A FURTHER EXPERIMENTAL STUDY ON EXCITATION OF INFECTIONS OF THE THROAT.

By SAMUEL B. GRANT, STUART MUDD, and ALFRED GOLDMAN.

(From the Department of Pathology of Washington University Medical School, St. Louis.)

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In experiments previously published it has been shown that chilling of the body surface causes vasoconstriction and ischemia—not, as theretofore assumed, congestion—in the mucous membranes of the palate, pharynx, and palatine tonsils.[1] Upon rewarming the subject this ischemia was shown to disappear only partially from the palate and pharynx, but, in a single experiment upon the palatine tonsil, promptly gave way to an actual hyperemia. Because of the peculiar importance of the tonsils as foci of infection, it was considered necessary to devote further study to their reactions. The present experiments amply confirm the occurrence in the tonsils of the reaction of ischemia to chilling of the body surface; a composite of the four recovery curves obtained bears out also the first observation that the tonsils, upon the subject's being rewarmed after chilling, show a considerably greater tendency than do the contiguous mucous membranes of the palate and pharynx to regain a full blood supply.

Concurrent bacteriological observations on the pharynx and tonsils of several of the subjects showed after the experiments in several instances apparently an increase in the relative number of some of the pathogenic bacteria, synchronous with the appearance of a clinical sore throat.

Urine analysis indicated secretion during an experiment of a more dilute and less acid urine. In no instance was albuminuria or glycosuria produced.

[1] Mudd, S., and Grant, S. B., *J. Med. Research*, 1919, xl, 53.

Method.

The thermopile method described in the earlier paper[2] was again used, but with several notable improvements in detail. The subject entered the experimental room, kept between 16.9° and 20.9°C., warmly wrapped in loose garments. Thoracic and abdominal pneumographs were adjusted to a moving drum writing in the subject's view. The terminals of a thermopile, borne on a carrier of galvanized iron wire, were strapped by adhesive tape to the subject's forehead. The terminals of a second thermopile were fixed by means of another galvanized iron applicator and a specially devised holder, to be described below, in apposition with the mucous membrane of one palatine tonsil. Thereafter the subject maintained his position as nearly as possible constant throughout the experiment. The proximal ends of the thermopiles were kept packed in cotton in a test-tube with the bulb of a sensitive thermometer, and were connected through a rocking key with a d'Arsonval galvanometer.

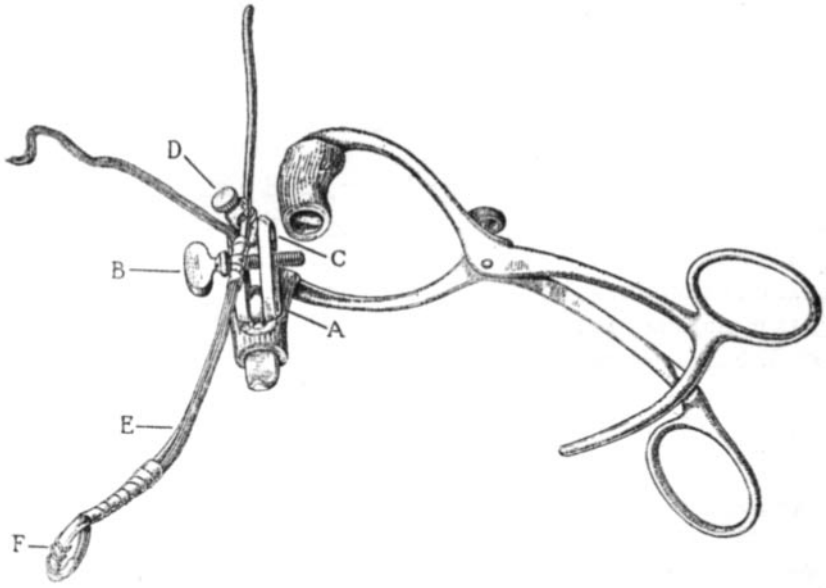
The subject's nostrils were plugged with cotton; breathing was through the open mouth. At least a part of the difficulty introduced by the excessive secretion of saliva under these circumstances was eliminated in the present experiments by keeping in the subject's mouth a glass saliva ejector of the type used by dentists, connected through a rubber tube to a suction pump on a water faucet.

When thermopiles, pneumographs, and saliva tube had once been properly adjusted, readings of galvanometer and thermometer were made at about 60 second intervals for a few minutes. Respiration was then deepened by an amount sufficient to increase the excursion of the pneumograph levers on the average for the experiments illustrated in the charts by about 73 per cent, the respiratory rate being kept constant throughout the experiment with the aid of a metronome. With the intake of cool room air thus increased, mucous membrane temperature usually fell slightly. When the readings showed themselves approximately constant, the subject's wraps were all removed and an electric fan was turned at short range on the lumbar region of the back; chilling continued in the experiments illustrated in the charts from 7 to 19 minutes, with an average duration

[2] Mudd and Grant,[1] pp. 54–60.

of 13.8 minutes. The subject was finally rewrapped and readings were continued until the end of the experiment.

From the thermometer and galvanometer readings thus made, skin and mucous membrane surface temperatures are readily computed and their changes accurately followed. It is to be borne in mind that these temperature changes under the conditions of the experiments have been shown to be satisfactory indices of local vasomotor changes.[3] Therefore, although the curves in the text-figures actually record



TEXT-FIG. 1. Applicator holder with tonsillar applicator and thermopile in position. *A* and *C*, ball and socket joints made by metal spheroids and blades of head mirror; *B*, set screw for tightening joints at *A* and *C*; *D*, set screw for fastening applicator in holder; *E*, galvanized iron wire applicator; *F*, applying surface bearing thermopile terminals.

variations in superficial temperature of the skin and exposed mucous membranes, what they indicate is alteration in vasomotor tone—a fall in temperature means local vasoconstriction and ischemia, a rise local vasodilation.

The most important improvement in method in the present study has been the devising of a special instrument by which accurate and

[3] Mudd and Grant,[1] pp. 58–60.

stable adjustment of the thermopile terminals to the tonsillar surface, or other site in mouth or throat, can be effected. Into one arm of a Doyen mouth gag (Text-fig. 1) a small brass spheroid was screwed. A second brass spheroid bearing a groove closed by a set screw (*D*) was made. The two spheroids were connected by means of the blades of an ordinary head mirror (*C*). The blades could be clamped stably upon the spheroids by means of a second set screw (*B*). The applicator (*E*) so shaped as to have its tip fit against the tonsil, was held in place in the groove by the set screw *D*. By varying the shape and position of the applicator and arranging properly the joints at *A* and *C* any desired application could be made. The subject's teeth were protected from the metal gag by rubber, as shown in the drawing.

As is evident, the iron wire applicators used with this new holder are somewhat simpler than the original types; they are also of slightly lighter wire; No. 13 has been found most satisfactory.

The subjects used, as in the earlier experiments, were all upper class medical students, except J. D. R. and B. J. F. in the first and W. G. E. in the present series, who were laboratory employees several years younger.

For calibration the unknown temperature terminals of the thermopiles were bound with elastic about the bulb of a sensitive thermometer, which was immersed in a suspended test-tube of distilled water or salt solution. In the earlier experiments heat in small amounts was applied at short intervals directly to the test-tube. The contained liquid was stirred, and, when equilibrium had been reached, the galvanometer deflection and temperatures of the two ends of the thermopiles were read. From these data the calibration curves for the thermopiles were constructed. Since these were apparently, within the temperature range of the experiments, virtually straight lines, the results were averaged for each thermopile and the calibration constants thus obtained; *i.e.*, the straight line $x = ky$, when y is the galvanometer deflection in millimeters, x the temperature difference in °C. between the two ends of the thermopiles, and k the calibration constant, in each case with a value of approximately 0.1.

In the experiments of the present series the test-tube of water containing the thermopile terminals and the thermometer was immersed in addition in a suspended beaker of water containing a stirrer, and heat was applied to the beaker at intervals. The water in the beaker and that in the test-tube were then stirred until a constant temperature had been reached, and the thermometer and galvanometer readings then taken. With the more accurate results thus obtained,

the calibration curves were found to deviate appreciably, though very slightly, from straight lines. Temperatures were therefore taken from the curves directly.

The deviations were such that with the larger deflections the temperatures calculated from the calibration constant were slightly higher than those actually shown by the curve; with the smaller deflections calculated temperatures were slightly too low. For instance, to take extreme values, with a galvanometer deflection of 206 mm., the thermopile constant temperature end being 17.75°C., the mucous membrane temperature calculated from the calibration "constant" (in this case 0.09904) is 38.15°C., that shown by the curve, 37.43°C. With a galvanometer deflection of 56 mm. and constant end at 18.5°, the calculated mucous membrane temperature is 24.05°, that shown on the curve is 24.47°C. The high mucous membrane temperature values mentioned previously[4] are thus at least in large part accounted for. To be corrected the curves of the first paper should be very slightly foreshortened along the vertical axis; however, the error introduced was obviously quite negligible from the point of view for which the curves were designed; *i.e.*, to show temperature variations through a small range.

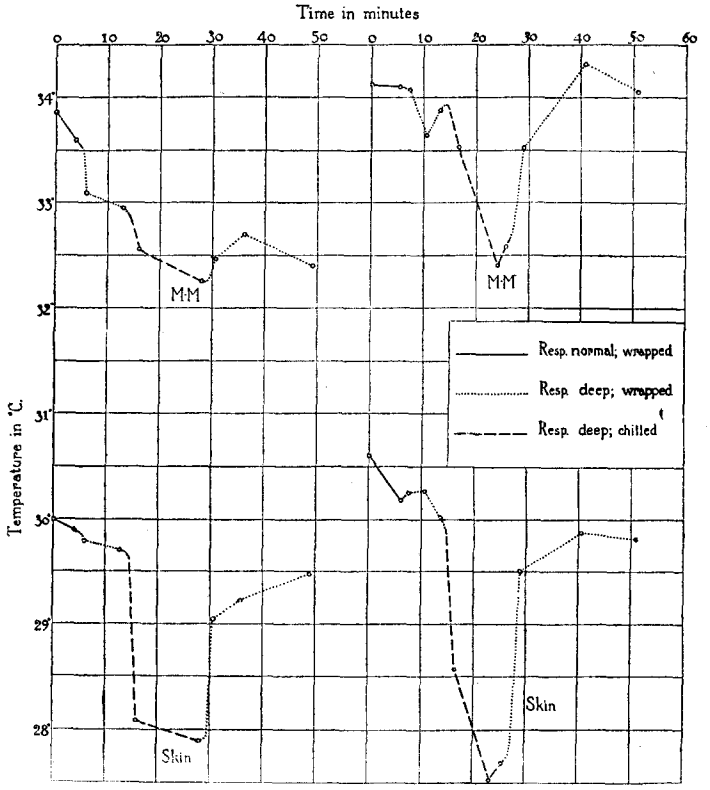
Vasomotor Reactions of Palatine Tonsils.

Composite Graphs.—The characteristic reactions of skin and mucous membrane to chilling of the body surface are shown in Text-fig. 2. The curves on the right are a composite of four experiments upon three different subjects; for the mucous membrane curve the thermopile tips were applied to the palatine tonsil surface; the synchronous lower curve is from the skin of the forehead. The curves on the left are a composite of three experiments upon the forehead, and, in two instances, mucous membrane of soft palate, in one instance, mucous membrane of oropharynx; two subjects were used. In each case the first and last point of the experiment, the point immediately before and after a change of conditions, and the point of maximum mucous membrane response to rewrapping were taken, and from their average values the curves were drawn. In the right hand curve the two points of maximum mucous membrane response to deepened respiration and to chilling are also included.

The palatine-oropharyngeal curve underwent the usual slight depression with deepened respiration. Upon chilling, the mucous membrane temperature fell 0.69°C. in 14 minutes; the corresponding point on the skin curve shows a depression of 1.80°. Upon rewrapping,

[4] Mudd and Grant,[1] p. 55.

the mucous membrane temperature rose in 7.3 minutes 0.40°, thereafter sinking slightly. The skin curve showed a maximum rise of 1.60° in 14.8 minutes. The maximum recovery exhibited within a 20 minute period after rewrapping was, then, for the palatine-oropharyngeal curve only 58 per cent of the fall in response to chilling; for the skin curve recovery was 88.8 per cent of the fall.



TEXT-FIG. 2. Reactions to chilling and to rewarming. On left, temperatures of skin and mucous membranes (*M.M*) of soft palate and oropharynx (composite graphs of Experiments 10, 12, and 13); on right, temperatures of skin and palatine tonsil (composite graphs of Experiments 1, 3, and 5 of the present series and Experiment 20 of the earlier series[5]).

[5] Mudd and Grant,[1] p. 85.

The palatine mucous membrane and skin curves responded to chilling by the usual depression, amounting to 1.47° for tonsil and 2.49° for skin. On rewarming, the mucous membrane reached a maximum rise of 1.72° in 14.1 minutes, the skin a rise of 2.33° in 14.5 minutes. Recovery was thus 117 per cent for tonsillar mucous membrane, 93.6 per cent for skin.

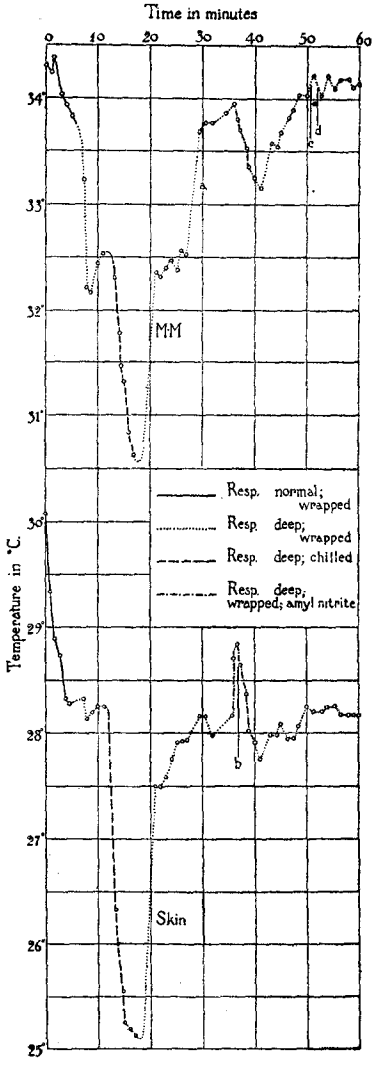
It is to be noted that, because the subject could not change position during the experiment and because of all the apparatus attached to him, he was practically never quite so warmly wrapped after chilling as he had been before. If conditions had been made identical before and after, doubtless all the recovery curves would have been somewhat higher.

Evidently the tonsils tend strongly to react to rewarming after chilling by becoming hyperemic, whereas the pharynx and palate, as was also shown in the earlier experiments, tend to remain somewhat ischemic for a considerable period after chilling. The skin occupies an intermediate position and returns approximately to its original condition.

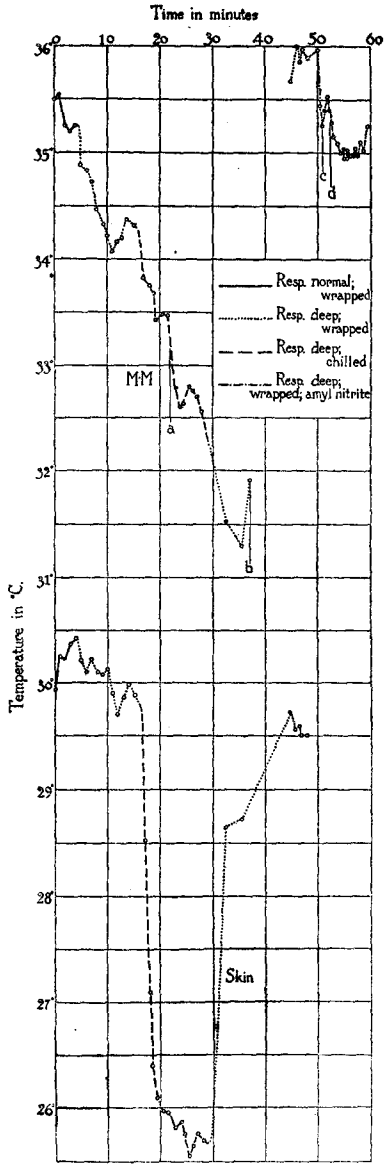
Experiment 1.—Subject 1, W. G. E. June 11, 1919, 11 a.m. to 12 m. Mucous membrane thermopile on left tonsil. Skin thermopile on forehead. Respirations 14 per minute. Mouth open; nostrils plugged. Thoracic and abdominal pneumographs. Room temperature 17.30–18.05°C.

Text-fig. 3 shows strikingly the characteristic tonsillar reactions. When the mucous membrane temperature had adjusted itself to deep respiration, chilling was begun at 0:12.[6] By 0:17 the mucous membrane temperature had fallen 1.91°, the skin temperature 3.11°. The subject was rewrapped at 0:17.5. 17 minutes later the tonsillar temperature had risen 3.24°, the skin temperature 3.04°. At 0:35 inhalation of an ampule of amyl nitrite was begun. The short transient rise in skin temperature, corresponding to the visible flush, at once developed; the peak, 0.66° higher, was reached in about 1.5 minutes, the maximum secondary fall to 0.42° below the original level in 6 minutes. The mucous membrane temperature, on the

[6] 0:12, 0:17, etc., indicate the time after the beginning of the experiment; *i.e.*, 0:12 signifies 12 minutes after the beginning of the experiment, 0:17, 17 minutes, etc.



TEXT-FIG. 3.



TEXT-FIG. 4.

TEXT-FIG. 3. Reactions to chilling, rewarming, and amyl nitrite. Temperatures of skin and mucous membrane of faucial tonsil, Experiment 1. *a*, applicator noted to be properly adjusted; *b*, flush of face fading; *c*, breathing shallow; *d*, breathing deeper.

TEXT-FIG. 4. Reactions to chilling, rewarming, and amyl nitrite. Temperatures of skin and mucous membrane of faucial tonsil, Experiment 2. *a*, fan faster; *b*, applicator loose; readjusted; *c*, face flushed; *d*, face fairly white.

other hand, which was already at the high level of 33.86°, fell with amyl nitrite to 33.17°, reached after 6 minutes, and then rose to a level slightly above 34° about 15 minutes after inhalation.

The tonsil here responded to amyl nitrite in the same way as did an acutely inflamed soft palate.[7] The mucous membrane vessels were already dilated; the effect of the relaxing of the mucous membrane blood vessel walls by amyl nitrite must have been overshadowed by the general lowering of blood pressure, the rate of circulation through the mucous membrane vessels was decreased, and the temperature fell. It is possible that increased depth of respiration with amyl nitrite also contributed to the observed fall.

Experiment 2.—Subject 2, L. J. O. June 7, 1919, 10.30 to 11.30 a.m. Mucous membrane thermopile on left tonsil. Skin thermopile on forehead. Respirations 14 per minute. Mouth breathing. Thoracic and abdominal pneumographs. Room temperature 17.12–17.87°C.

Text-fig. 4 shows the usual depression of skin and mucous membrane temperatures; the latter in this case continued to fall for about 6.5 minutes after cessation of chilling, possibly because of faulty adjustment of the applicator, which at 0:38 was noted to be loose, and was readjusted. The next reading showed a mucous membrane temperature 1.37° above the last reading before chilling. This curve thus probably records a reaction of hyperemia to rewrapping, but it was excluded from the composite graph because of the readjustment of the thermopile. On inhalation of amyl nitrite at 0:49, the response was again a drop in tonsillar temperature—0.94° in 6 minutes; the increase in respiratory amplitude was at most 30 per cent. The increase in respiratory amplitude at 0:4.5 amounted to 84.6 per cent and was followed within 6.5 minutes by a depression of only 1.16°. The temperature fall after amyl nitrite was, then, evidently due in part both to respiratory increase and to general blood pressure fall.

Experiment 3.—Subject 3, S. B. G. June 6, 1919, 5 to 6.30 p.m. Mucous membrane thermopile on left tonsil. Skin thermopile on forehead. Respirations 14 per minute. Mouth open; nostrils plugged. Thoracic and abdominal pneumographs. Room temperature 18.60–20.0°C.

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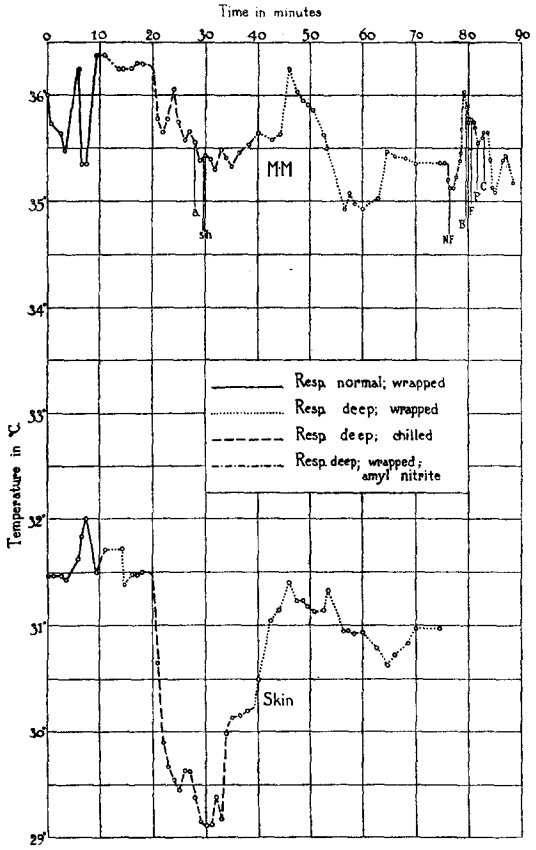
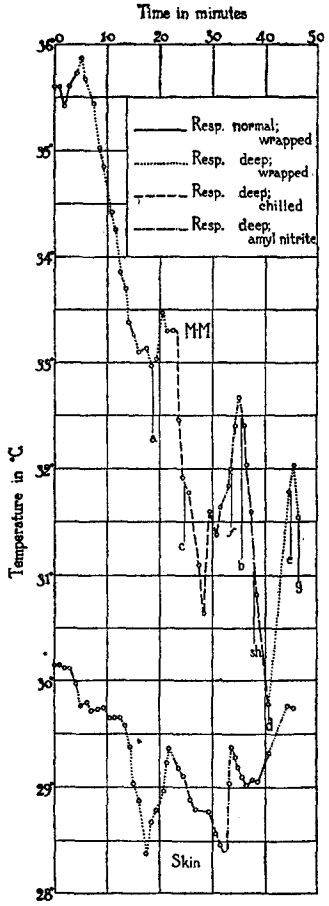
[7] Mudd and Grant,[1] p. 92.

In Text-fig. 5 the chilling and recovery curves proceed normally until 0:46, after which both skin and mucous membrane temperatures fall again, presumably on account of the subject's being inadequately wrapped. This curve is included in the composite although it makes less striking the hyperemia reaction to rewarming. The

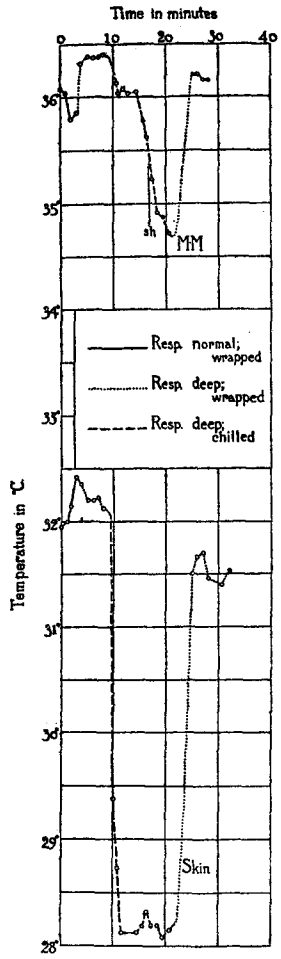


TEXT-FIG. 5. Reactions to chilling, rewarming, and amyl nitrite. Temperatures of skin and mucous membrane of faucial tonsil, Experiment 3. *a*, fan faster; *sh*, starts shivering; *NF*, face not flushed; *B*, second ampule of amyl nitrite inhaled; *F*, face flushed; *P*, still inhaling amyl nitrite; face paler; *C*, stops inhaling.

mucous membrane response to amyl nitrite is here a momentary fall of 0.23° in 1 minute, followed by a sharp rise of 0.90° in 2 minutes, with a more gradual return to normal in about 5 minutes. The predominating factor is evidently the local vasodilation.



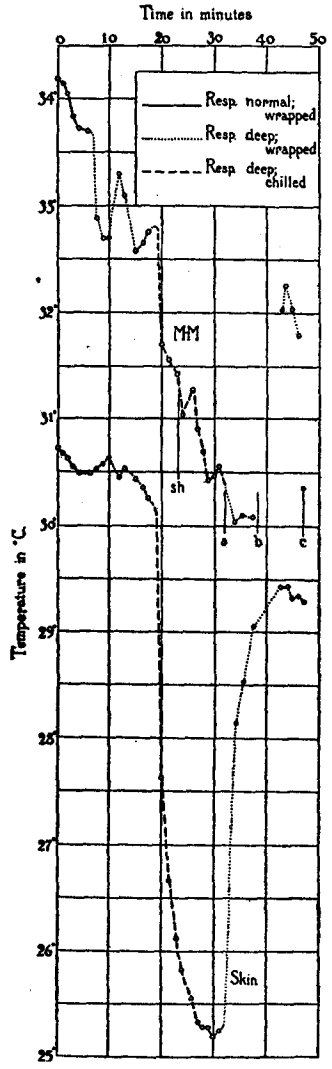
TEXT-FIG. 6.



TEXT-FIG. 7.

TEXT-FIG. 6. Reactions to chilling and amyl nitrite. Temperatures of skin and mucous membrane of faucial tonsil, Experiment 4. *a*, clears throat; *c*, coughed; *f*, face flushed; *b*, flush passing; stops inhaling amyl nitrite; *sh*, is shivering; *d*, clears throat; *e*, respiration too shallow; deepened; *g*, subject fainted.

TEXT-FIG. 7. Reactions to chilling and rewarming. Temperatures of skin and mucous membrane of faucial tonsil, Experiment 5. *sh*, is shivering.



TEXT-FIG. 8. Reaction to chilling. Temperatures of skin and mucous membrane of faucial tonsil, Experiment 6. Tonsil hypertrophic. *sh*, shivers; *a*, applicator holder seemed to be slipping; *b*, applicator off; reapplied; *c*, applicator tip off tonsil.

Experiment 4.—Subject 4, R. L. A. June 9, 1919, 10.56 to 11.46 a.m. Mucous membrane thermopile on left tonsil. Skin thermopile on forehead. Respirations 14 per minute. Mouth open; nostrils plugged. Thoracic and abdominal pneumographs. Room temperature 17.47–18.55°C.

In Text-fig. 6 the mucous membrane depression with chilling is great—3.52° in 18 minutes; the maximum skin fall, on the other hand, is only 0.88°, in 7.5 minutes, and is obliterated after amyl nitrite inhalation. Amyl nitrite, administered at 0:32.5 during chilling, produced a sharp rise in both mucous membrane and skin temperatures—1.02° in 2.5 minutes, and 0.89° in 1 minute, respectively. The recovery curves started up characteristically, but were interrupted by the subject's fainting.

Experiment 5.—Subject 3, S. B. G. June 11, 1919, 4.37 to 5.09 p.m. Mucous membrane thermopile on left tonsil. Skin thermopile on forehead. Respirations 10 per minute. Mouth breathing. Thoracic and abdominal pneumographs. Room temperature 19.65–20.12°C.

Text-fig. 7 shows characteristic chilling curves. Recovery is not quite complete either for skin or mucous membrane, perhaps due to inadequate wrapping. The tonsillar curve was cut short at 0:28 by the slipping of the thermopile applicator.

Experiment 6.—Subject 5, A. G. June 10, 1919, 11.30 a.m. to 12.17 p.m. Mucous membrane thermopile on right tonsil. Skin thermopile on forehead. Respirations 16 per minute. Mouth open; nostrils plugged. Thoracic and abdominal pneumographs. Room temperature 16.90–17.80°C.

The tonsils of this subject had been diagnosed in the Army and in the Washington University as hypertrophic. Text-fig. 8 shows characteristic chilling curves for both tonsil and skin, of large amplitude in each case. The applicator holder seemed to be slipping at 0:31.5, and satisfactory application was not thereafter obtained.

Discussion of Vasomotor Reactions to Chilling.[8]

The difference in recovery of blood supply upon rewarming after chilling exhibited by the palatine tonsils on the one hand, and the palate and pharynx on the other, is of interest, and suggests a corollary

[8] Compare Galeotti, G., *Riforma Med.*, 1920, xxxvi, 205; abstracted in *J. Am. Med. Assn.*, 1920, lxxiv, 1491.

hypothesis. It is well known that persons in robust health and inured to rigorous physical circumstances of living react better after chilling, as for instance by a sea bath, than the less vigorous. It seems possible that one factor in the hardening process of cold bathing, outdoor life, and so forth, with its incident heightened resistance to colds and sore throats, is a training of the vasomotor system in the direction of development of a quick reaction of hyperemia in the pharynx following chilling, such as has been shown to exist in the tonsils of the subjects of the present experiments.

We would reiterate in order to minimize any possibility of misunderstanding. We are concerned in our experiments with excessive chilling of the body surface, which, like overdosage of a useful drug, we believe may have ill effects. Certainly we would not encourage the unreasoning fear of slight drafts and exposure so often encountered. Good ventilation and circulating air in buildings, cold weather, and out-of-door living are needed for vigorous health; many people are unquestionably benefited by cold bathing. But excesses in this direction should also be avoided.

Autoinfections only are under consideration in the present paper. However, it should be clearly borne in mind that colds dependent primarily upon contagion from outside sources are probably of more frequent and widespread occurrence.[9]

Concurrent Bacteriological Studies.

Several instances during the experiments of 1918 seemed at least suggestive of experimental excitation of infection. The case of S. M. (Subject 6) in particular seemed to point to chilling as the exciting factor. The experiment was a blood temperature control in which he sat from 4 to 6.09 p.m., December 4, 1918, with closed mouth, the bulb of a thermometer beneath his tongue. He forced respiration from 4.12 to 6.09 p.m., and was chilled by a fan from 4.47 to 5.09 p.m. Shivering began at 4.48 p.m., and had become very severe by 4.52 p.m. The subject had not been aware of other recent exposure to cold or infection. By the morning of December

[9] For a discussion of this phase of the subject the reader is referred especially to Hill, L., The science of ventilation and open-air treatment. Part 1, *Gt. Britain Med. Research Com., Special Rep. Series, No. 32,* 1919.

5, nasopharyngeal stuffiness had developed sufficiently to cause the remark by a friend that he had a cold. The symptoms persisted 3 or 4 days.[10]

A study of the flora of the nose and throat during the experiments of the summer of 1919 seemed, then, to be well worth while.

Material and Method.—The medium employed was a 5 per cent rabbit blood meat infusion agar. Baked blood agar was also used in each instance as a special medium for *Bacillus influenzæ*. Sputum from each subject was injected into a mouse for typing pneumococcus. Cultures were taken from the nose through the anterior nares, from the tonsil, and from the posterior pharyngeal wall by means of separate swabs. Each swab was immersed in sterile broth and then applied both to a red and baked blood agar plate; the remaining area of the plate was inoculated by means of a platinum loop. Films were made directly from the same swab.

The cultures were incubated for 36 hours. The plates were then divided into eight segments, and every colony in two to four segments of the plate was counted and its nature determined. An attempt was made to count approximately the same total number of colonies daily, in order to detect any marked changes in the flora and particularly in the relative proportions of the bacteria present. On account of the difficulty of differentiating pneumococcus from *Streptococcus viridans* by morphology these two were put in the same group.

Results.—Four different subjects were used in this study. Two developed clinical sore throats; a third had some symptoms of malaise and headache; a fourth was unaffected. The results obtained with the nose cultures were entirely negative. Subjects 5 and 6 showed *Staphylococcus aureus*, Subjects 1 and 3 *Staphylococcus albus*. No attempt was made to sterilize the vestibule of the nose before swabbing. The flora obtained from the nose, as has been found by other investigators[11] was at all times exceedingly sparse, but the above organisms were always found to be present. They showed no changes with exposure. The results obtained from pharynx and tonsil in each instance are given in Tables I to III.

[10] Similarly we have noted what we believe to be an excitation of infection after, and presumably due to chilling in a number of carefully observed instances in our everyday experience.

[11] Thomson, St. C., Diseases of the nose and throat, New York, 1913, 7.

TABLE I.

Subject 6. Bacteriology of Tonsil and Pharynx.

Date.	Place cultured.	*S. viridans* and Pn. II.		*S. hæmolyticus.*		*B. influenzæ.*		Undetermined.		Remarks.
		No. of colonies counted.	Per cent of all colonies.	No. of colonies counted.	Per cent of all colonies.	No. of colonies counted.	Per cent of all colonies.	No. of colonies counted.	Per cent of all colonies.	
1919										
June 4	Left tonsil.	28	93	0	0	2	7	0	0	
	Pharynx.	36	100	0	0	0	0	0	0	
						Present in baked blood.				
" 5	Left tonsil.	43	100	0	0	" " " "		0	0	
	Pharynx.	31	94	0	0	" " " "		4	6	
" 6	Left tonsil.	35	100	0	0	" " " "		0	0	
	Pharynx.	24	86	0	0	" " " "		4	14	
" 7*	Left tonsil.	52	94	0	0	3	6	0	0	Subject of experiment. Application on left tonsil. Cultures after experiment.
	Pharynx.	40	87	0	0	4	13	0	0	
" 8	Left tonsil.	57	65	13	15	7	8	11	12	Subjective sore throat. Pharynx shows injection with white exudate; tonsillar ring injected.
	Pharynx.	26	56	14	31	6	13	0	0	
" 9	Left tonsil.	35	76	6	13	1	2	4	8	Very slight soreness. Throat no longer injected.
	Pharynx.	34	79	9	21	Present in baked blood.		0	0	
" 11	Left tonsil.	34	94	1	3	1	3	0	0	Throat normal.
	Pharynx.	30	91	3	9	Present in baked blood.		0	0	

* Experiment 7.

TABLE II.

Subject 1. Bacteriology of Tonsil and Pharynx.

Date.	Place cultured.	*S. viridans.*		*S. hæmolyticus.*		*B. influenzæ.*		*S. albus.*		Remarks.
		No. of colonies counted.	Per cent of all colonies.	No. of colonies counted.	Per cent of all colonies.	No. of colonies counted.	Per cent of all colonies.	No. of colonies counted.	Per cent of all colonies.	
1919										
June 10	Left tonsil.	18	42	4	9	9	21	12	28	
	Pharynx.	13	52	0	0	12	48	0	0	
" 11*	Left tonsil.	28	68	3	8	8	20	2	4	Subject of experiment. Application on left tonsil. Cultures after experiment.
	Pharynx.	24	72	0	0	6	18	3	9	
" 12	Left tonsil.	31	55	3	5	5	9	17	31	No after effects.
	Pharynx.	18	54	0	0	12	36	4	9	
" 16†	Left tonsil.	26	53	0	0	6	12	18	35	Subject of experiment. Application on soft palate. Cultures taken before experiment.
	Pharynx.	32	60	0	0	9	17	12	23	
" 17	Left tonsil.	14	45	2	7	8	26	7	22	Subject complains of general malaise; slight headache; no sore throat. Film from swab shows mostly Gram-negative bacilli with a few cocci.
	Pharynx.									
	Red blood.	0	0	0	0		100	0	0	
	Baked blood.	0	0	0	0		100	0	0	
" 19	Left tonsil.	19	56	2	6	5	15	8	24	
	Pharynx.	21	60	0	0	14	40	0	0	
" 20	Left tonsil.	21	50	3	7	7	17	11	26	
	Pharynx.	19	58	0	0	11	33	3	9	

* Experiment 1.

† Experiment 8.

TABLE III.

Subject 5. Bacteriology of Tonsil and Pharynx.

Date.	Place cultured.	*S. viridans.*		*M. catarrhalis.*		*S. aureus.*		*S. albus.*		Remarks.
		No. of colonies counted.	Per cent of all colonies.	No. of colonies counted.	Per cent of all colonies.	No. of colonies counted.	Per cent of all colonies.	No. of colonies counted.	Per cent of all colonies.	
1919										
June 7	Left tonsil.	29	85	0	0	0	0	5	15	
	Pharynx.	21	91	0	0	0	0	2	9	
" 8*	Left tonsil.	49	90	0	0	0	0	5	10	Subject of experiment. Application on
	Pharynx.	27	75	0	0	2	6	7	19	left tonsil. Cultures after experiment.
" 9	Left tonsil.	21	60	3	9	0	0	11	31	No symptoms.
	Pharynx.	31	57	15	27	1	2	7	14	
" 10†	Left tonsil.	27	52	4	8	2	4	19	36	Subject of experiment. Application on
	Pharynx.	34	81	0	0	3	7	5	12	right tonsil. Cultures after experiment.
" 11	Left tonsil.	34	85	1	2	0	0	5	13	
	Pharynx.	39	93	0	0	0	0	3	7	
" 12	Right tonsil.	30	73	0	0	4	10	7	17	
	Pharynx.	34	87	2	5	1	3	2	5	
" 13‡	Right tonsil.	40	88	2	5	0	0	3	7	Subject of experiment. Application on
	Pharynx.	27	70	7	19	0	0	4	11	pharynx. Cultures after experiment.
" 14	Right tonsil.	21	58	12	34	0	0	3	8	
	Pharynx.	15	45	4	11	11	39	2	5	
" 15										No cultures. Subject has soreness on swallowing.

June 16§	Right tonsil.	21	52	11	27	0	0	8	20	Subject of experiment. Application on pharynx. Marked congestion of tonsillar ring and pharynx.
	Pharynx.	29	60	15	31	0	0	4	9	
" 17	Right tonsil.	34	72	3	7	8	17	2	4	Throat injection milder. No soreness on swallowing.
	Pharynx.	27	75	6	16	3	8	0	0	
" 18‖	Right tonsil.	25	59	2	5	15	36	0	0	Subject of experiment. Application on soft palate. Cultures after experiment.
	Pharynx.	31	77	4	10	5	13	0	0	
" 19	Right tonsil.	28	54	15	28	9	18	0	0	Soreness on swallowing. Injection of tonsillar ring.
	Pharynx.	32	64	11	22	7	14	0	0	
" 20										No cultures. Sore throat disappeared.
" 21	Right tonsil.	35	83	0	0	4	10	3	7	No soreness. No injection.
	Pharynx.	31	93	1	3	0	0	1	3	
" 23	Right tonsil.	31	81	2	5	1	2	4	11	" " " "
	Pharynx.	27	81	1	3	2	6	3	9	

* Experiment 9.
† Experiment 6.
‡ Experiment 10.
§ Experiment 11.
‖ Experiment 12.

From the pharynx and tonsil of Subject 6 before the experiment there were cultured *Streptococcus viridans*, Pneumococcus Type II atypical, and *Bacillus influenzæ*. He was then subject of Experiment 7. Within 24 hours he had a clinical sore throat; coincident with this, there was a sudden appearance of *Streptococcus hæmolyticus* in the cultures from both tonsil and pharynx. During the days following, with the disappearance of the sore throat, the number of colonies of *Streptococcus hæmolyticus* fell off rapidly. The remaining bacteria showed no evident change.

Experiment 7.—Subject 6, S. M. June 7, 1919, 3.45 to 6 p.m. Mucous membrane thermopile on left tonsil. Respirations 14 per minute. Mouth open; nostrils plugged. Room temperature 18.10–19.60°C. 0:00 to 0:31.5. Wrapped; normal breathing; swallowed many times. 0:31.5 to 0:44. Wrapped; deep breathing. 0:44 to 0:55.5. Unwrapped; fan on back; deep breathing. 0:52. Shivers. 0:55.5. Coughs, chokes, applicator removed; blood flecks seen about terminals. 4.57 p.m. Experiment started again. 0:00 to 0:06. Wrapped; deep breathing. 0:06 to 0:13.5. Unwrapped; fan on; deep breathing; shivering; swallows many times. 0:13.5 to 0:33.5. Wrapped; deep breathing. 0:33.5. Conditions the same; amyl nitrite inhaled. 0:35 to 0:44. Wrapped; deep breathing; some coughing and swallowing. 0:44 to 0:53. Hot water bag around subject; wrapped; deep breathing.

On the following morning the feeling of soreness had practically left the traumatized tonsil, but the posterior wall of the oropharynx felt sore. On inspection a localized area of injection bearing a whitish exudate was seen on the posterior wall of the oropharynx. In culturing, the contact of the swab on this area was a little painful, and the culture yielded streptococci, as explained above. The tonsillar ring was injected, but the feeling of soreness on the tonsil entirely passed off during the day and contact of the swab in culturing was hardly felt. Thus the traumatized tonsil showed less evidence of being the site of an active infection than the posterior pharyngeal wall, which was thought not to have been directly traumatized, but of course we cannot exclude the possibility that the oropharynx was infected by hemolytic streptococci from the tonsillar crypts—so commonly a habitat for them—which were missed in the earlier cultures and were disseminated by the experimental trauma and swallowing.

In Subject 1 there were present *Streptococcus viridans*, *Bacillus influenzæ*, *Streptococcus hæmolyticus*, and *Staphylococcus albus*. Following Experiment 1 there were no noteworthy changes. The plate inoculated from the pharynx about 26 hours after Experiment 8, however, showed a pure culture of *Bacillus influenzæ;* the tonsillar

plate showed also a slight relative increase. The film from the pharynx showed practically all Gram-negative bacilli with an occasional coccus. The subject had no sore throat, but complained of general malaise, slight headache, and some chilly sensations.[12] The pharynx culture made 96 hours after Experiment 8 was practically the same as before the experiment, *Streptococcus viridans* and *Staphylococcus albus* appearing as before.

Experiment 8.[13]—Subject 1, W. G. E. June 16, 1919, 3.20 to 4.07 p.m. Mucous membrane thermopile on anterior half of soft palate, left side. Respirations 16 per minute. Mouth open; nostrils plugged. Room temperature 20.22–20.90°C. 0:00 to 0:05.5. Wrapped; normal breathing. 0:05.5 to 0:11. Wrapped; deep breathing. 0:11 to 0:32. Unwrapped; fan on back; deep breathing. 0:32 to 0:47. Wrapped; deep breathing.

With the applicator resting against the anterior soft palate there is no reason for supposing trauma to the tonsils and pharynx. Organisms could hardly have been introduced from outside by the applicator, for this, with the thermopile terminals attached, was freshly coated with shellac in alcoholic solution before being adjusted for an experiment.

Subject 5 was the subject of five experiments, June 8, 10, 13, 16, and 18. On June 15 he noted a soreness on swallowing, and on June 16 the entire posterior pharynx and tonsillar ring were distinctly injected. The experiment of June 16 produced no sudden increase in symptoms; on June 17 the sore throat had practically disappeared. On June 19, 36 hours following an experiment, the subject again developed a soreness on swallowing, with congestion of the posterior pharynx and tonsillar ring. On June 20 the symptoms had subsided. On June 21 the wares no longer any injection or soreness.

This subject had present in his throat *Streptococcus viridans*, *Staphylococcus aureus*, and *Staphylococcus albus*. 24 hours following the first experiment there was noted for the first time the appearance of *Micrococcus catarrhalis*. Subsequently there appeared to be a certain degree of correlation between the appearances of sore throat and the rises in relative numbers of *Micrococcus catarrhalis* colonies. No other change in the bacterial flora was apparent.

[12] Compare the effect of infecting monkeys with *B. influenzæ* (Blake, F. G., and Cecil, R. L., *J. Am. Med. Assn.*, 1920, lxxiv, 170).

[13] For Experiment 1 see p. 93.

Experiment 9.—Subject 5, A. G. June 8, 1919, 3.38 to 5.06 p.m. Mucous membrane applicator on left tonsil. Respirations 10 per minute. Mouth open; nostrils plugged. Room temperature 18.1–19.45°C. 0:00 to 0:06. Wrapped; normal breathing. 0:06 to 0:15. Wrapped; deep breathing. 0:15 to 0:43. Unwrapped; fan on back; deep breathing; some swallowing, coughing, and clearing of throat; after 0:17, shivering. 0:43 to 1:20. Wrapped; deep respiration. 1:07. Inhales amyl nitrite. 1:20 to 1:28. Hot water pad to back; deep respiration.

The possibility that trauma to the tonsil was responsible for the appearance of *Micrococcus catarrhalis* after this experiment cannot be excluded.

Experiment 10.[14]—Subject 5, A. G. June 13, 1919, 3 to 3.46 p.m. Mucous membrane applicator on posterior wall of oropharynx. Respirations 16 per minute. Mouth open; nostrils plugged. Room temperature 18.45–19.05°C. 0:00 to 0:04.5. Wrapped; normal breathing. 0:04.5 to 0:15. Wrapped; deep breathing. 0:15 to 0:26. Unwrapped; fan on back; deep breathing; coughed; cleared throat; contraction of pharyngeal muscles; after 0:22, shivers. 0:26 to 0:46. Wrapped; deep breathing; coughed and cleared throat several times; pharynx appeared normal.

Experiment 11.—Subject 5, A. G. June 16, 1919, 10.30 to 11.30 a.m. Mucous membrane applicator on posterior pharyngeal wall. Respirations 14 per minute. Mouth open; nostrils plugged. Room temperature 18.90–19.80°C. 0:00 to 0:04.5. Wrapped; normal breathing; contractions of pharyngeal muscles. 0:04.5 to 0:23.5. Wrapped; deep breathing. 0:23.5 to 0:32. Unwrapped; fan on back; deep breathing. 0:32 to 1:00. Wrapped; deep breathing; contractions of pharyngeal muscles.

Experiment 12.—Subject 5, A. G. June 18, 1919, 10.20 to 11.12 a.m. Mucous membrane applicator on soft palate, middle part. Respirations 14 per minute. Mouth open; nostrils plugged. Room temperature 18.75–19.55°C. 0:00 to 0:05.5. Wrapped; normal breathing. 0:05.5 to 0:15.5. Wrapped; deep breathing. 0:15.5 to 0:27. Unwrapped; fan on back; deep breathing. 0:27 to 0:52. Wrapped; deep breathing.

In Subject 3 there were present in the throat *Streptococcus viridans*, Pneumococcus Type IV, and *Staphylococcus albus*. Cultures were made daily from June 4 to 19; he was the subject of an experiment on June 6, 9, 14, and 17. There was practically no change in the bacterial flora of this subject throughout the entire period studied. Neither did subjective or objective signs of sore throat or cold develop. Frequently the cultures from the pharynx were almost sterile, there being from three to ten colonies over the entire plate.

[14] For Experiment 6 see p. 99.

Discussion of Bacteriological Results.

Streptococcus viridans was found in all four of the individuals studied, *Bacillus influenzæ* in two, pneumococcus in two, and *Micrococcus catarrhalis* in one subject.

In Subject 6 the increased number of *Streptococcus hæmolyticus* was definitely synchronous with the presence of a sore throat. There appears to have been a correlation between the high *Micrococcus catarrhalis* counts and the presence of sore throats in Subject 5. The pure culture of *Bacillus influenzæ* in the pharynx of Subject 1 was not coincident with sore throat but with malaise, slight chilliness, and headache.

These results in no sense prove, however, that the sore throats were caused by the increased number of bacteria cultured from the mucous membranes, or that the apparent increase of microorganisms was caused by the ischemia of the mucous membranes incident upon chilling of the body surface. The method is subject to so many sources of error, and the amount of data thus far obtained is so small, that we do not feel justified in drawing any conclusions. To attribute the apparent proliferation of pathogenic microorganisms to the effect of chilling would seem to be in harmony with the great wealth of clinical and common observation which points to excessive chilling, under proper circumstances, as an efficient excitant of infection of the mucous membranes by their indigenous pathogenic bacteria. Although it is possible that the apparent proliferation was due to the local ischemia incident upon chilling, the inaccuracy of the bacteriological method and the insufficient data make it impossible to assume that this is so. The effect of trauma by the thermopiles, the possibility of transient changes in the flora of the mucous membranes caused by swallowing, gagging, or other muscular activity in the pharynx pressing a plug of bacteria from the tonsillar crypts, the fact that the subject's mouth was held open throughout the experiments, with the accompanying accumulation of mucus on the membranes, the errors necessarily introduced in each stage of making the cultures, and the inaccuracy of any method depending upon swab cultures, all tend to confuse the results. We present the data given above as a contribution to the etiology of upper respiratory infections, and not with the idea that the study is in any sense complete in itself.

TABLE IV.

Observations on Concentration and Reaction of Urine.

Experiment No.	Increase in respiration.	Deep respiration.	Deep respiration; chilled.	Deep respiration.	Reaction to litmus.		Color.		Clarity.		Decrease in acidity in amount of 0.1 N NaOH neutralized by 10 cc. of urine.
					Before experiment.	After experiment.	Before experiment.	After experiment.	Before experiment.	After experiment.	
	per cent	*min.*	*min.*	*min.*							*cc.*
9*	77.9	9	28	45					Clear.	Cloud of phosphates.	
4*	88.9	18.5	17.5	6		Neutral.	Dark yellow.	Light yellow.			
13*		17.5	19.5	21	Acid.	Acid.	Yellow.	Very slightly lighter.			
6	75.4	12	13.5	15	"	Alkaline.	"	Light yellow.	Clear.	Phosphates.	4.25 (titrated next day).
1	42.7	6	5.5	42.5	"	"	"	" "	"		1.76
14	45.4	11.75	22	17	"	Neutral to alkaline.	"	Slightly lighter yellow.	"	Cloudy.	1.24
15											
10	69.2	10.5	11	20	"	Alkaline.					2.54
16	54	7.5	22	20	"	"					2.16
11	30.1	19	8.5	28	"	"					4.90
8	30.1	5	21	15.5	"	Acid.					0.00
17	44.6	6	16	19.5	"	"					2.28
12	52.3	10	11.5	28	Neutral.	Alkaline.					0.95
Average.	49.3	9.75	14.56	22.83							2.23

* Not included in average.

Observations on Urine.

It was thought that the chilling in the experiments might produce sufficient renal congestion to give albuminuria. This, however, was not the case. In fourteen experiments in which urine specimens were taken before and after the experiment the results were in all instances negative. The room temperature in these experiments varied from 16.9–20.9°C.; the time of exposure, unwrapped, to the draft of the electric fan was from 5.5 to 28 minutes, the average 16.75 minutes. Severe shivering was often produced. In twelve of the experiments urinalysis for sugar was done, also with negative results in all.

In all of five experiments in which the color was noted it was lighter after than before the experiment, denoting the secretion of a more dilute urine during the experiment.

The most interesting change in the urine produced by the experimental conditions was a decrease in its acidity. Specimens were titrated with phenolphthalein against 0.1 N sodium hydroxide in nine experiments; in eight a decrease in acidity after the experiment was noted, amounting to the equivalent of from 0.95 to 4.90 cc. of 0.1 N sodium hydroxide per 10 cc. of urine; the average decrease was 2.23 cc. This lowered titer was doubtless due in part to dilution of the urine, but in part also represented a true fall in hydrogen ion concentration, as is shown by the fact that a change in the urinary reaction demonstrable with litmus paper was noted in seven out of ten experiments. The mechanism of the experimental alteration in the reaction of the urine has been further analyzed by Grant and Goldman;[15] the decreased acidity has been found to be referable to the forced respiration rather than to the chilling.

The results of the observations on concentration and reaction of urine are given in Table IV.

SUMMARY.

Improvements are described in the method of following temperature changes, and thus alterations in vasomotor tone, in exposed mucous membranes. Invention of an applicator holder, by means of which

[15] Unpublished investigation.

more sure and stable apposition of the thermopile terminals to the mucous surface may be effected has been the chief advance. Minor improvements have been the use of a saliva ejector and of better calibration technique.

The palatine tonsils, like the palate, pharynx, and skin, react to chilling of the body surface with reflex vasoconstriction and ischemia. On rewarming the subject the tonsils quickly more than recover their former blood supply, actually becoming hyperemic; the skin returns to about its control condition; the pharynx and palate remain somewhat ischemic.

The hypothesis is advanced that one factor in the beneficial hardening effect of cold bathing and outdoor living, with its incident heightened immunity to respiratory infection, may be the training of the vasomotor system in the direction of development in the pharynx of a reaction of hyperemia following chilling, similar to that observed in the tonsils of the present subjects.

With inhalation of amyl nitrite, the skin temperature has always shown a sharp transient rise. The mucous membrane, if relatively ischemic, responds by a rise corresponding to the skin flush. If already hyperemic, local vasodilation in the mucous membrane with amyl nitrite is more than counterbalanced by the lowering of the general blood pressure, and the temperature falls.

The flora of the pharynx and tonsils, studied by the unsatisfactory method described, showed, in several instances, after experimentation changes apparently due to proliferation of one of the microorganisms already present. In one case *Streptococcus hæmolyticus*, in one *Micrococcus catarrhalis*, and in a third *Bacillus influenzæ* was the organism showing a relative increase in numbers. The first two instances were associated with sore throat, the third with slight constitutional symptoms.

The chilling in the experiments in no instance produced albuminuria or glycosuria, although a more dilute urine was apparently excreted during the experiments. A fall in hydrogen ion concentration, referable to the forced respiration, was noted.

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