Sham operation produced no change in systolic blood pressure in 3 dogs which were followed for 6 weeks. Subsequent operations in which periadrenal blood vessels and tissues were ligated in dog No. 390 and No. 386, Fig. 1, caused elevation of blood pressure which has persisted until the present, 4 months later. To date, there have been no significant changes in the urine analysis or blood NPN levels of the hypertensive dogs.

Conclusion. A prompt and sustained hypertension was produced in 6 dogs by unilateral subtotal ligation of periadrenal blood vessels and tissue.

It is a pleasure to thank Miss Goldie Spierer and Mr. Dominick Triolo for their assistance in these observations.

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The Production of Shock in Rats by the Drum Method.*

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Noble and Collip[1] described a method by which rats were subjected to graded degrees of trauma by tumbling in drums for varying periods of time. Animals subjected to this type of trauma did not develop complications of hemorrhage and infection. The undesirable factor of an anesthetic was likewise eliminated. Hemoconcentration and other pathological changes ascribed to the condition of shock did develop. These workers found that the drum method produced a better graded and controlled type of trauma than any other method they tried, and made use of it in subsequent experiments.[2,3] Zahl, Hutner, and Cooper[4] used the method and confirmed Noble and Collip's results as to the number of turns, percentage of deaths, survival time, and reproducibility. Chambers, Zweifach, and Lowenstein[5] employed the method to study circulatory reactions of rats, and Clarke and Cleghorn[6] used the drug method to study tissue potassium and phosphorus in shocked rats. In our laboratory we were interested in finding a method for producing shock which would give as nearly uniform and reproducible results as possible in animals to be used for biochemical studies. We wished to determine the chemical changes in the blood and tissues of animals in shock, and in animals which had received sublethal stimuli under conditions which could be readily controlled so that a quantitative relationship between the sublethal and lethal stimuli could be defined. As the tissues were to be analyzed for extremely labile substances they had to be frozen *in situ* with liquid air. The necessity for rapid freezing precluded the use of any animal larger than a rat. The method of Noble and Collip for production of shock was chosen because it seemed best to meet the requirements for the chemical investigations and also because it simulates battlefield conditions insofar as it has the elements of violent exercise and excitement as well as trauma.

The blood and tissue studies of rats which had been shocked by the drum method will be reported in other papers.[7,8]

This report is concerned with results ob-

* The work described in this paper was done under a contract, recommended by the Committee on Medical Research between the Office of Scientific Research and Development and the University of Wisconsin.

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2 Noble, R. L., and Collip, J. B., *ibid.*, 201.

3 Noble, R. L., *Am. J. Physiol.*, 1942, **138**, 346.

4 Zahl, P. A., Hutner, S. H., and Cooper, F. S., *J. Pharm. and Exp. Therap.*, 1943, **77**, 143.

5 Chambers, R. W., Zweifach, B. W., and Lowenstein, B. E., *Am. J. Physiol.*, 1943, **139**, 123.

6 Clarke, A. P. W., and Cleghorn, R. A., *Endocrinol.*, 1942, **31**, 597.

7 McShan, W. H., Potter, V. R., Goldman, A., Shipley, E. G., and Meyer, R. K., *Am. J. Physiol.*, 1945, **145**, 93.

8 LePage, G. A., unpublished data.

tained with the Noble-Collip method of producing shock in the Sprague-Dawley strain of albino rats, in a strain of cancer-resistant rats, and in adrenal enucleated rats of the Sprague-Dawley strain.

Materials and Methods. The apparatus used for producing shock was like that described by Noble and Collip except that the drums had a diameter of 16 inches as recommended by the authors.[1] Each of the drums had two baffles and the drums were set to rotate at 40 r.p.m. Metal screen was used to replace the glass in the doors so as to provide better ventilation.

Adult male albino rats of the Sprague-Dawley strain, weighing 250-300 g were used. These rats had been in the laboratory 5 days or longer before being used in any of the experiments. The cancer-resistant strain of rats were those maintained by Dr. M. F. Guyer of the Zoology Department and we are indebted to him for supplying us with them. Males weighing 250-300 g were used.

The adrenal-enucleated rats were Sprague-Dawley rats in which the adrenal capsule had been opened and the cortex and medulla removed by applying light pressure to the capsule. The animals were maintained on 1% NaCl as drinking water for 10 days until the adrenal remnant had regenerated sufficiently to maintain the animals. The rats weighed 125 to 175 g at the time of adrenal enucleation. They were used for the experiment five to six weeks later, at which time the weight ranged from 260 to 360 g. It was obvious that their appetites had been normal and that normal growth had ensued since the average weights were approximately doubled.

Rats were considered to survive if they lived more than 24 hours after tumbling in the drums. To eliminate the possibility of protection from jumping over the baffles the forepaws were fastened together with adhesive tape before the rats were placed in the drums.

Results and Discussion. The animals dying from drum trauma showed essentially the same changes in appearance as described by Noble and Collip.[1] These included extreme vascular dilatation in the intestine and its mesentery, reddening of the muscles of the abdominal wall, frequent hemorrhage into the lumen of the intestine and petechiæ in the intestinal walls. Lungs sometimes showed either petechiæ or marked congestion. The heart contained little blood and it was thick and viscid. Rarely did an animal show any subcutaneous, cranial, or muscular hemorrhage. Teeth and claws were frequently broken and the feet were often slightly bruised. The liver was engorged and sometimes small breaks and tears occurred. No broken or torn places were ever observed in the spleen. Both adrenals and kidneys often showed congestion.

TABLE I.
Survival of Rats to Drum Shock.

No. of rats	Time,* min.	% survival
14	4	100.0
44	8	65.6
42	10	71.4
125	12	47.2
63	13	9.5
16	15	4.3

* Drum revolved 40 times per minute.

The data in Table I show the results obtained by use of 304 male rats of the Sprague-Dawley strain. The per cent of animals surviving is less in almost all cases than was obtained by Noble and Collip at comparable periods of rotation. These results together with ours on conditioning[11] indicate that the Sprague-Dawley strain of rats is not as resistant to trauma of this type as are the rats of the strain used by Noble and Collip.

Table II summarizes the results of testing the effect of varying one factor at a time on survival of groups of rats. The first factor which was modified was that of taping all paws in contrast to taping only the front paws as was done regularly when producing Noble-Collip shock. Slightly better survival was obtained when both pairs of paws were taped together. The survival was 42.9% as compared to 21.5% when only the front paws were taped.

[9] Freeman, N. E., Freedman, H., and Miller, C. C., *Am. J. Physiol.*, 1941, **131**, 545.

[10] Bulbring, E., and Burn, J. H., *J. Physiol.*, 1942, **101**, 289.

[11] Shipley, E. G., Meyer, R. K., and McShan, W. H., unpublished data.

TABLE II.
Alteration in Resistance of Rats to Drum Shock by Various Factors.

No. of rats	Time run,* min.	Factor modified	% survival
14	12	Taping paws—all taped	42.9
14	12	" " fore paws taped	21.5
19	12	Bled one week previously	5.1
8	12	Without abdominal girdle	0.0
14	12	With " "	50.0
6	12	Adrenal enucleation	0.0
6	12	Intact adrenals	16.7
24	10	Adrenal enucleation	8.3
12	10	Intact adrenals	50.0
20	12	Cancer resistant	20.0
10	10	" "	30.0

* Drum revolved 40 times per minute.

To determine the effect of protection to the abdomen on survival, 2 groups of rats were run simultaneously in the Noble-Collip drums for 12 minutes. One group was without protection and the second group was protected by having a strip of heavy muslin wrapped snugly around the abdomen of the rat and fastened in place with adhesive tape. The strips were wide enough to cover the space between the fore and hind legs and was long enough to make 4 or 5 thicknesses when in place. Some degree of protection against the development of shock was afforded by girdling the abdomen but this protection was not complete, as is indicated by the data in Table II. Chambers, Zweifach, and Lowenstein[5] found that protection of the abdomen during tumbling prevented the development of a shock-like state in rats subjected to rotation up to 1000 revolutions. Fifty per cent of our rats with abdominal protection survived while none of the controls survived.

Four groups of rats which had survived bleeding to produce hemorrhagic shock were subjected, one week later, to 12 minutes of Noble-Collip shock to see if protection had developed as a consequence of the bleeding. Only 1 rat out of 19 survived the Noble-Collip shock. Comparing the 5.2% survival in these rats with the 47.2% survival in normal rats, it is obvious that a decreased rather than an increased resistance resulted.

The adrenal-enucleated rats were run simultaneously with control rats. Ten or 12-minute periods of tumbling were used. None of the adrenal-enucleated and only 1 control survived 12 minutes. At 10 minutes 8.33% of 24 adrenal-enucleated and 50% of 12 unconditioned rats survived. All of the adrenal-enucleated rats were autopsied and the regenerated adrenals were removed to determine whether regeneration had occurred. In all cases regeneration of the cortex had occurred. Thus it would seem that loss of the adrenal medulla or perhaps inadequate regeneration of cortical tissue had decreased the percentage of survival. Freeman, Freedman, and Miller[7] produced a shock-like state by the infusion of adrenaline. Bülbring and Burn[10] found that small amounts of adrenaline augment transmission in sympathetic ganglia and adrenaline in large amounts depresses transmission. The authors concluded that sudden liberation of large amounts of adrenaline was more likely to produce permanent circulatory damage than small amounts. If liberation of adrenaline contributes to the production of shock, then the removal of the adrenal medulla should increase the percentage survival in shocked animals, which have been subjected to overwhelming sensory stimuli. However, the results of our experiments do not support this conclusion but it is to be emphasized that the cortex was also largely removed, leaving remnants under the capsule for regeneration. Several investigations have shown that adrenalectomized animals are more susceptible to all types of

shock than are normal animals.[2,12,13,14] Numerous investigators have tried the effects of adrenal-cortical extracts as prophylactic and as therapeutic agents in shock produced by various means in both normal and adrenalectomized animals. Some of them have found the adrenal cortical hormones of benefit[15-17] and others found no beneficial effects from use of these hormones.[18-25] In general it may be said prophylaxis with adrenal cortical extracts was found to be of more benefit than therapeusis, and that a greater increase in survival was found in treated adrenalectomized than in treated intact animals. The findings of these authors together with our results in adrenal-enucleated rats suggest that a minimum quantity of adrenal cortical hormones are needed to protect an animal against trauma and that increasing the amount of the extracts is of no further benefit, whereas a decrease in quantity is detrimental.

As a cancer resistant strain of rats was readily available it became of interest to determine whether resistance to cancer might be linked with resistance to trauma. Included in Table II are the results obtained from subjecting 30 adult male rats of the cancer-resistant strain to graded degrees of trauma in the Noble-Collip apparatus. The survival at 12 minutes and 10 minutes were respectively 20% and 30%. These results do not seem to show any marked variations from those obtained with the Sprague-Dawley strain, but the percentages of survival are slightly lower.

Summary. 1. Varying degrees of shock can be produced in rats by subjecting them to various periods of trauma in Noble-Collip drums. The method appears to be suitable for use where graded and reproducible degrees of trauma are desired.

2. The percentages of survival were: for 5 minutes of tumbling, 100%; for 8 minutes, 65.6%; for 10 minutes, 71.4%; for 12 minutes, 47.2%; for 13 minutes, 9.5%; and for 15 minutes, 4.3%.

3. The Sprague-Dawley strain and a cancer-resistant strain of rats were found to be less resistant to trauma of the Noble-Collip type than were rats used by other investigators.

4. Survival of previous hemorrhage did not increase resistance to Noble-Collip trauma, but appeared to decrease resistance to some extent.

5. Adrenal enucleation decreased the resistance of rats to Noble-Collip trauma although regeneration of cortical tissue had been sufficient to support normal growth and to maintain the rats in a healthy state.

6. Protection to the abdomen and taping of the paws gave only limited protection to the rats of the Sprague-Dawley strain subjected to Noble-Collip shock.

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