the evoked pinocytosis operates with approximately one quarter the efficiency of that existing normally in capillaries having intense macromolecular transport.

Of the microvesicles evaluated, the pinocytotic vesicles are in general presumed to be of non-selective transporting elements[7], whereas the coated vesicles are thought to absorb selectively and carry proteins[8] into the blood capillaries. Recent studies on the permeability of toad urinary bladder to water and certain other small molecules, in relation to the pinocytosis of mucosal cells, have clearly indicated that the well-known permeability-modifying effect of neurohypophyseal hormones is firmly associated with cAMP mediated induction of pinocytosis[9].

Increase in pinocytosis of brain capillaries has long been observed in several cases of pathological damage to the 'blood-brain' barrier[10,11]. No hypothesis has, however, as yet been put forward to explain the altered cellular activity resulting from any pathological circumstance. From our results, the fact that cAMP plays a key role in the regulation of pinocytosis in the brain capillaries can be readily established. For this reason, it might be assumed that an increase in level of cAMP may also occur during the evoked breakdown of the 'blood-brain' barrier, regardless whether it is of experimental or pathological origin.

Whether the described facilitation of pinocytosis, by means of which certain macromolecules can be readily transported through the endothelium, is effected directly by cAMP generated in the tissue or is a secondary effect, still remains to be elucidated[12].

Zusammenfassung. Die Anzahl der pinocytotischen und stachligen Vesicula wurde unter normalen Bedingungen mit Bezug auf einheitliche Gebiete der pinocytotischen Aktivität der Kapillaren von Mäusegehirnen quantitativ charakterisiert. Die Pinocytose der Gehirnkapillaren war durch das substitutielle cyclische N^6O^2-Dibutyrylderivat des 3′, 5′-Adenosinmonophosphats signifikant gesteigert.

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Effect of Serum from Depressed and Manic Patients on Maze Behavior of Rats

In 1961 Poliakova[1] reported that serum from patients with manic-depressive illness had differential effects on the behavior of dogs in a maze. Dogs injected intravenously with serum from depressed patients ran the maze more slowly than controls. Those injected with serum from manic patients ran slightly, but consistently, faster and made more errors. This study has been cited in reviews of affective illness[2,3], but no further work in this area has been reported. The present study was designed to further investigate the effect of serum from manic-depressive patients on animal behavior.

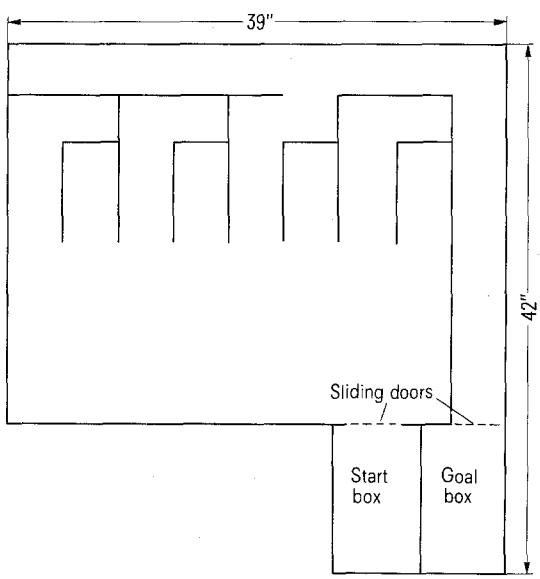

Fig. 1.

Methods. Male Sprague-Dawley rats were trained to run the maze illustrated in Figure 1 (adopted from Poliakova). This maze requires a choice of 9 alleys and a left-right discrimination for reward of moist food. Animals were food deprived daily from 07.00 h. Trials were conducted between 14.00 h and 15.00 h following which food was given ad libitum. Time from leaving start box to reaching goal box and number of errors were recorded for each trial. All rats were trained to a criterion of 5 consecutive trials, each under 10 sec with less than 2 errors. On experimental days, rats were run immediately before and at 0, 10, 20 and 30 min after tail-vein injection of 0.4 ml[4] of serum from manic and depressed patients or normal controls. Serum was injected within 1 h of being drawn and the investigator running the animals was blind to its source.

Seven depressed patients donated serum a total of 14 times for trials in 20 different rats. Six manic patients' serum was used 12 times in 12 different rats. All patients were drug free for at least 1 week prior to the experiment. Control serum from 5 euthymic investigators was used in 24 trials.

Patients were hospitalized on 2 psychiatric research units at the NIMH designed for intensive longitudinal study of manic-depressive illness. All patients were diagnosed by 3 staff psychiatrists and a social worker, and patients with other than primary affective illness were excluded from the study. Depression and mania were

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[4] This amount of serum exceeds by 50% that used by Poliakova in dogs (10 ml) on a ml/kg basis.

rated on a 15-point multi-item scale derived from that of BUNNEY and HAMBURG[5]. The degree of depression ranged from moderately severe to severe with patients exhibiting symptoms of marked psychomotor retardation, sleep and appetite disturbance, depressive delusions, and suicidal ideation. Five of the depressed patients were bipolar, i.e., had histories of manic episodes. The 6 manic patients exhibited flight of ideas, pressure of speech, euphoric or angry mood and intrusive, demanding behavior. Four of the 6 manic patients required seclusion. A cross-over design was employed where rats receiving one type of serum were given a different serum during the trials on the next day.

Results. There were no significant differences in the maze behavior of rats following injection of serum from depressed and manic patients or normal controls (Figure 2).

In 6 trials the animals appeared acutely ill after injection – similar to the dogs injected with depressed serum described by POLIAKOVA. However, this syndrome occurred equally among groups receiving manic, depressed and control serum (2 in each). The rats became prostrate and tremulous with labored respiration, yet attempted to drag themselves into the correct alley. This syndrome lasted 5–10 min. After recovery all but 1 of the animals were able successfully to complete the maze, often running a successive trial in less than 10 sec. The exclusion of animals with this effect did not alter the results as summarized in Figure 2.

There was no difference in the number of maze errors among groups of rats receiving manic-depressive or control sera. In the cross-over design where the same animal received injections of many different sera, no individual rat showed a clear pattern of faster or slower runs with manic or depressed serum.

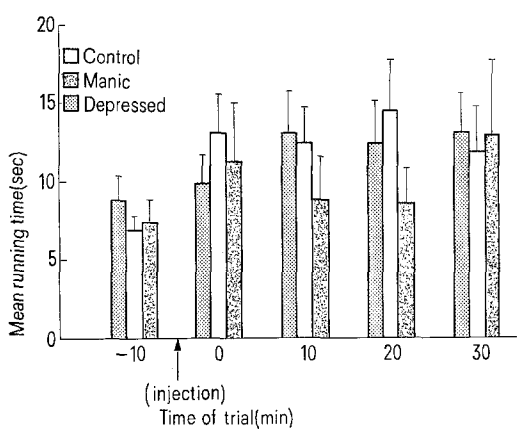

Fig. 2. Effects of manic and depressed serum on maze running time.

Discussion. Our failure to find any differences in the behavior of rats injected intravenously with serum from manic-depressive patients and controls raises questions about POLIAKOVA's findings, but does not rule out the possibility of a species specific effect in dogs.

As is evident in Fig. 2 all groups of animals showed an increase in maze running time following injection of serum. This may have been due to nonspecific serum effect or the stress of the injection procedure. Rats were immobilized in a restraining device before tail-vein injection. This procedure, equally stressful for experimental and control injections, could also have increased excitatory levels to the point where small differences in behavior mediated by a serum factor would not be evident.

No mention of medications is made in POLIAKOVA's study, while all of our patients were drug-free at least 1 week prior to sampling of serum. It is possible that psychotropic drug effects could explain POLIAKOVA's findings.

A number of animals, equally distributed between patient and control groups, appeared to have a toxic reaction to the injection of serum. This effect appears to be non-specific and was probably not related either to acute volume overload or anaphylaxis, as animals that had repeated injections did not have an increased likelihood of adverse reaction. It may be that this non-specific toxic reaction to injection of serum fortuitously accounted for the differences between depressed and control groups in POLIAKOVA's study.

Zusammenfassung. Serum von depressiven und manischen Patienten und von normalen Kontrollen wurde in die Venen von Ratten injiziert und deren Labyrinthlaufen beobachtet. Bedeutende Unterschiede bei Laufzeit und Fehlern wurden nicht festgestellt.

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Ring Shaped Nucleoli in the Primary Spermatocytes of Rats and Mice

Ring shaped nucleoli have been described in normal plasmocytes[1], oocytes[2–4], lymphocytes[5], smooth muscle and endothelial cells[1] as well as in hepatocytes during vital hepatitis[6], leukemic lymphoblasts[7] and Ehrlich ascitic cells[1].

In experimental studies ring nucleoli were obtained in a variety of cells under the influence of actinomycin D in vitro and in vivo[8–10] and chromomycine A_3 in vitro[1]. Starvation in some insects could also induce the appearance of ring nucleoli[11].

In the course of cytological study of spermatogenesis, using techniques described in previous papers[12–14], we commonly observed ring shaped nucleoli in primary spermatocytes of normal rat and mouse. It seemed therefore of interest to ascertain, whether the ring shaped nucleoli were a characteristic feature of these cells.

Material and method. Observations were made on testicles of 40 animals: 20 Wistar rats (Carworth Farm, N.Y.) weighing 120–240 g, and 20 Swiss mice CF-1 (Carworth Farm, N.Y.) weighing 20–40 g. All the animals were fed with standard Purina Chow (Ralson Purina Comp., St. Louis, Missouri) and water ad libitum.

Under general ether anesthesia the animals were unilateraly (right side) castrated. The testes were cut in halves with a razor blade and smears and imprints were prepared from the surface section.

After drying, the preparations were stained with the Giemsa-Ionescu solution[15], composed of: May-Grunwald