

recollect any detail of the dream. Of 23 interrogations during ocular inactivity, 19 disclosed complete failure of recall, while the remaining 4 were evenly divided into the other 2 categories. Recognizing the inadequacies of employing a χ^2 test for the independence of the 2 groups of interrogations, the probability nevertheless on a χ^2 basis is that the ability to recall dreams is significantly associated with the presence of the eye movements noted, with a p value of less than 0.01.

Eleven subjects in one series of 16 experiments were permitted to sleep uninterrupted throughout the night. The mean duration of sleep was 7 hr. The first appearance of a pattern of rapid, jerky eye movements was from 1 hr 40 min to 4 hr 50 min (3 hr 14 min, mean) after going to bed. This pattern of eye motility was of variable duration and frequently disappeared for a fraction of a minute or for several minutes only to reappear and disappear a number of times. The period from the onset of the first recognizable pattern to the disappearance of the last pattern was from 6 to 53 min with a mean of 20 min. A second period of eye movement patterns appeared from 1 hr 10 min to 3 hr 50 min (2 hr 16 min, mean) after the onset of the first eye motility period. With lengthier sleep there occurred a third and, rarely, a fourth such period. The electrooculogram disclosed vivid potentials with amplitudes as high as 300–400 μ v, each potential lasting about 1 sec. This was further striking in comparison with simultaneously recorded monopolar EEG's, from the frontal and occipital areas, which were invariably of low amplitude (5–30 μ v) and irregular frequency (15–20/sec and 5–8/sec predominating).

In another series of experiments involving 14 subjects, the respiratory rate was calculated for a minimum of $\frac{1}{2}$ min during eye motility and compared with the rate for a similar duration 15 min before and after an eye motility period. The respiratory rate had a mean of 16.9/min during eye motility in contrast with 13.4/min during ocular quiescence. By using Fisher's t method, the difference in rates was found to be statistically significant with a probability of less than 0.001. Experiments now in progress suggest that heart rate also is probably higher in the presence of these eye movements. Body motility records were secured in 6 experiments by attaching a sensitive crystal to the bed spring and leading the output through a resistance to a Grass preamplifier. In every case the eye motility periods were associated with peaks of overt bodily activity although the latter were frequently present in the absence of eye movements.

Data obtained from the 2 female subjects used in these experiments were at least qualitatively similar to that obtained from males.

The fact that these eye movements, EEG pattern, and autonomic nervous system activity are significantly related and do not occur randomly suggests that these physiological phenomena, and probably dreaming, are very likely all manifestations of a particular level of cortical activity which is encountered normally during sleep. An eye movement

period first appears about 3 hr after going to sleep, recurs 2 hr later, and then emerges at somewhat closer intervals a third or fourth time shortly prior to awakening. This method furnishes the means of determining the incidence and duration of periods of dreaming.

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Manuscript received April 3, 1953.

Inactivating Medium for Hexachlorophene (G-11) Types of Compounds and Some Substituted Phenolic Disinfectants

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A previous report presented evidence of the use of synthetic, nonionic wetting agents for the inactivation of the bacteriostatic activity of hexachlorophene (G-11) upon bacteria (1). With the evidence obtained of the marked interfering action of Tween-80² on the bacteriostatic effects of hexachlorophene, it appeared desirable to extend these studies to several other chemical disinfectants, two of which are closely related in chemical constitution to hexachlorophene, G-4 (2,2'-dihydroxy-5,5'-dichlorodiphenylmethane) and Actamer (2,2'-dihydroxy-3,5,3',5'-tetrachlorodiphenyl sulfide). In addition to the latter, several substituted phenolics and related compounds were evaluated in the presence and absence of the nonionic surface-active agent. The compounds studied and their chemical designations are given in Table 1.

Due to the relative insolubilities of several of the compounds in distilled water (Nos. 1–8) these were first dissolved in 1 ml of 10% sodium hydroxide and then diluted to 1.0% with distilled water. The remaining disinfectants were dissolved directly in distilled water or in beef extract broth (0.3% Bacto beef extract, 1% Bacto peptone, 0.5% sodium chloride in water). In all instances 9 ml of sterile broth, with or without 1% Tween-80, were added aseptically to the first of a series of sterile test tubes and 5-ml amounts in the remaining, or 9 additional tubes. To the first tube was added 1 ml of the stock germicide to be tested. After thoroughly mixing the latter in the medium, 5 ml was transferred to the second tube containing 5 ml of broth. This process of mixing and transferring was then continued through the remain-

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² Atlas Powder Company, Delaware, brand of polyoxyalkylene derivative of sorbitan monooleate.

TABLE 1
TRADE NAMES AND CHEMICAL CONSTITUTION OF DISINFECTANTS

| Trade name | Chemical constitution | Manufacturer |
|---------------------|---|--|
| 1. G-11 | 2,2'-Dihydroxy-3,5,6,3',5',6'-hexachlorodiphenylmethane | Sindar Corporation, New York. |
| 2. G-4 | 2,2'-Dihydroxy-5,5'-dichlorodiphenylmethane | Sindar Corporation, New York. |
| 3. Actamer | 2,2'-Dihydroxy-3,5,3',5'-tetrachlorodiphenylmethane | Monsanto Chemical Co., St. Louis, Mo. |
| 4. Santophen-1 | Orthobenzyl-para-chlorophenol | Monsanto Chemical Co., St. Louis, Mo. |
| 5. Dovicide-4 | 2-Chloro-4-phenylphenol (85%) | Dow Chemical Co., Midland, Mich. |
| 6. Dovicide-A | Sodium orthophenylphenate | Dow Chemical Co., Midland, Mich. |
| 7. Dovicide-2 | 2,4,5-Trichlorophenol | Dow Chemical Co., Midland, Mich. |
| 8. Dovicide-32 | Mixture of 4-chloro-2-phenylphenol and 6-chloro-2-phenylphenol | Dow Chemical Co., Midland, Mich. |
| 9. Lysol | Orthohydroxydiphenyl with soap, alcohol, cresylic acid, propylene glycol, glycerol, and water | Lehn and Fink, Corp., Bloomfield, N.J. |
| 10. Osyl | Potassium ricinoleate, orthohydroxydiphenyl, alcohol, propylene glycol, glycerol, and water | Lehn and Fink, Corp., Bloomfield, N.J. |
| 11. Amphyl | Potassium ricinoleate, orthophenylphenol, para-tertiary-amyl phenol, alcohol, propylene glycol, glycerol, and water | Lehn and Fink, Corp., Bloomfield, N.J. |
| 12. Phenol | Hydroxybenzene— | — |
| 13. Metaphen | 4-Nitroanhydrohydroxymercury orthoeresol | Abbott Laboratories, North Chicago, Ill. |
| 14. Merceresin | Orthohydroxyphenylmercuric chloride, secondary amyltrieresols, alcohol, and acetone | Upjohn Company, Kalamazoo, Mich. |
| 15. Hexylresorcinol | Hexylresorcinol (0.1%) in a glycerol-water solution. | Sharp and Dohme, Co. |

ing tubes; finally, 5 ml of the test solution was discarded from the last tube.

The germicide-broth dilutions were inoculated with a 4-mm loopful of a 24-hr-broth culture of *Micrococcus pyogenes* var. *aureus* and incubated for a week, during which time the presence or absence of visible growth was recorded. In those instances where a turbid solution resulted upon adding the germicides to broth or a similar condition resulted upon combining the germicides with the Tween-80 broth, these mixtures were tested for the presence of viable bacteria at the end of 48-hr incubation by transferring a 4-mm loopful of the suspension to tubes containing sterile broth and broth with 1% Tween-80. The latter tubes were also incubated at 37° C for several days. The results of this study are presented in Table 2.

From the data given in the table it may be noted that with the exceptions of Merceresin and phenol, the remaining germicides are markedly affected by Tween-80 in so far as their bacteriostatic activities are concerned. The exceptionally high bacteriostatic actions of the hexachlorophene types of compounds (G-11, G-4, Actamer) is evident from these results in which approximately 1 part of these compounds in 2,000,000–5,000,000 parts of plain broth inhibited the growth of *M. pyogenes*, var. *aureus*. However, when the same test was carried out in the presence of Tween-80 in broth, concentrations greater than 1:1000 of the G compounds and a 1:2000 concentration of Actamer are required to inhibit the growth of the same organism. A distinct interfering action was also obtained with the nonionic agent against Santophen-1 and Dovicide-A. The remaining Dovicides, Metaphen, hexylresorcinol, and the cresylic acid types of disinfectants showed somewhat less, but a fairly proportionate loss in activity when tested in the presence of Tween-80.

Preliminary studies reveal that Tween-80 will interfere with the antibacterial activity of certain quaternary ammonium surface-active germicides and the antibiotic tyrothricin. No inhibition was noted in the use of the nonionic agent against the activities of penicillin, streptomycin, aureomycin, neomycin, chloromycetin, bacitracin, and terramycin against *M. pyogenes*, var. *aureus*. While this report primarily proposes the use of nonionic surface-active compounds for distinguishing between the bactericidal and bacteriostatic activities of certain antimicrobial agents,

TABLE 2
INHIBITING EFFECTS OF TWEEN-80 ON SOME
SUBSTITUTED PHENOLICS

| Disinfectant | Limiting dilution inhibiting in plain broth | Limiting dilution inhibiting in 1% Tween-80 in broth |
|------------------------------------|---|--|
| 1. G-11 | 1 : 2,048,000 | < 1 : 1,000* |
| 2. G-4 | 1 : 5,096,000 | < 1 : 1,000 |
| 3. Actamer | 1 : 2,048,000 | 1 : 2,000 |
| 4. Santophen-1 | 1 : 128,000 | < 1 : 1,000 |
| 5. Dovicide-4 | 1 : 32,000 | 1 : 2,000 |
| 6. Dovicide-A | 1 : 4,000 | < 1 : 1,000 |
| 7. Dovicide-2 | 1 : 64,000 | 1 : 4,000 |
| 8. Dovicide-32 | 1 : 64,000 | 1 : 2,000 |
| 9. Lysol | 1 : 3,200 | 1 : 200 |
| 10. Osyl | 1 : 2,560 | 1 : 160 |
| 11. Amphyl | 1 : 5,120 | 1 : 320 |
| 12. Phenol | 1 : 400 | 1 : 200 |
| 13. Metaphen (1 : 500 aq.) | 1 : 2,560 | 1 : 640 |
| 14. Merceresin (1 : 250 tinc.) | 1 : 5,120 | 1 : 2,560 |
| 15. Hexylresorcinol (1 : 1,000) | 1 : 20 | < 1 : 5 |

* Figures preceded by symbol < indicate highest concentration of disinfectant tested failed to inhibit growth of organisms.

it also poses the question concerning the indiscriminate use of the nonionics as solubilizing, wetting, or detergent agents in various germicide and drug formulations without preliminary biological compatibility data.

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Manuscript received April 22, 1953.

A Rapid Titrimetric Method for Determining the Water Content of Human Blood¹

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The use of the Karl Fischer reagent to determine blood and tissue water *in vivo* and *in vitro* in rats has been reported by Cook, Cramer, and Kenyon (1). Such a method, if applied to human beings, may have physiological, diagnostic, and therapeutic applications, since a determination can be made in a matter of 10 min. The most convenient tissue to use is the blood, which is relatively sensitive to changes in body water.

References to the literature have given rather diverse and incomplete figures for human plasma water and whole blood water. The accompanying chart shows this diversity.

TABLE 1

| Reference | Total H ₂ O whole blood % | Plasma water % | Cellular water % |
|-------------------------|--------------------------------------|----------------|------------------|
| U.S.A.F. (2) | 83 (81-86) | 94 (93-95) | 72 (70-75) |
| Cushny (3) | | 90-93 | |
| Best & Taylor (4) | | 92 | |
| (Modified after Cushny) | | | |
| Everett (5) | | 92 | 65 |
| Davis, Kenyon, Kirk | 80.5 (79-82) | 92.4 (91-93) | 66 (63-70) |

To obtain values of blood water in normal humans by the Karl Fischer method, we obtained an unselected group of blood donors at the Los Angeles County Hospital. Our procedure is as follows. A small amount of venous blood is drawn into a medicine dropper. Capillary blood from a finger puncture can also be used (1). The medicine dropper is weighed and one drop of blood (more would obscure the end point) is discharged into a flask containing 20 ml of anhydrous methanol previously brought to an orange-red end point with Fischer reagent. The medicine dropper is again weighed and the flask is brought to the same orange-red end point by titrating a meas-

¹ Support for this study from Harold V. Kirk and Edward Pollard is gratefully acknowledged.

TABLE 2

| Substance | Percentage water found by | |
|-------------|---------------------------|--------------------------------------|
| | Oven drying | Titration (Av. of duplicate samples) |
| Whole blood | 80.2 | 80.2 |
| | 80.5 | 80.0 |
| | 80.2 | 79.9 |
| Plasma | 92.3 | 91.5 |
| | 92.6 | 91.6 |
| | 92.0 | 91.6 |
| | 90.8 | 90.4 |
| | 91.3 | 90.5 |

ured volume of Fischer reagent. The Fischer reagent is dispensed from an anhydrously maintained all-glass buret assembly.

By using a special double necked flask containing a twin platinum electrode and attached to an aquameter, an electrometric end point can also be used. Up to 8 drops of blood can be used in this instance, hence greater accuracy can be obtained. However, we found that both methods gave the same values on the same blood. All of the work reported in this paper was done using the electrometric end point method.

Mitchell and Smith (6) have written the only book on the subject at the present time, but we found the methods and formulae for the Fischer reagent used by Shell Development Company, Emeryville, California, to be superior in producing a more stable end point. We strongly advise against using the commercially available material as the end point is extremely unstable.

Hematocrit values by the Wintrobe method and specific gravity values by the copper sulfate method were routinely done on the same samples.

In all, 100 whole blood samples were used including 23 females and 77 males. The female extremes were 78 and 84%. The average was 80.8% and the bulk of the samples fell in the range 80-82%. The male extremes were 74 and 84%. The average was 80.4% and the bulk of the samples fell in the range 79-82%. The combined average was 80.5%.

We found a nonsignificant correlation of -0.17 between the percentage whole blood water and the hematocrit. We found a significant correlation of -0.49 between the specific gravity and the percentage whole blood water. There was no correlation between age and percentage whole blood water.

A smaller group of 15 additional samples was obtained in the same manner. The whole blood water was obtained and the samples were then centrifuged. The plasma water content was obtained and the cellular water content calculated. Extremes of whole blood were 76-84% with an average of 80.5%, the bulk falling between 79 and 83%. Plasma water extremes were 90 and 94%. The average was 92.5%, the bulk falling between 91 and 93%. The cellular water extremes were 56 and 74%, the average was 66% and