



Fig. 2. Desaturation curve of calcium-45 for rabbit atria washed out in non-isotopic Krebs solution after soaking in Krebs solution containing tracer amounts of calcium-45 for 3 min (●, group 1b) and for 2 h (○, group 2b). Each point is the mean of five experiments. Vertical bars represent standard error of the mean. Δ, Curve obtained after linear portion of group 2b curve is extrapolated to zero time and then subtracted from original curve.

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<sup>1</sup> Heilbrunn, L. V., and Wiercinski, F. J., *J. Cell. Comp. Physiol.*, **29**, 15 (1947).  
<sup>2</sup> Niedergerke, R., *J. Physiol.*, **134**, 569, 584 (1956).  
<sup>3</sup> Niedergerke, R., *J. Physiol.*, **138**, 506 (1957).  
<sup>4</sup> Niedergerke, R., and Harris, E. J., *Nature*, **179**, 1068 (1957).  
<sup>5</sup> Niedergerke, R., and Lüttgau, H. C., *Nature*, **179**, 1066 (1957).  
<sup>6</sup> Lüttgau, H. C., and Niedergerke, R., *J. Physiol.*, **143**, 486 (1958).  
<sup>7</sup> Frank, G. B., *J. Physiol.*, **151**, 518 (1960).  
<sup>8</sup> Weber, A., and Winicour, S., *J. Biol. Chem.*, **236**, 3198 (1961).  
<sup>9</sup> Sandow, A., *Pharmacol. Rev.*, **17**, 265 (1965).  
<sup>10</sup> Bianchi, C. P., and Shanes, A. M., *J. Cell. Comp. Physiol.*, **56**, 67 (1960).  
<sup>11</sup> Winegrad, S., *J. Gen. Physiol.*, **48**, 455 (1965).  
<sup>12</sup> Locke, F. A., and Rosenheim, O. T., *J. Physiol.*, **26**, 213 (1907).  
<sup>13</sup> Mines, G. R., *J. Physiol.*, **46**, 188 (1913).  
<sup>14</sup> Loewl, O., *J. Pharmacol.*, **114**, 90 (1955).  
<sup>15</sup> Winegrad, S., *Circulation*, **24**, 523 (1961).  
<sup>16</sup> Winegrad, S., and Shanes, A., *J. Gen. Physiol.*, **45**, 371 (1962).  
<sup>17</sup> Sekul, A. A., and Holland, W. C., *Amer. J. Physiol.*, **197**, 752 (1959).  
<sup>18</sup> Langer, G. A., *Circulat. Res.*, **15**, 393 (1964).  
<sup>19</sup> Langer, G. A., *Circulat. Res.*, **17** (1965).

**PATHOLOGY**

**Effect of Chlordiazepoxide on Stomach Ulcers in Rabbit induced by Stress**

In an earlier communication<sup>1</sup> we reported that premedication with chlordiazepoxide (CDP), a 1,4-benzodiazepine derivative, prevented the eosinopenia caused by emotional stress in rabbits, acting in a manner antagonistic to adrenocorticotrophic hormone (ACTH). Furthermore,

CDP behaves antagonistically towards another hormone involved in stress, namely, antidiuretic hormone<sup>2</sup>. The effect of premedication with CDP on stomach ulcers induced by stress has now been investigated.

Male rabbits weighing 1.5–2.0 kg were used. Emotional stress was applied daily for 21 days as previously described<sup>1</sup> using the method of Colfer *et al.*<sup>3</sup>. Three rabbits received electroshock only and acted as controls. Three rabbits received daily intraperitoneal injections of CDP (50 mg/kg) 30 min before electroshock. Daily blood counts showed that eosinopenia occurred in the control group only. After 21 days the animals were killed and the stomachs examined with a hand lens. Stomachs from the control group all showed extensive congestion, numerous haemorrhages, shedding of the epithelium over large areas and distinct ulceration. Among the experimental group there was slight shedding of epithelium in one rabbit and some congestion in all three, but no haemorrhage and no ulceration.

It thus appears that premedication with CDP affords protection against the effects on the stomach of emotional stress. It is unlikely that gastric acidity played any part in these experiments, because the pH of the stomach contents was the same in both groups. In a separate investigation<sup>4</sup>, it has been shown that premedication with CDP prevents the stomach damage in rats usually caused by the stress of restraint. In other experiments, we have found that stomach ulcers produced by chronic administration of cortisone to rats were not prevented by similar premedication with CDP.

It may be assumed that stomach lesions following emotional stress are caused by adrenocortical hormone released in response to increased concentrations of ACTH in the blood. It seems reasonable to infer from the present investigations that the antagonism between CDP and ACTH prevents the release of adrenocortical hormones in amounts sufficient to damage the stomach.

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<sup>1</sup> Dasgupta, S. R., and Mukherjee, B. P., *Nature*, **213**, 199 (1967).  
<sup>2</sup> Dasgupta, S. R., and Sikdar, S., *Bull. Cal. Univ. Coll. Med.*, **3**, 31 (1965).  
<sup>3</sup> Colfer, H. F., De Groot, J., and Marris, G. W., *J. Physiol.*, **111**, 328 (1950).  
<sup>4</sup> Dasgupta, S. R., and Mukherjee, B. P., *Brain News* (in the press, 1967).

**Pyrogen in the Urine of Febrile Patients with Hodgkin's Disease**

THE mechanism whereby bacterial infections induce fever has been elucidated in some detail<sup>1,2</sup>. Bacteria and bacterial pyrogens (exogenous pyrogen) interact with polymorphonuclear granulocytes of the host, resulting in release into the circulation of a soluble product of the granulocyte (endogenous pyrogen) which is the proximate cause of the fever through its action on the temperature control centre of the host. Exogenous pyrogen and endogenous pyrogen may be distinguished in several ways, but the most striking difference between their actions is that tolerance to the first develops rapidly, whereas endogenous pyrogen continues to cause fever after a long sequence of daily injections.

Less is known about the mechanisms responsible for fever not associated with bacterial infection. Such fever is frequently seen in patients with Hodgkin's disease. This study was undertaken to determine whether an analogous mechanism (that is a circulating pyrogen of the "endo-