—	—
⋮	—	—
46	1.8	1.8
48	1.7	1.8
50	1.7	1.8
52	1.68	1.8
54	1.6	1.8
56	1.5	1.8
58	1.42	1.8
60	1.3	1.8
62	1.1	1.8
64	—	1.8

Result: This extract proves to possess distinct inhibiting power, since only after 64 minutes the nerve becomes irresponsive (normally after 22 minutes).

CONCLUSIONS.

1. Our experiments produced evidence for our assertion that the action of cocain can be considerably inhibited by the addition of:

a. the serum of man, dog, rabbit and cavia;

b. the brain-substance of rabbit and cat;

c. ether-extract of dried cat's brains;

d. lecithin.

BIER's and SANO's experiments are hereby supported and extended.

2. This inhibition of cocain, is not brought about by a chemical decomposition of the cocain but by a physical adsorption; for, through extraction with hydrochloric acid and alcohol of a mixture with a reduced cocain action, all the cocain can be restored, which has still retained its activity. The melting point of this cocain also lies very near to normal values.

3. Serum, brain-substance and lecithin are of themselves not deleterious to the frog's nerve, nor when these materials (in control experiments) were extracted with hydrochloric acid and alcohol.