five normal persons (P. II.) The following Table shows the highest serum dilutions which gave an index higher than normal saline.

	Highest dilution of Serum which shows a greater phagocytic index than normal saline.									
	Before Inoculation.	3 days.	4 days.	5 days.	6 days.	7 days.	8 days.	9 days.	10 days.	
R. St. J. B.	—	1/1024	1/768	1/1024	1/1536	1/512	—	1/512	—	
P. I.	—	1/512	1/512	1/1024	1/1024	1/512	1/512	1/256	—	
P. II.	less than 1/32	1/128	1/128	1/256	1/384	1/256	—	—	1/192	

Except in two cases in the third series, the effects, on inoculation, were very slight and in no case was any increase in pulse rate or temperature observed. In the third series the opsonic response is not as great as in series I. or II. In the case of the two groups of pooled sera the number of persons in each group is so small that one would hesitate to draw any definite conclusions from these results, but as far as they go, they tend to show that pre-existing sensibility has an influence on the opsonic index in human plague vaccination.

CONCLUSIONS.

1. The substance which produces a rise in the opsonic index in immune pest serum is the nucleo-protein contained in the bodies of the bacilli.
2. The washed bodies of the bacilli when used as a vaccine do not cause any increase in the opsonic index.
3. Within limits, the larger the dose the greater the opsonic response.
4. A repeated dose of vaccine raises the index above the maximum of the first inoculation, even after the curve has fallen to its normal level.
5. In the early stages, in rats, the opsonic response and the degree of protection aroused rise together.
6. In human beings the maximum response is observed to be much later than in the case of laboratory rats, and the response in a series of previously sensitised persons is somewhat greater than in a series of persons not previously vaccinated.
7. The local and constitutional effects of nucleo-protein vaccination compare very favourably with those observed in other methods of protective inoculation.

I desire to express my thanks to Dr. C. J. Martin, F.R.S., Director of the Lister Institute, and to Dr. J. C. G. Ledingham, Chief Bacteriologist, Lister Institute, for valuable advice and suggestions throughout the enquiry, and particularly to Dr. Sydney Rowland, of the Yersin Laboratory, Elstree, Herts, without whose constant advice and help the experiments could not have been carried out.

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THE DESTRUCTION OF ALKALOIDS BY EMULSIONS OF THE BODY TISSUES.

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DURING recent years many workers have investigated both the natural tolerance to drugs, that occurs in certain animals, and also the tolerance that is acquired when certain drugs are administered repeatedly. We now know that the protective mechanism, which causes tolerance, differs in the case of different drugs, and that, with the same drug, tolerance may be produced by different mechanisms in different animals. This evidence has been recently reviewed by Dixon⁽¹⁾; it appears that tolerance may be established by the following mechanisms: (1) Diminished absorption. (2) Increased rapidity of excretion. (3) Increased resistance of the tissues upon which the drug acts. (4) Linkage of the drug with other bodies to form an inert substance. (5) Absorption of the drug by organs upon which it has no action. (6) Destruction of the drug by the body tissues. All of these six mechanisms, except the third, have been shown to exist in mammals, the third has been demonstrated chiefly in protozoa and may depend upon physical causes. The sixth mechanism, the destruction

of the drug by the body tissues, has been studied in various ways, both in the intact animal, in isolated surviving organs, and in emulsions made of excised organs; the present paper is concerned only with results obtained by the last method.

1. HISTORY.

Numerous investigators have examined the power of emulsions of the tissues to destroy alkaloids, and the method employed has usually been the following: An organ is excised from a freshly killed animal, and made into a fine emulsion with normal saline, a small quantity of alkaloid is added, and the mixture incubated for some time at body temperature, in the presence of oxygen; after incubation the alkaloid is extracted and estimated. Using this method Buys⁽²⁾ showed that the livers of the frog and the rabbit could destroy hyoscyamine, but that the frog's blood, and the dog's liver did not do so. Cloetta^(3 and 4) showed that the rabbit's liver could destroy atropine, he also considered that the rabbit's brain, and the cat's liver and brain could destroy atropine. Fleischmann^(5 and 6), and Metzner⁽⁷⁾ both showed that the rabbit's serum could destroy atropine, but that this power varied greatly according to the locality from which the rabbit came; they noted particularly that the serum of rabbits suffering from goitre did not destroy atropine. Fleischmann moreover showed that normal human serum did not destroy atropine, but that the serum of patients suffering from exophthalmic goitre could do so. Cloetta and Fischer⁽⁸⁾ showed that neither the dog's liver, brain, nor heart could destroy digitoxin.

Several investigators have compared the action, which emulsions of the organs of normal animals have upon a drug, with the action of emulsions of the organs of animals made tolerant to the drug. Albanese⁽⁹⁾ showed that liver emulsions from normal dogs did not destroy morphine, but that liver emulsions from dogs made tolerant to morphine could destroy considerable quantities of the drug. Dixon⁽¹⁾ showed that the liver of normal rabbits possessed a slight power of destroying nicotine, and that this power was increased in rabbits in which tolerance to the drug had been induced. Cloetta⁽⁴⁾ compared the destruction of atropine, produced by the livers of normal cats and rabbits, with that produced by the livers of cats and rabbits made tolerant to atropine; he showed that the tolerant rabbits possessed increased powers of destruction, but that there was no such increase in the tolerant cats.

2. METHOD.

The method adopted by the writer was similar to that already outlined. A freshly excised organ was made into a fine emulsion by pounding in a mortar with sand and normal saline, and then filtering through muslin: a few drops of toluol were added to prevent sepsis, a minute quantity of the alkaloid to be tested was next added, and the mixture well shaken, and then incubated for a few hours at body temperature; after incubation the alkaloid was extracted by the Staas method, and the amount recovered estimated. It was found by experiment that heating to 60°C. completely removed the power of emulsions to destroy alkaloids; control experiments were therefore made by always taking two equal portions of emulsion, and heating one portion to 60°C. for 30 minutes before adding the alkaloid; the two portions were then treated in an exactly similar manner, and the amount of alkaloid recovered from each at the end was compared. In all cases small quantities of alkaloid (usually less than 1 mgm.) were added, and destruction of the alkaloid was only considered to have been proved, when, firstly the unheated portion was found to contain either no alkaloid, or at most a trace, and secondly there was a large difference between the amount recovered from the heated and the unheated portions; in this manner errors due to the extraction and estimation of such minute amounts of alkaloid were eliminated as far as possible.

3. MODE OF DESTRUCTION OF ATROPINE BY THE TISSUES.

The livers of frogs and rabbits were used, since emulsions of these organs were known to possess the power of destroying atropine (Buys⁽²⁾). The atropine was estimated by Vitali's test; the extracted alkaloid being diluted until Vitali's test was only just positive. When 1 c.c. of fluid was taken I found that 0.003 mgm. of sulphate gave a distinct violet colour, and that 0.002 mgm. gave a very feeble violet colour; smaller quantities showed a red colour, but no violet colour. The sensitiveness of the test depends upon the fuming nitric acid used, and upon the freshness of the alcoholic solution of caustic potash. Cloetta⁽⁴⁾ found the end point with this method to lie between 0.005 and 0.01 mgm. of atropine, but the end point is so indistinct that no two observers are likely to obtain exactly similar results.

TABLE I.
POWER OF FROG'S TISSUES TO DESTROY ATROPINE.
1 or 2 c.c. of Emulsion of the organ mixed with Atropine Sulphate and incubated
for some hours at 22° C.

Nos.	Date.	Organ.	Quantity of Emulsion in c.c.	Quantity of Atropine Sulphate added in mgm.	Length of Incubation in hours.	Quantity of Atropine Sulphate (in mgm.) recovered.	
						i. From unheated Emulsion.	ii From Control. (Emulsion previously heated to 60° C.)
1	4.12.11	Liver	2	0.2	3	Nil	Atropine present
2	10.11.11	"	2	0.4	2	"	"
3	14.11.11	"	2	2.5	15	"	"
4	4.12.11	Heart	1	0.2	3	0.01	over 0.02
5	4.12.11	"	1	0.1	3	nil	"
6	8.1.12	"	1	0.04	2	less than 0.002	0.04
7	21.11.11	Kidney	1	0.05	4	nil	Atropine present
8	18.1.12	"	1	0.04	2	"	"
9	8.1.12	Skeletal muscle	2	0.02	2	0.01	"
10	14.11.11	"	2	0.025	19	over 0.01	"
11	21.11.11	Pancreas	1	0.03	4	Atropine pres.	"
12	4.12.11	"	1	0.02	4	"	"
13	18.1.12	Blood	1	0.04	2	0.02	0.01
14	8.1.12	"	1	0.02	3	Atropine pres.	Atropine present
15	18.1.12	Intestinal mucous membrane	1	0.04	2	"	"
16	4.12.11	Testicles	0	0.2	2	"	"

Cloetta (4) used this method and apparently considered it accurate within 10 per cent., as he draws conclusions upon differences of 10 or 20 per cent. I consider that the method cannot be relied upon to show a difference of less than 50 per cent. I found it possible to recover about 0.002 mgm. of atropine from 1 c.c. of tissue emulsion mixed with 0.01 mgm. of atropine. No atropine could be isolated when 0.005 mgm. of atropine was added to 1 c.c. of tissue emulsion. The unavoidable loss of atropine, therefore, is about 0.005 mgm. per c.c. of emulsion used.

In some experiments the organ emulsion itself was tested, without extraction, by putting a drop of it into the eye of a kitten or rat. This test, when positive, was considered to prove the presence of atropine, but when negative the result was confirmed by extracting and testing by Vitali's test.

With a rat one drop of a solution of 0.01 mgm. atropine sulphate per c.c. always caused dilatation within forty-five minutes; a solution of 0.005 mgm. per c.c. did not always produce dilatation. With a kitten three instillations of one drop with intervals of ten minutes produced dilatation in sixty minutes with a dilution of 0.002 mgm. per c.c.; this corresponds to about 0.0004 mgm. actually introduced into the eye. Metzner (7) found that about 0.0001 mgm. of atropine sulphate put into a kitten's eye produced a well-marked dilatation. I made a few experiments with excised frogs eyes but found that they were much less susceptible; a concentration of 0.2 mgm. atropine sulphate per c.c. was required to produce dilatation.

(a) *The Rate at which Atropine is Destroyed.*

Expt. i.: Frog's liver emulsion 0.05 c.c. + 3.5 c.c. 0.65 NaCl. 1 c.c. of mixture put in four test tubes—1 drop of toluol in each tube. 0.04 mgm. of atropine sulphate added to each tube. Incubated at 22°C. for varying times, killed by heating to 100°C., atropine extracted and estimated by Vitali's test.

Test Tube.	Length of Incubation.	Atropine originally present.	Atropine recovered.
1	Killed at once	0.04 mgm.	0.03 mgm.
2	Killed after 5 min. incubation	0.04 mgm.	0.02 mgm.
3	" " 30 " "	0.04 mgm.	0.008 mgm.
4	" " 130 " "	0.04 mgm.	0.000 mgm.

This experiment shows that the destruction of atropine proceeds slowly, and that the action resembles that of a ferment rather than that of an ordinary chemical combination.

(b) *The Nature of the Atropine Destroying Substance.*

As already mentioned, the power of emulsions to destroy atropine was found to be completely abolished by heating to 60°C. The action was not however dependent upon the presence of living cells, for if an emulsion of liver was smeared upon

glass plates and dried, the dried material when made into an emulsion with saline could destroy atropine and retained this power for several weeks; after keeping for a few months this power to destroy atropine disappeared. On filtering a liver emulsion through a Berkefeld filter the filtrate was found to possess the power of destroying atropine, but after filtering through a Pasteur-Chamberland filter the filtrate was inactive. The destruction of atropine is therefore due to a body which resembles a ferment in its general characteristics, it acts slowly, it is destroyed by heating, but it does not depend upon the presence of intact cells.

4. THE DISTRIBUTION OF THE ATROPINE DESTROYING FERMENT IN THE BODIES OF THE FROG AND THE RABBIT.

A series of experiments was made according to the method already described, using emulsions prepared from the different organs of the body. If, on prolonged incubation, an organ emulsion did not destroy nearly all of the minute quantity of atropine introduced, it was considered that the organ had no power to destroy atropine, and in these cases it was not considered necessary to make an exact determination of the atropine recovered.

From these results it appears that the frog's liver can destroy considerable quantities of atropine, the heart and kidney can destroy minute quantities, but the other organs possess no such power; it is especially noteworthy that the frog's blood possesses no power of atropine destruction, a conclusion also obtained by Buys (2).

The destruction of atropine by the frog's heart was further tested upon the surviving excised heart. The heart was perfused with a small quantity of fluid by means of a cannula introduced into the ventricle through the sinus venosus.

Expt. ii.: 7/2/12. 2 c.c. of saline in frog's heart, 0.04 mgm. atropine. Heart maintained a good beat for twenty-four hours. One drop of fluid tested on rat's eyes at intervals. Atropine disappeared after five hours.

After twenty-four hours fluid and heart extracted, and the extracts tested for atropine. No atropine found in either.

A control was made by leaving 0.04 mgm. atropine in contact with a dead heart under similar conditions. No destruction of atropine occurred.

From these experiments it appears that the rabbit's liver and serum can destroy atropine. This result confirms the experiments of Buys (2), Cloetta (3), Fleischmann (5 and 6), and Metzner (7).

The other organs of the rabbit appear to have no power to destroy minute doses of atropine, even on prolonged incubation. Cloetta (7 and 8) used a similar method, but obtained a different result. He took 10 gms. of the organ emulsion and added 5 mgm. of atropine sulphate, and incubated for thirty minutes. He found that the rabbit's brain, as well as the liver, possessed the power of destroying atropine. I have been unable to confirm this result. Cloetta also found that the muscles destroyed about 20 per cent. of the atropine introduced, but I consider that this difference lies within the limits of the experimental error of the method used.

TABLE II.
POWER OF RABBIT'S TISSUES TO DESTROY ATROPINE.
Emulsions incubated at 37° C.

Nos.	Date.	Organ.	Quantity of Emulsion in c.c.	Quantity of Atropine Sulphate added in mgm.	Length of Incubation in Hours.	Atropine Sulphate (in mgm.) recovered from	
						i. Unheated Emulsion.	ii. Control (Emulsion previously heated to 60° C.)
1	24.11.11	Liver	1	0.1	4	Nil	Atropine present
2	9.12.11	"	1	0.5	5	"	"
3	2.1.12	"	2	0.1	15	"	" 0.1 "
4	5.1.12	Serum	1	0.01	5	"	" 0.01 "
5	27.11.11	Heart	2	0.4	15	Atropine present	Atropine present
6	16.11.11	"	2	0.2	5	" 0.02 "	" 0.02 "
7	9.1.12	"	2	0.04	5	" 0.02 "	" 0.02 "
8	16.11.11	Brain	1	0.1	15	Atropine present	Atropine present
9	9.1.12	"	2	0.04	5	" 0.02 "	" 0.02 "
10	27.11.11	Intestinal mucous membrane	2	0.4	15	Atropine present	Atropine present
11	4.12.11	"	1	0.2	5	"	"
12	27.11.11	Stomach mucous membrane	2	0.4	15	"	"
13	8.12.11	"	1	0.2	4	" 0.02 "	" 0.02 "
14	9.1.12	"	2	0.04	5	" 0.02 "	" 0.02 "
15	27.11.11	Pancreas	1	0.2	15	Atropine present	Atropine present
16	27.11.11	Kidney	2	0.4	15	"	"
17	27.11.11	Bone marrow	1	0.2	15	"	"

5. THE POWER OF THE TISSUES OF OTHER ANIMALS TO DESTROY ATROPINE.

In the rat, the liver, serum, heart, pancreas, kidney and intestinal mucous membrane were all tested, quantities of atropine varying from 0.2 mgm. to 0.02 mgm. were found not to be destroyed after incubation for four hours, there is therefore no evidence that any of the rat's organs can destroy atropine.

In the cat similar experiments were performed with the liver, heart, brain, pancreas, kidney and intestinal mucous membrane, in no case was there any evidence that atropine was destroyed, even after incubation for sixteen hours.

Cloetta (³ and ⁴) using a similar method, but using larger quantities of atropine (4 to 5 mgm.) concluded that the cat's liver destroyed 50 per cent. and the brain 25 per cent. of the atropine introduced, as already mentioned, I consider that the method he used was unsuitable for estimating accurately the total quantity of atropine recovered. If the cat's tissues possess any power to destroy atropine, minute quantities of atropine should be almost completely destroyed after prolonged incubation; as I have shown, such a destruction occurs regularly with the rabbit's liver, but is never observed with any of the cat's tissues. A few experiments were made with the dog's liver, this was found to have no power to destroy atropine, a result previously obtained by Buys (²).

6. THE DESTRUCTION OF PHYSOSTIGMINE BY THE TISSUES.

The drug was extracted in the same manner as atropine, and the extracted drug estimated by dropping into the eye of a kitten. When three drops of a solution of physostigmine were put into the kitten's eye at intervals of ten minutes, it was found that a concentration of 0.02 mgm. per c.c. produced contraction within one hour, but that a concentration of 0.01 mgm. per c.c. produced no contraction. Experiments were made with the frog's liver and the rabbit's liver, in neither case was there any evidence that physostigmine was destroyed.

7. DISCUSSION.

It is interesting to consider what relation there is between the power of the tissues of an animal to destroy atropine, and the degree of tolerance shown by the animal to this drug. I have shown that the frog's liver, the rabbit's liver, and the rabbit's blood can destroy atropine, but that there is no evidence that any of the tissues of the cat, dog or rat possess this power.

Unfortunately it is difficult to determine the relation between the power of an animal to destroy atropine, and its tolerance to the drug, as measured by the minimal lethal dose per kilo of body weight, because there is no general agreement as to the latter. Different observers give widely different numbers for the minimal lethal dose of atropine both for the rabbit and dog. This diversity of opinion may be explained by the fact noted by Fleischmann, that rabbits from different localities show different powers of resistance to atropine. I determined the minimal lethal dose of atropine administered subcutaneously for rats, but found that it varied greatly, being much lower in young rats: 0.5 grms. atropine per kilo body weight killed young white rats weighing about 50 grms., but over 2 grms.

atropine per kilo were required to kill older rats weighing 200 grms. Cloetta (⁴) compared the minimal lethal subcutaneous dose of atropine in cats and rabbits and found it to be 0.03 grms. per kilo and 0.5 grms. per kilo respectively: thus showing that the rabbit whose liver can destroy atropine is much more tolerant than the cat whose liver possesses little or no such power.

Heffer (¹⁰) compared the minimal lethal dose of atropine in rabbits and dogs, and obtained the following figures:—

TABLE III.

Animal.	Mode of Administration.	Dose of atropine Sulphate in grm. per kilo.
1. Rabbit ..	By mouth	1.4-1.5
2. " ..	Subcutaneous	0.65-0.7
3. " ..	Intravenous	0.068-0.074
4. Dog ..	Subcutaneous	0.401
5. " ..	Intravenous	0.07.

The rabbit therefore shows greater power of resistance to the drug administered subcutaneously, but both animals are equally susceptible to the drug when it is given intravenously; as already mentioned the rabbit's liver can destroy atropine but the dog's liver cannot do so. Cloetta also compared the action of atropine upon normal rabbits, and upon rabbits in which tolerance to the drug had been induced. The tolerant animals were more resistant to atropine given subcutaneously, but when atropine was given intravenously, and the minimal dose ascertained which would paralyse the vagi, it was found that this dose was the same both in the normal and in the tolerant animals.

In the cases recorded therefore it appears that there is some relation between the power of an animal to destroy atropine and its tolerance of the drug, when measured by the subcutaneous minimal lethal dose; this is shown by the following table:—

TABLE IV.

No.	Animal.	Subcutaneous Minimal Lethal Dose of Atropine in grms. per kilo body weight.	Authority.	Power of Liver to Destroy Atropine.
1	Frog	3.0	Determined by the writer	Well marked
2	Rabbit	0.7	Heffer (¹⁰)	Well marked
3	Rat	2.0	Determined by the writer	Nil
4	Cat	0.03	Cloetta (³)	Nil
5	Dog	0.4	Heffer (¹⁰)	Nil

This comparison is not satisfactory because of the uncertainty as to the true minimal lethal dose in any species. It will be seen that some of the more tolerant animals possess the power of destroying atropine, but that the rat is exceptional since it is very tolerant to atropine, but none of its tissues have any power to destroy the drug.

Both Cloetta and Heffter show that an animal may be tolerant to subcutaneous doses but show no tolerance to intravenous doses, this is only natural because, when given intravenously, the drug exerts its specific action before sufficient time has elapsed for any appreciable destruction to occur. This rule probably holds good for most other drugs in which tolerance is observed, and with the development of intravenous therapy it may become of considerable practical importance.

CONCLUSIONS.

1. The livers of the frog and rabbit possess the power of destroying atropine; this power persists when all living cells are destroyed, and is due to a soluble body, resembling a ferment in its action.

2. In the frog the liver has a marked power, and the heart and kidneys have a slight power, to destroy atropine; no other tissues have any such power.

3. In the rabbit the liver has a marked power, and the blood a less marked power, to destroy atropine; no other tissues have any such power.

4. None of the tissues investigated in the cat, the rat, and the dog have any power to destroy atropine.

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STUDY OF EXPERIMENTAL PURPURA.

BY

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Although it is now easier to interpret the phenomena of purpura on theoretical grounds, yet it is still difficult to explain many cases clinically, and more difficult to produce the condition experimentally. The experiments generally quoted in the large text-books are those of Grenet, carried out in 1904. This author claimed to have produced purpura in a rabbit by introducing three pathological factors:—(1) Hepatic derangement; (2) nervous disturbance; (3) presence of toxin. These are old observations, but, as far as I know, have neither been confirmed nor disproved. My first experiments were therefore repetitions of Grenet's, using, as far as possible, the same technique.

Grenet took rabbits, ligatured the "hepatic pedicle" for twenty minutes, and then in five to seven days injected an alcoholic extract of serum from a hæmophilic patient into the spinal canal. Paraplegia of varying degrees followed, but within a week ecchymoses on the hind legs invariably appeared. Control injections, without preliminary ligature of the pedicle, and also of simple fluids with ligature, always gave negative results.

In the four rabbits in which these proceedings were repeated, apart from some paresis of the hind limbs, no change was produced. No sign of purpura ever appeared. In six other rabbits intraspinal injections were made to investigate the curious tetaniform convulsions which occur when the cord is irritated. Using any fluid, it was found that 1 c.c., the amount employed by Grenet, caused death in a few minutes; with 0.5 c.c. recovery with paresis followed.

Sections of the liver, cut at different dates after ligature of the pedicle, showed no histological changes.

Charrin in 1892 described the easy production of purpura by injecting either organisms and their toxins into animals. *B. pyocaneus* was said to give purpura readily. I found, however, that repeated doses of sterilised twenty-four hours' growth of this organism produced negative results. Animals dying with a *pyocaneus* septicæmia even developed no purpura. Other bacterial toxins, as diphtheria and coli, also injected into guinea-pigs, failed to give a positive result. The mere presence of potent bacterial toxins is not sufficient to produce purpura; some other factor must be present before lysis of the capillary endothelium can occur.

The number of blood platelets is said to be greatly reduced in the hæmorrhagic conditions. Duke has studied the subject, and finds the platelet count is 30,000-80,000 instead of the normal 500,000-600,000 per c.mm. Selling, by injecting benzol subcutaneously into dogs, claims to have been able to reduce the number of platelets. It seemed, therefore, that by diminishing the platelets and then giving the animal toxins, that purpura should follow. Unfortunately I have not been able to confirm Selling's work, using rabbits and guinea-pigs. In counting the platelets Pratt's method was used. Careful microscopic examination of the liver and spleen of these animals failed to show free iron. It is difficult to imagine a drug affecting platelets without at the same time destroying the red corpuscles.

Appended are the tables of blood counts, showing the effect of benzol:—

Date.	Hb%	Reds	Whites	Platelets	Inj. Benzol.
Jan. 22	85	5500000	14000	690000	nil.
" 23	90	6000000	15000	600000	*3cc.
" 24	—	—	—	—	1cc.
" 25	85	5160000	11900	480000	1.5cc.
Feb. 1	60	4200000	11250	450000	1cc.
" 6	90	5060000	15000	500000	1.5cc.
" 9	80	5000000	12000	550000	1.5cc.
" 20	90	6500000	12500	480000	1.5cc.
" 21	95	6800000	19000	540000	nil.
"	Animal killed.				
Jan. 23	99	6500000	12500	400000	*3cc.
" 24	—	—	—	—	*2cc.
Feb. 1	95	6000000	13000	600000	*2cc.
" 6	95	6500000	14000	620000	*5cc.
" 9	98	6000000	15000	580000	*5cc.
" 10	animal killed.				

CONCLUSIONS.

Unfortunately, as regards the production of experimental purpura, my results have been negative. It appears that the oft-quoted positive experiments must, at any rate, not be accepted at present.

It is doubtful whether benzol has any effect on the blood platelets.

Although the lytic body at work in purpura is undoubtedly allied to its hæmolysin, yet its action seems to be different, since in two fatal cases of purpura neonatorum I have been able to microscope the organs without finding traces of free iron.

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SOME CLINICAL AND EXPERIMENTAL OBSERVATIONS ON THE OPERATIVE TREATMENT OF FRACTURES,

WITH ESPECIAL REFERENCE TO THE USE OF INTRA-MEDULLARY PEGS.

BY

ERNEST W. HEY GROVES, M.S., F.R.C.S.

The use of intra-medullary pegs for the fractures of the long bones is, of course, no new invention. Various modifications of these, in shape and material, have often been suggested. But for two chief reasons they have not been used very widely, first because of the fear of sepsis being introduced into the marrow cavity, and secondly because of the mechanical difficulty of introducing the peg into the interior of the closely-apposed fractured ends.