

- Process. Academic Press, New York, 1965, p. 245.
8. Mulholland, J. H., Ed.: Postoperative Wound Infection: The Influence of Ultraviolet Irradiation of the Operating Room and of Various other Factors. Report of an Ad Hoc Committee of the Committee on Trauma, Division of Medical Sciences, National Acad. of Sciences, National Research Council. Ann. Surg., 160:1 (Supp), 1964.
 9. Sbarra, A. J., Shirley, W., Selvaraj, R. J., Ouchi, E. and Rosenbaum, E.: The Role of the Phagocyte in Host-Parasite Interactions. I. The Phagocytic Capabilities of Leukocytes from Lymphoproliferative Disorders. Cancer Res., 24:1958, 1964.
 10. Sbarra, A. J., Shirley, W., Selvaraj, R. J., McRipley, R. J. and Rosenbaum, E.: The Role of the Phagocyte in Host-Parasite Interactions. 3. The Phagocytic Capabilities of Leukocytes from Myeloproliferative and other Neoplastic Disorders. Cancer Res., 25:1199, 1965.
 11. Starzl, T. E., Lerner, R. A., Dixon, F. J., Groth, C. G., Brettschneider, L. and Terasaki, P. I.: Shwartzman Reaction After Human Renal Transplantation. New Eng. J. Med., 287:642, 1968.

DISCUSSION

DR. HENRY H. BALCH (Washington): I have not seen the manuscript and am not able to comment on the technic used but I have been involved in this type of work in the past and would like to make a few observations.

It is tempting to feel that there are basic defects in host defense against infection in a variety of surgical states, traumatic or otherwise.

I have studied neutrophil function and antibody synthesis in a wide selection of surgical disease and have had difficulty in finding significant defects in host defense. My observations have shown that severely traumatized and very ill patients can synthesize large quantities of antibody globulin on stimulus. Furthermore, neutrophils from such patients can phagocytose and destroy pathogenic micro-organisms as well as neutrophils from normal subjects and in acutely burned patients better than those from normal subjects.

Technic of studying blood bactericidal capacity have to be carefully controlled to be able to compare one study with another. Ratios of white cells to bacteria and the bacterial species used significantly influence the end result. The coagulase positive staphylococcus is particularly hard to work with because of the difficulty in obtaining a satisfactory control baseline for comparison. With this micro-organism there is a wide variety in bactericidal effect in studying leucocytes from different normal subjects and in consecutive studies of leucocytes from individual normal subjects. The coagulase negative staphylococcus is easier to work with but even here the ratio of leucocytes to bacteria in the test system must be about 10 to 1 to ensure a 95% kill. If this ratio is adjusted in favor of the bacteria then the percentage destruction of bacteria is much less.

My studies showing a marked increased bactericidal effect of leucocytes-plasma suspensions from severely burned patients during the early

days following burn injury were all done in triplicate and I am sure that the observations were accurate. They reflect therefore in an *in vitro* system the functional capacity of leucocytes from burned patients suspended in their own plasma. In the paper presented this afternoon leucocytes were removed from the blood of burned patients and resuspended in heterologous immune serum—also an *in vitro* study but an artificial system. Findings from such a study may or may not reflect the functional capacity of leucocytes suspended in their natural environment.

Another significant finding of mine in acutely burned patients is that the mobilization of white blood cells to peripheral tissues is markedly depressed following burn injury for a number of days. Such cells as do appear in response to repeated minor injury during this 7- to 10-day period are mostly juvenile neutrophils but they are actively phagocytic and as stated, have an increased capacity to kill test bacteria. However, there is a marked delay in the appearance of lymphocytes during this period. This impaired cellular response following burn injury is probably very important in permitting invasive bacterial infection as the bacterial growth in the burn wound increases, changing the ratio of leucocytes to bacteria in favor of the latter. If pathogenic bacteria such as coagulase positive staphylococci are present in the burn wound, then invasive infection is probably easier because these micro-organisms have a well known capacity for producing serious infection in apparently normal subjects in the right circumstances. This is even more likely in the burned patient as the early increased post-burn blood bactericidal capacity is returning to normal levels after the first week.

DR. HARRIS B. SHUMACKER, JR. (Indianapolis): I never thought I would relate the story which I am about to tell, but since it is fairly close to the cocktail hour and since we have just

heard a very fundamental paper dealing with leukocyte function, it does seem appropriate. I am especially impressed by the contrast between the sophistication of the present investigation and the naivete of the one that I shall describe.

When I went to the Johns Hopkins Medical School in 1928, the spirit of Sabin, Cunningham and Doan still pervaded the institution and similar work was being carried on in a very invigorating way by Dr. George Wislocki with whom I know many Bostonians subsequently became well acquainted. We were all interested in supra-vital technics of observing blood cells. During my first year in medical school, I and others became interested in such observations and one of my very nicest classmates, Dr. Lydia Edwards, and I worked together on a number of projects for a number of years. She continued to be interested in the motility of leukocytes and she was following her own blood with reference to possible influences of the menstrual cycle.

She called me up one day from the clinical laboratory and said, "Harry, please come up quickly. I've seen the most extraordinary things happen to my neutrophils!" She had been to a cocktail party but was quite sober, I thought. At any rate her neutrophils were absolutely without mobility! I looked at them and confirmed what she had observed. It was a very unusual observation and we decided we would set up a little pertinent experiment.

This was during the time of Prohibition, you will remember. Though we thought about using animals, we weren't quite sure how this would work out and it seemed simpler anyway to use humans. Furthermore, one could buy Maryland "Red Eye" whiskey for \$3 a gallon! We agreed we would meet the next Sunday and flip a coin to see who would drink a tall glass full of whiskey and the other one of us would then do repeated studies of cell motility. We flipped the coin and I lost. I had to drink the glass of whiskey and when I woke up—she told me that my neutrophils had behaved precisely as hers did and that instead of having normal mobility they had just sat still during this whole period apparently, anesthetized completely!

It was obvious that one person couldn't make so many observations and that we needed more help. We let it be known that we would furnish the whiskey if we could get any of our fellow

students to volunteer. I am not sure that his participation constitutes the reason he subsequently became a professor of psychiatry. We brought the proper apparatus up to my apartment so we could make observations relatively undisturbed over a long period of time. Our volunteer said that if I could drink one glass he could drink two and he did. His cells did not move at all over a period of many hours and we were really quite excited about this. The experiment ended when I found him wandering around the Pennsylvania Station the next day apparently not knowing where he was or where he had been, and we decided to stop the investigation for the time being.

It was several years later that another member of this Association, Dr. Kenneth Pickrell, before he became interested in plastic surgery, carried out some animal experiments with a somewhat different orientation. They, in a very simple way, demonstrated that the leukocyte response to infection was quite abnormal in inebriated animals.

It makes one wonder whether one might go back to this very simple supra-vital technic of observing the motility of leukocytes and see whether there is any correlation between them and these very impressive observations which have been reported today.

DR. J. W. ALEXANDER (Closing): I would like to emphasize that the functional capability of neutrophils is but one aspect of resistance of a host against bacterial infection, albeit an important one. We did indeed find several contrasting results from those reported by Dr. Balch, and I think, as he stated, this probably represents a variation in methodology. It took about a year of almost full-time work to look at the variables in this test and to be reasonably confident that we had a technic with which we could measure the important aspects of neutrophil function.

One of the important differences in contrast to Dr. Balch's study was that we used a pool of human serum as a source of opsonins instead of autologous plasma. In addition, even very small concentrations of antibiotics in the extracellular medium, such as may be present in patient serum, can strikingly influence the ingestion and intracellular killing of bacteria even when the antibiotics are in sub-inhibitory concentrations.