rise to necrosis of the skin under the same conditions. After intramuscular injection in rats all three drugs gave an early inflammatory response characterized by the appearance of a polymorphonuclear exudate. In the case of Thiomerin this exudate was entirely resorbed without evidence of residual damage. After injection of Mercuzanthin, or Mercuhydrin, however, the irreversible nature of the response was indicated by marked fibroblastic proliferation.

These results would seem to furnish an adequate experimental basis for the clinical use of Thiomerin by subcutaneous injection.

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17059. Observations of Nitrite-Induced Postural Syncope in Patients with Mental Disease.

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Earlier work[1] discussed the vasomotor system in schizophrenia; it was concluded that no structural vascular defect exists and that schizophrenic patients often exhibit acral vasoconstriction. Investigation of the reactivity of postural vasoconstrictor mechanisms has also been made. Nitrite dilates vessels by relaxing smooth muscle. but does not prevent the action of nervous impulses on this muscle; accordingly, the degree to which the vasoconstriction overcomes the effect of nitrite affords data on the reactivity of postural vasoconstrictor mechanisms.

Material and methods. Twenty-four patients were studied. Their diagnoses varied (Table I). Four (Table II), all schizophrenics were studied only after lobotomy. Twenty-four normal subjects were also observed. After reassurance the subjects came to the laboratory fasting or 3 or 4 hours after a last meal. Patients were not permitted to smoke before or during experiments. Each subject was given 3 grains of sodium nitrite by mouth and allowed to rest for 30 minutes. He then lay on a board which had no protuberances except for a bicycle seat at right angles to it; this the patient straddled. After control observations were made, the board was tilted 60 degrees leaving the patient head-up with legs hanging. Systolic blood pressure was measured every few minutes by palpation. Auscultatory measurements were not made since they may be markedly in error with changing vasomotor tone; an arterial cannula was considered undesirable for measuring arterial pressure in this study. If syncope did not occur within forty minutes after tilting the patient, the observations were ended and were repeated no sooner than 2 days later, using 7 grains of sodium nitrite.

Observations. Subjects were classified as follows:

Group I. Syncope during tilting after 3 grains of sodium nitrite, *i.e.*, no increase in vasomotor reactivity (Fig. 1).

Group II. Syncope during tilting after 7 grains but not after 3 grains of sodium nitrite, *i.e.*, possible increase in vasomotor reactivity (Fig. 2).

Group III. Fall in blood pressure during tilting but no syncope after 7 grains of sodium nitrite, *i.e.*, definite increase in vasomotor reactivity (Fig. 3).

Group IV. Rise in blood pressure during tilting after 7 grains of sodium nitrite, *i.e.*, marked increase in vasomotor reactivity (Fig. 4).

Twenty-two normal subjects were in Group I and 2 in Group II. Seven of the 11 nonlobotomized schizophrenic patients exhibited

[1] Altschule, M. D., and Sulzbach, W. M., *Arch. Neurol. and Psychiat.*, 1949, **61**, 44.

TABLE I.
Vasomotor Response to Tilting After Administration of Nitrite.

Diagnosis	No. of cases				
	Groups I	II	III	IV	Total
Normal	22	2	—	—	24
Schizophrenia	3	1	5	2	11
Organic disease—post asphyxial	—	—	1	—	1
Involutional psychosis, paranoia	1	—	—	—	1
Manic-depressive, manic	—	1	—	—	1
Anxiety neurosis	—	—	1	—	1
Psychoneurosis, reactive depression	1	—	1	—	2
Chronic alcoholism	—	2	1	—	3
Total, non-schizophrenic	2	3	4	0	9

TABLE II.
Vasomotor Response to Tilting After Administration of Nitrite in Lobotomized Patients.

Case	Group		Diagnosis
	Before	After	
We	III	I	Schizophrenia, paranoid
Wi	II	III	" "
B	—	I	" catatonic
S	—	III	" "
L	—	IV	" "
Wo	—	IV	Schizophrenia, other types
Z	I	I	" " "

a definite or marked increase in postural vasomotor reactivity. Of the 9 patients, with diagnoses other than schizophrenia, 4 exhibited a definite increase. Of the 7 schizophrenic patients studied at least 4 months after lobotomy, 4 showed definite or marked increases (Table II). No consistent change in vasomotor reactivity developed after operation.

The schizophrenic patient showed no correlation between the presence of acral cyanosis under control conditions and increase of vasomotor reactivity; however, acral cyanosis developed, or if present, became intensified when the patients were tilted to the head-up position.

Mood or thought content changed sharply in some instances. A patient with involutional psychosis was studied 11 times; each time

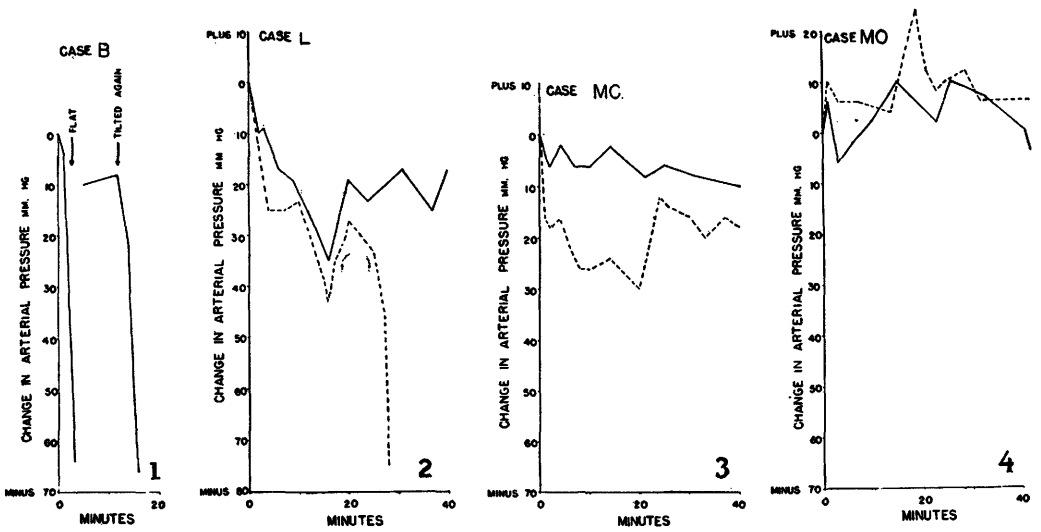

FIG. 1. Group I Reaction. Syncope after 3 grains of sodium nitrite.
FIG. 2. Group II Reaction. Syncope after 7 grains (dotted line) but not after 3 grains of sodium nitrite (solid line).
FIG. 3. Group III Reaction. Fall in blood pressure but no syncope after 3 grains (solid line) or 7 grains (dotted line) of sodium nitrite.
FIG. 4. Group IV Reaction. Rise in blood pressure after 3 grains (solid line) and after 7 grains (dotted line) of sodium nitrite.

distressing hallucinations of violent events developed a few minutes after she had been tilted up and when decreases in blood pressure were only slight. They persisted until she was returned to the flat position, when they disappeared, leaving the patient shaken but cognizant that the visions had been hallucinations. A patient with psychosis due to asphyxial cerebral damage became fearful when her blood pressure began to fall after she was tilted up. She spoke spontaneously for the first time of the fire during which she had almost died and which marked the onset of her illness. She described how her son had died and she also brought out other material previously suppressed. A manic-depressive patient in the manic phase became more active when her blood pressure began to fall after she was tilted up; she showed excitement and rambling speech alternating with moodiness and weeping. The patients with reactive depressions, psychoneurosis and chronic alcoholism showed no change in mood or mental content. The 15 schizophrenic patients observed showed various psychological reactions. In 3 instances syncope occurred so quickly that no evaluation of changes in thinking could be made. Two young patients with recent onset of schizophrenia became more self-absorbed and showed expressions suggestive of hallucinatory mental content when their blood pressures were falling. The remaining patients, all examples of schizophrenia of long duration, showed no definite psychological change when tilted in the head-up position although there was some decrease in blood pressure in half of them.

Discussion. The data indicate that increased reactivity of the vasomotor mechanisms involved in postural changes may exist in patients with mental and emotional disorders. This finding is not limited to schizophrenia. The mechanism of the increased vasomotor reactivity observed here is not evident. The vasomotor phenomena here observed are of interest in that they indicate the occurrence of disturbances of functions other than those concerned with thought, mood or perception in mental disease. The similarity of findings in schizophrenia and in non-schizophrenic disorders does not support the concept that the former is accompanied by a specific change in autonomic function. Moreover, the presence of increased reactivity of the postural vasomotor mechanisms in schizophrenia, negates the belief that the autonomic nervous system is less responsive than normal in this disease. The common finding of increased reactivity of vasomotor mechanisms in schizophrenic patients here and as previously discussed[1] suggests that the conclusion that such increased vasomotor reactivity is the precursor of hypertension is erroneous since the incidence of the latter is low in schizophrenia. The patients who developed activation of their psychoses when placed in the head-up position are of interest. These changes began and often became marked at a time when changes in the general circulation were too small to be noteworthy; nevertheless, at this time significant changes in cerebral circulation already must have been in progress.[2] The events in these patients suggest the wisdom of caution in ascribing the onset of, or changes in overt psychotic manifestations definitely to psychological factors whenever evidences of changes in physiological status of the brain are absent on superficial examination.

Studies made here on lobotomy, though few, indicate that it causes no distinctive change in postural vasomotor reactivity if time for complete healing is allowed. Rinkel *et al.*[3] found increases in the response to injected epinephrin in patients after lobotomy. These findings may possibly indicate overreactivity of the sympathetic nervous system, or, on the other hand, may merely indicate an altered pharmacological response to a substance given greatly in excess of physiological quantities. At any rate, the fact that Rinkel *et al.*[3] made their studies a few weeks after lobotomy, suggests that the changes they found are manifestations of an irritative phenomenon and are not due to division of the tracts cut during the operation.

2 Lennox, W. G., Gibbs, F. A., and Gibbs, E. L., *Arch. Neurol. and Psychiat.*, 1935, **34**, 1001.

3 Rinkel, M., Greenblatt, M., Coon, G. P., and Solomon, H. C., *Arch. Neurol. and Psychiat.*, 1947, **58**, 570.

Summary and conclusions. In patients with mental or emotional disorders, increased activity of vasomotor mechanisms responsive to postural change may occur; this is observed irrespective of diagnosis. In some psychotic patients disturbances in mental content and mood, consisting of intensification of pre-existing psychotic manifestations, occurred at times when it may be assumed that cerebral blood flow was diminished. Observations suggest that lobotomy causes no distinctive change in postural vasomotor reactivity when time for complete healing is allowed.

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17060. Effect of Autolyzed Yeast, Yeast Nucleic Acid and Related Substances on Body-Temperatures of Rats.*

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It is common practice to produce fever experimentally in rats by means of the subcutaneous injection of a solution of autolyzed yeast. During the routine use of this procedure, we found that administration of the autolyzed yeast intraperitoneally produced a fall instead of a rise in body-temperature. In the present paper we are reporting this phenomenon and some efforts to determine what constituent or constituents of the yeast may be responsible for the temperature effects. The activities of autolyzed yeast, yeast nucleic acid, and the nucleic acid derivatives, guanine, uracil, xanthine, and allantoin were investigated.

Materials. The autolyzed yeast was prepared in the usual way by making a suspension of 15 g of commercial baker's yeast in 100 cc of water. This suspension was allowed to stand for several days at 37°C with occasional shaking. The solid material was then separated in the centrifuge and the clear, dark brown, supernatant "autolysate" was used as the experimental material. The magnesium salt of yeast nucleic acid was prepared according to the method of Baumann.[1] All nucleic acid derivatives used were Eastman products and when necessary were brought to essentially neutral condition before administration.

Experimental. The experimental animals were young adult white rats about equally divided between males and females in each experiment. The animals were fasted overnight before use. High colonic temperatures were taken with mercury thermometers by means of the technic previously described.[2] As soon as the initial temperature was obtained, the substance under investigation was injected either intraperitoneally in the lower left abdominal quadrant or subcutaneously craniolaterally to the base of the tail. After injection, the animals were kept at room temperature in individual wire cages without food or water. The room temperature varied between 25.5 and 28.5°C.

With the exception of the yeast, which was given as a "15%" autolysate, all test substances were administered in 0.1% solution.

Results. Fig. 1 shows the response in temperature following the intraperitoneal injection of 2 cc of a "15%" yeast autolysate contrasted with that after the subcutaneous injection of 2 cc of the same material. The average maximum rise in body-temperature after subcutaneous administration was 1.9°C and appeared at about the 5th hour. After

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1 Baumann, E. J., *J. Biol. Chem.*, 1918, **33**, XIV.

2 Hill, R. M., Ware, A. G., and Schultz, F. H., *Cancer Research*, 1943, **3**, 839.