

A Technic for Appraising Ability to Resist Gravitational Shock in the Rabbit.

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The day to day and hour to hour changes in ability to resist the pull of gravity against the venous return to the heart are of importance not only to the clinical problem of orthostatic hypotension and to the tactical problem of pilot failure under combat conditions but also to the more general problem of maintaining health and efficiency at occupations requiring prolonged, unrelieved sitting or standing. Tests have been proposed for the recognition of impairment and exploratory information gathered as to the extent of effect contributed by infection, lack of exercise and fatigue.¹⁻⁶ Little has been done in the way of quantitative appraisal of the possibilities for correction, stabilization and control. Mechanical aids have been suggested,^{1,7,8} and vasoconstrictive drugs.⁷⁻⁹

The upright position imposes gravitational restrictions on circulation regardless of species.¹⁰ Rabbits accustomed to small cages become markedly affected by enforced standing.¹¹ Circulatory interferences are established sufficient to cause a 30 to 100% decrease in ability to warm up after chilling. The effect is adapted to quantitative meas-

ure¹² and is shown below to be modified by infection and by lack of exercise in the same way that has been observed for man. The converse effects of ascorbic acid and desiccated thyroid also are described as instances of a use of the method for further exploration.

Method. The rabbits were dropped into water held at 66°F and allowed to swim freely until the rectal temperature had fallen to a point near 95°F. They were then removed from the water and dried. The course of the subsequent temperature rise was determined and recorded as indicated in Fig. 1, using identical clinical thermometers inserted to a depth of 2½ inches for 1½ min. When the temperature had risen to a point near 96.5°, the rabbits were placed in boxes enforcing an erect, vertical position for one-half hr following which serial temperature measurement was resumed until 100° had been passed. The completed temperature records were examined for the number of degrees rise accomplished during the half hour of enforced standing. A rise of 0.2° was considered to be indicative of a greater degree of interference with circulation, during the half hour of enforced standing, than a rise of 2.0°, etc.

The highest rise observed was 4.0°, in an exceptional rabbit, following preliminary hardening. The lowest was -0.9°, in a rabbit 4 years old. All of the rabbits were in sufficiently good condition¹² to make a rise of 2 to 4°, in one-half hour, when free of the gravitational stress of the upright position.

Reproducibility. Spontaneous changes, possibly associated with week to week changes in health, occurred to an extent re-

¹ Sewall, H., *Am. J. Med. Sc.*, 1919, **158**, 786.

² Weiss, S., *J. Am. Med. Assn.*, 1942, **118**, 529.

³ Lewis, T., *The Soldier's Heart and the Effort Syndrome*, 1919.

⁴ Crampton, C. W., *Am. J. Med. Sc.*, 1920, **160**, 721.

⁵ Schneider, E. C., *J. Am. Med. Assn.*, 1920, **74**, 1507.

⁶ Scott, V. T., *J. Am. Med. Assn.*, 1921, **76**, 786.

⁷ Fulton, J. F., *Science*, 1942, **95**, 207.

⁸ MacLean, A. R., and Allen, E. V., *J. Am. Med. Assn.*, 1940, **115**, 2162.

⁹ Jeffers, W. A., Montgomery, H., and Burton, A. C., *Am. J. Med. Sc.*, 1941, **202**, 1.

¹⁰ Hill, L., *J. Physiol.*, 1895, **18**, 15.

¹¹ MacLeod, J. J. R., *Physiology and Biochemistry in Modern Medicine*, 1926, p. 471.

¹² Locke, A., *J. Infect. Dis.*, 1937, **60**, 106; *J. Immunol.*, 1939, **36**, 159.

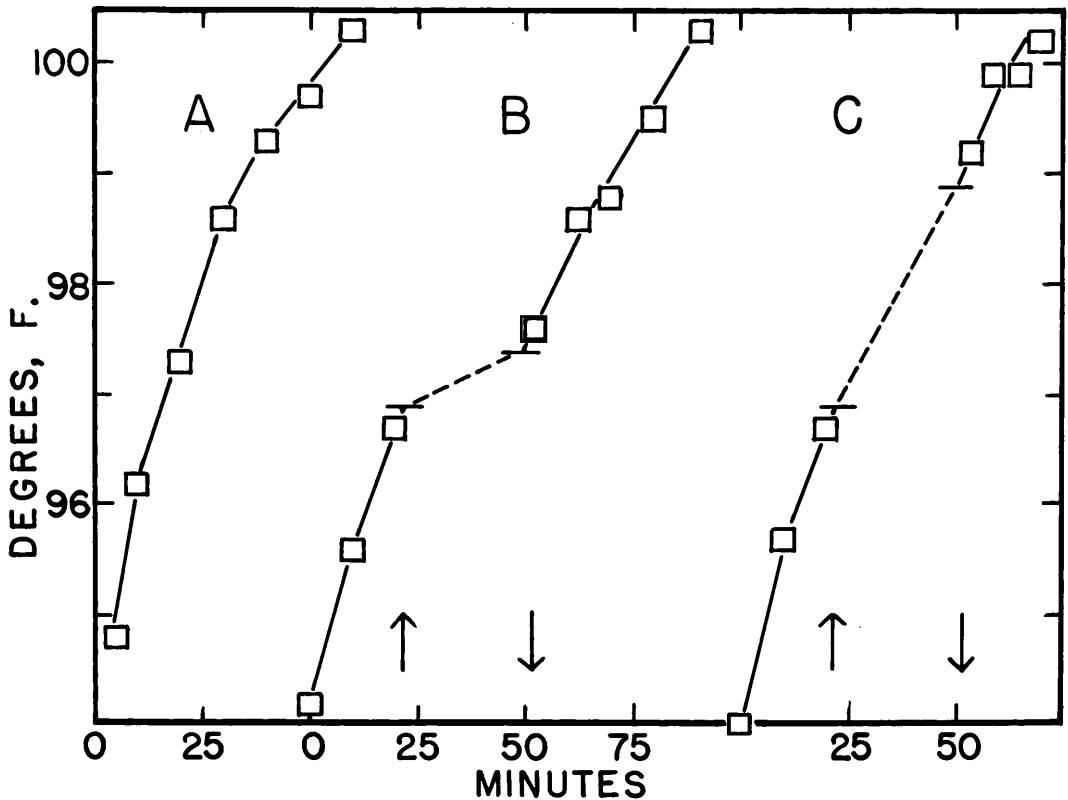


FIG. 1.

A typical record of the rate of temperature recovery after chilling in a rabbit (A) kept in the normal horizontal position throughout the test and (B and C) forced to stand upright for the half hour indicated by the arrows. The rabbit had not been chilled during the week prior to test B and had been chilled on each of the two days preceding test C. The chillings were given as an incentive to exercise (shivering, etc.).

quiring the use of groups large enough to give a stable average (Table I).

Infection. Rabbits so commonly harbor low-grade infections and infestations that freedom from such handicap cannot be assumed even when no evidence of snuffles, wet adherent feces, ear or skin conditions, abscesses, or periods of elevated temperature or weight loss is apparent. Those of the rabbits in Table I with manifest evidence of infection were, on the whole, the least able to endure enforced standing.

Exercise. The most effective hardening procedure appeared to be that given by the test itself. Consecutive, daily repetition of the test caused a progressive increase in tolerance for the erect position, reaching a peak on the third day. A control sequence of periods of enforced standing, without ac-

companied chilling, was without substantial hardening effect. The benefit was not maintained in the absence of further, supportive chillings at intervals of not longer than 3 days.

Ascorbic acid. An increased tolerance for the erect position was apparent in rabbits given a single feeding of 300 mg of ascorbic acid 2 hr before the time of test, providing a preliminary chilling had been given not longer than 3 days before. No clear effect from ingested ascorbic acid was apparent in the absence of the reinforcing chilling. As great an improvement was produced by the one preliminary chilling plus ascorbic acid as was produced by 2 preliminary chillings without ascorbic acid. The improvement was transient and usually entirely lost within one to 2 weeks of the time of ascorbic acid

TABLE I.

Reproducibility of Effect of Enforced Standing on Ability of the Rabbit to Warm Up After Chilling; Influence of Infection.

No. of rabbits	Presence of recognized low-grade infection	Preparation*	Avg. temp. rise, °F, during the half hour of standing		Probable error of the difference, °F†
			Test 1	Test 2	
14	+	R	0.85	0.84	0.05
20	—	R	1.39	1.33	.09
20	+	H	1.25	1.24	.05

*R: No preliminary chilling for 4 days or longer, preceding test; H: One preliminary chilling within 3 days of test.

†As computed by Peter's formula (J. W. Mellor, *Higher Math.*, etc., 1926, p. 524).

administration.

The rabbits used were New Zealand White males, between 2.5 and 5.0 kg in weight, with continuous access (excepting during the periods of test) to clover hay, oats, carrot, salt and water. No opportunity for unusual ascorbic acid depletion had been given prior to test nor were unusually low plasma ascorbic acid levels present in those of the group tested for this factor.

Isoascorbic acid. This substance, chemically similar to ascorbic acid but with only

a fraction of the latter's antiscorbutic activity,¹³ appeared to be practically devoid, also, of effect on sensitivity to gravitational interference with circulation. It was given exactly as the ascorbic acid was given and to the same rabbits, in part before the tests for response to ascorbic acid and in part after.

*Desiccated thyroid.** Feedings of 200 mg per day for 8 days produced a marked decrease in sensitivity to gravitational effect, further decreased by a continuance of the

TABLE II.

Effect of Preliminary Hardening, Ascorbic and Isoascorbic Acids and Desiccated Thyroid.

No. of rabbits	Preparation*	Avg temp. rise in °F during the half hour of forced standing		% change
		Before the indicated preparation	After	
30	H	1.14	1.46	28±7†
18	H, IA	1.08	1.45	34±11
27	H, AA	1.01	1.77	76±13
23	HH	1.03	1.75	70±15
15	PAA	.92	.77	—17±11
17	T	1.19	1.98	66±14
12	TT	.98	1.86	90±24
17	H, T	1.19	2.28	92±19
12	H, TT	.98	1.99	103±24
13	PT	1.14	1.36	19±11

*H: One preliminary chilling within 3 days of the test.

HH: Two or more chillings during the 3 days preceding test.

IA: Isoascorbic acid, Pfizer, 300 mg by mouth, 2 hr before test.

AA: Ascorbic acid, Pfizer, 300 mg by mouth, 2 hr before test.

T: Desiccated thyroid, Parke-Davis, 200 mg by mouth daily for 8 days.

TT: Desiccated thyroid as indicated under T followed by 100 mg daily for 6 days longer.

PAA: Seven to 14 days after the administration of ascorbic acid:

PT: Seven to 14 days after the discontinuance of the thyroid feedings.

†Probable error of the estimate. See Table I.

¹³ Dalmer, O., *Deut. med. Wchnschr.*, 1934, **60**, 1200.

* Trial of this principle was suggested by Broda Barnes who observed instances of improvement in

toleration for the erect position in a series of university students given thyroid feedings (personal communication).

feedings for 6 days at a level of 100 mg per day, and by one preliminary chilling on the day prior to test (Table II). Adjuvant hardening was not required for the production of the thyroid effect. Discontinuance of the thyroid feedings was followed by a return toward the original sensitivity to gravitational effect within 5 to 7 days.

Summary. A technic is proposed through which changes in degree of tolerance for the upright position can be followed in the rab-

bit. Through use of the technic, a minimum tolerance is demonstrated in rabbits harboring depleting infections, and in rabbits softened by maintenance for a week or more in cages too small to permit exercise, and a heightened tolerance following subjection to either a preliminary chilling sequence, a single preliminary chilling followed by ascorbic acid administration, or a sequence of feedings of desiccated thyroid.

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Effect of Heparin on Retrograde Blood Flow.

EUGENE LEITER. (Introduced by Claude S. Beck.)

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The use of heparin in the treatment of thrombosis is chiefly prophylactic.^{1,2} There is some speculation that thrombi already formed are reduced in size by heparin, but no convincing evidence to that effect. It has also been suggested that heparin may increase the rate of blood flow, by reducing viscosity. If true, this fact would lend further reason for its use in the treatment of occluded vessels, by improving circulation through collaterals. This experiment is intended to show whether retrograde blood flow (*i.e.*, through a collateral circulation bed) is improved by administration of heparin.

Experiments. Dogs and cats were used. Under pentobarbital anesthesia, a femoral artery was ligated and severed. The amount of back-flow in 1-3 min from the distal end of the severed artery was then measured until constant readings were obtained, allowing sufficient time for opening of the femoral collateral circulation. Between readings, the free distal end was kept closed by a clamp, preventing excess loss of blood. Carotid pressure was recorded. Blood pressure was kept as constant as possible. A femoral vein

was cannulated for infusions and for injection of heparin. After consistent control readings were obtained, the animals were given single doses of heparin (Liquæmin), the dose varying from 1000 to 3000 Howell cat units per kg. Readings were taken for one-half to 4 hr after heparinization—that is, until the clotting time had returned to normal or at least until the peak of heparinization was well passed.

The method was shown to be sensitive to changes in blood pressure, to blood dilution by saline infusion in excess of 100 cc and to excessive blood loss. Infusion of 200-300 cc of saline in dogs consistently produced a change in the rate of flow, varying from 15% to 30% increase—obviously a factor of dilution and consequent alteration of viscosity. This procedure was utilized at the conclusion of each experiment to check the reliability of the method.

Observations. Experiments were completed on 11 animals, including 9 dogs and 2 cats. In 7 of the 11 experiments, there was no increase of flow after heparinization; in 4 there was an increase of 15% to 30%, attributable to changes in the control conditions.

Conclusion. From the data obtained, hep-

¹ Mason, M. F., *Surgery*, 1939, **5**, 451, 618.

² Murray, G., *Surg., Gynec., and Obstet.*, 1941, **72**, 340.