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Schick Reaction and Menstrual Cycle.

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The possibilities of changes in resistance to infection at the time of menstruation have been widely discussed but there are few direct observations on the subject. Only in the case of the common cold,[1] herpes febrilis[2] and hemolytic streptococcus infections[3] has it been shown, with any degree of certainty, that resistance may be lowered at this time. A number of attempts have been made to measure periodic fluctuations in the anti-infectious agencies of blood and tissues. Thus, Geller[4] has demonstrated that the bactericidal titer of blood is depressed premenstrually, and Fisher[5] reports a lowering in the disinfecting power of the skin at menstruation. In studying the virucidal properties of the blood at different times of the cycle, Jungeblut and Engle[6] found that, although the ability to neutralize poliomyelitis virus changed, there was no uniform correlation with any given phase of the cycle. Ross[7] reports the titer of natural protective substances against type II pneumococci as being higher during the first days of the menstrual cycle than during the latter part; and Dressel and Keller[8] found that serum from menstruating women was bactericidal for the anthrax bacillus while serum from women who were not menstruating exhibited no such power. It is clear from the references quoted above that the effect of the menses on resistance to different diseases is not uniform and that each disease must be studied individually.

The physiological changes in capillary function that occur at the beginning of the menses are far from being understood; but Brewer[9] has recently contributed data to suggest that capillary fragility may be greatly increased during the first 2 days of the menstrual period.

1 Maciejewski, K., Thesis, Berlin, 1930.

2 Lauda, E., and Luger, A., *Ergeb. inn. Med.*, 1926, **30**, 377.

3 Geller, F., and Sommer, W., *Arch. Gynœkol.*, 1927, **131**, 293.

4 Geller, R., *Muench. Med. Woch.*, 1925, **72**, 1686.

5 Fisher, V., PROC. SOC. EXP. BIOL. AND MED., 1931, **28**, 952.

6 Jungeblut, C. W., and Engle, E. T., *J. Immunol.*, 1933, **24**, 267.

7 Ross, V., and Peizer, L. R., PROC. SOC. EXP. BIOL. AND MED., 1936, **35**, 432.

8 Dressel, E., and Keller, W., *Z. Hyg.*, 1922, **97**, 51.

9 Brewer, J. I., *Am. J. Obst. and Gynekol.*, 1938, **30**, 597.

Before, Benda[10] had already noted that cell permeability is increased during the time of the flow. In view of the fact that one of the outstanding properties of diphtheria toxin is its ability to produce capillary damage,[11] it seemed of interest to investigate whether the Schick reaction could be used as an indicator for any possible changes in capillary resistance at different phases of the cycle.

Fluctuations in Schick-reactivity have previously been observed in connection with seasonal studies.[12] However, when Schick tests are repeated in the same individual over short periods of time—and specific exposure can be ruled out—a remarkable tendency for stability of the reaction becomes evident.[13] The only exception to this rule, apparently, is the influence that fatigue[14] and ultraviolet irradiation[15] may exert in changing negative reactions temporarily to positive ones or making positive reactions more strongly positive.

Thirteen female medical students, aged from 20 to 25 years, were given repeated Schick tests. This number included 9 who were previously known to be positive reactors, and 4 who were Schick negative. These individuals were divided into 2 groups: The first group of 6 was given the initial Schick test at the beginning of the menses and the second test during the interval; in the other group of 7, the procedure was reversed. This arrangement was made so as to eliminate any possible error that might be introduced through partial immunization resulting from the initial antigenic stimulus. No evidence was found, however, that any such immunity developed since many of the second reactions were stronger than the first.

For the purpose of additional control, a group of 6 male students were Schick tested twice, at 14-day intervals. This was done in order to determine the uniformity of the test in repeated injections in the same individual, in the absence of any cyclic changes.

All injections were done intradermally on the flexor surface of the forearm, alternating arms being used for successive tests. One lot of toxin (N. Y. City Board of Health) was used throughout and all reactions were controlled by tests with heated toxin. Read-

10 Benda, R., *Muench. Med. Woch.*, 1925, **72**, 1686.

11 Gautrelet, J., and Gautrelet, M., *Presse méd.*, 1935, **43**, 961.

12 St. Tubiaz, M., *Office internat. d'hyg. publ.*, 1932, **24**, 2000; Nelis, P., *C. R. Soc. Biol.*, 1934, **115**, 1178.

13 Pintozzi, V., *C. Bakt. Ref.*, 1933-34, **112**, 59.

14 Zlatogoroff, S. I., and Kostereff, S. A., *C. R. Soc. Biol.*, 1931, **106**, 96; Feullie, P., Thiry, P., and Blancardi, C., *C. R. Soc. Biol.*, 1934, **115**, 367.

15 Bratusch-Marrain, A., and Asperger, H., *Med. Klin.*, 1932, **28**, 1310.

ings were taken at 24, 48 and 72 hours and the size of the area of inflammation was recorded as well as the degree of redness and edema. The last reading was used for final evaluation.

No significant changes were found in the male group. In the female group, however, the majority of the individuals showed considerable variation in intensity of the reaction. These changes involved the area and the degree of redness as well as the extent of edema; if one or more of these criteria was more pronounced whereas the others remained stable, the whole reaction was listed as more severe in our records. On the basis of such an interpretation it was found that of 9 Schick-positive individuals, 6 exhibited a severer reaction at the beginning of the menstrual period than during the interval while one reacted less strongly and 2 showed no change whatsoever. Among the 4 Schick-negative reactors, 3 remained negative on repeated injections; however, one individual who had given a completely negative reaction during the interval showed a distinct but mildly positive reaction at the beginning of the menses. Two individuals in the Schick-negative group gave pseudoractions to the heated toxin. In one instance this pseudoraction remained unchanged; in the other, a definite increase in severity was noted at the time she was menstruating.

The above data are of interest in demonstrating that susceptibility to a capillary poison, like diphtheria toxin, may be increased during the onset of menstruation.

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Sulfanilamide in Experimental Tuberculosis.*

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Rich and Follis[1] reported an inhibitory effect of sulfanilamide on experimental tuberculosis in guinea pigs. Doses of 200 and 500 mg were given daily, beginning 3 days before the animals were infected subcutaneously with human tubercle bacilli, and treatment

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1 Rich, A. R., and Follis, R. H., Jr., *Bull. Johns Hopkins Hosp.*, 1938, **77**, 621.