per and iron to an adequate diet when the supplements were given for a period of 10 days prior to splenectomy and continued after splenectomy. Seventy-five percent of 12 adult rats fed copper and 75% of 8 adult rats fed copper and iron were protected. The period of observation is one month following the operation. Copper was definitely more effective than iron, and copper plus iron slightly more effective than copper alone. Fifty percent of 10 rats fed iron were protected. The adult rats were protected in twice as many instances as were the immature rats. This is due to the fact that the severity of the infection with *Bartonella muris* (without anemia) is much greater in the immature rat with intact spleen than in the adult rat in which the infection is entirely latent. Copper protects 75% of the rats against this anemia if it is added as a supplement to an adequate diet for a period of 10 days prior to splenectomy.

These experiments suggest that the utilization of copper and of iron in the body is intimately concerned with the function of the spleen. Copper is involved in some way in the mechanism of resistance in the body as well as in the production of hemoglobin. We have been able to demonstrate an active substance in the spleen[12] which when injected into albino rats from the day of splenectomy protects in a large percentage of instances against *Bartonella muris* anemia. This extract contains neither copper nor iron. The relation of copper to the spleen may be somewhat analogous to the relation of calcium to the parathyroid gland. The small amount of copper in the adequate diet is insufficient for the needs of the rat in the absence of the splenic hormone. An excess of the metallic element may compensate for a deficiency of the hormone. Further, the copper as administered cannot be utilized at once but must be converted into a form that is more readily utilizable by the body in the mechanism of resistance to *Bartonella muris* anemia.

6182

Fever in Certain Cases of Heart Failure.

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The great frequency with which fever occurs during the course of heart disease is well known and has been frequently commented

[12] Perla, D., and Marmorston-Gottesman, J., in press.

upon. Its presence has generally been attributed to infection or infarction, usually of the lungs even when no sound proof of their existence was obtainable. In several patients elevations of temperature were so intimately and characteristically associated with the appearance and increase of the signs of heart failure and the return of the temperature to normal so promptly attendant upon the disappearance of these signs, that the processes themselves of heart failure were regarded as responsible for the presence of fever. These phenomena obviously warranted analysis further than the attempt to discover their relation to infection and infarction. The temperatures of patients suffering from heart failure, both during and after recovery, were accordingly studied. The temperatures of the surface (skin) and of the interior (rectum) of the body were recorded simultaneously. Such observations afford a rough estimate of the thermal gradient of the body.

The temperature of the skin being dependent upon environmental as well as upon internal conditions, it was necessary to keep the conditions of the room constant in order to detect changes of temperature in the body. The temperature of the room was maintained constant (21.5 to 22.5°C.). When changes occurred, the temperatures of the skin were corrected according to Vincent's observation; for each degree of change in room temperature, the temperature of the skin was adjusted by 0.3 of a degree.

The temperature, movement of air and humidity were maintained fairly constant. The total effect of these on cooling was measured by recording the cooling power of the air with a Kata-thermometer. This varied between 4.7 and 5.2 millicalories per square centimeter per second for the dry Kata- and 14 and 16 for the wet Kata-thermometer.

The temperatures of the skin were measured with a copper-constantan thermocouple (Benedict, somewhat modified), the rectal ones by ordinary clinical recording thermometers previously compared with the thermometer used for calibrating the thermocouple.

The patient remained undisturbed for 2 hours in a room, the temperature and cooling power of which remained constant, before the first observations were made, and remained there during the whole period of examination. Observations of the temperatures of the skin at 16 points, of the rectal temperature, of the heart rate and pulse rate were usually made every two hours except at 4 a. m. and 6 a. m. The periods of examination varied in length from one to 3 days, before, during or after, the administration of digitalis.

One patient, aged 70, the subject of advanced arteriosclerosis,

enlargement of the heart, rapid auricular fibrillation and heart failure with congestion was relieved by taking digitalis. When digitalis was withheld congestion recurred. Three attacks of heart failure were observed; on each occasion fever was present during the period of failure. No evidence of infection was obtained.

A comparison of skin and rectal temperatures during and after recovery from heart failure showed uniformly that during failure, the temperatures of the skin, more especially those of the extremities, were lower, that of the rectum higher than after recovery. When improvement had taken place, the surface temperatures were closer to each other and closer to the rectal temperatures. The thermal gradient from the interior to the surface of the body was greater during heart failure than after recovery.

This state of affairs is different from that observed in infections in which fever is present in persons whose circulation is supposedly normal for, as is well known, the skin under these conditions suffers an elevation of temperature. The inference which has naturally been drawn is that the elevated rectal temperature in heart failure is due to the difficulties which the embarrassed circulation encounters in distributing properly the heat which is produced within the body.

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Relation of Absorption Coefficients to Rate of Penetration of Dye into the Cell.

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Crystal violet penetrates slowly into the vacuolar sap of *Nitella*. Is this connected with the presence of 0.1 M KCl in the sap? To what extent can such an effect be interpreted by the multiple absorption coefficient theory? This theory deals only with rates and steady states (not with equilibrium); its basic principle is as follows: Other things being equal the rate of penetration of dye into the sap is a function of the concentration gradient (D'_o—D'_s) of the dye in the plasma membrane: D'_o and D'_s represent the concentrations of dye in the plasma membrane at the outer and inner phase boundaries, and are functions of the absorption coefficient* of the dye between the plasma membrane and the aqueous solution at the

* The absorption coefficients may represent solubility or chemical combination or both.