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

E. MARSHALL COWELL, M.D., F.R.C.S.

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.