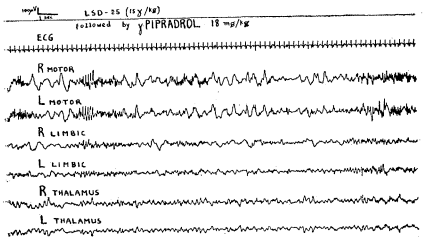

Fig. 2. The abnormalities induced by LSD-25 in the cerebral electric activity of the rabbit are corrected by administration of alpha-4-piperidyl benzhydrol hydrochloride (indicated in the figure as gamma-pipradrol). Notice the reappearance of the high-voltage slow activity and the 14-cy/sec spindles, predominantly in the motor cortex.

the electric brain activity. In all our experiments (five animals with LSD-25, five animals with mescaline) we observed that, within 2 to 10 min after the administration of alpha-4-piperidyl benzhydrol hydrochloride, the normal pattern of brain electric activity was restored. The slow waves and 14-cy/sec spindles, which were eliminated by the hallucinogenic drugs, returned after alpha-4-piperidyl benzhydrol hydrochloride (Fig. 2). The doses of the drug necessary to correct the abnormal electric activity ranged between 12 and 24 mg/kg. We found that there is a direct relationship between the amount of hallucinogen administered and that of alpha-4-piperidyl benzhydrol hydrochloride necessary to reverse the electric changes. Alpha-4-piperidyl benzhydrol hydrochloride when administered alone does not influence the EEG. Neither does it enforce the sleep pattern nor depress the mesodiencephalic activating system, the hyperactivity of which is responsible for the pattern of alertness (*10*).

Di-isopropylfluorophosphate (DFP), amphetamine and Meratran (alpha-2-piperidyl benzhydrol hydrochloride) are other drugs that, like the hallucinogenic substances, evoke a permanent pattern of alertness (*11*). We administered alpha-4-piperidyl benzhydrol hydrochloride to animals that had received enough DFP, amphetamine, and Meratran to produce a continuous alert electric pattern. In no instance, however, did alpha-4-piperidyl benzhydrol hydrochloride correct the effects of DFP, amphetamine, or Meratran, even though the last is a positional isomer of alpha-4-piperidyl benzhydrol hydrochloride. So far it seems that the described action of alpha-4-piperidyl benzhydrol hydrochloride in restoring normal electric patterns in the rabbit is limited to, and perhaps is specific for, the changes induced by the hallucinogenic drugs, LSD-25 and mescaline. Probably the antagonism between alpha-4-piperidyl benzhydrol hydrochloride and the hallucinogenic agents is restricted to the central nervous system, for we have observed that alpha-4-piperidyl benzhydrol hydrochloride does not correct the mydriasis associated with the action of LSD-25 or mescaline. Fabing (*7*) also observed the rectification of the psychic symptoms but not of the autonomic and other physiological alterations wrought by LSD-25.

FRANCO RINALDI*
HAROLD E. HIMWICH
Thudichum Psychiatric Research Laboratory, Galesburg State Research Hospital, Galesburg, Illinois

References and Notes

1. W. A. Stoll, *Schweiz. Arch. Neurol. Psychiat.* 60, 279 (1947).
2. P. H. Hoch, *Am. J. Psychiat.* 107, 607 (1951).
3. J. Delay *et al.*, *Rev. Neurol.* 86, 7 (1952); J. Elkes, C. Elkes, P. B. Bradley, *J. Mental Sci.* 100, 125 (1954).
4. P. B. Bradley, C. Elkes, J. Elkes, *J. Physiol. (London)* 121, 50p (1953); H. Gastaut, S. Ferrer, C. Castells, *Confinia. Neurol.* 13, 102 (1953).
5. P. A. Davis, *Am. J. Psychiat.* 98, 851 (1940); F. Lemere, *Brain* 59, 366 (1936), and *Psychosomat. Med.* 3, 152 (1941).
6. F. Rinaldi and H. E. Himwich, *Arch. Neurol. Psychiat.* 73, 387 (1955); *ibid.* 73, 396 (1955).
7. H. Fabing, *Science* 121, 208 (1955).
8. Frenquel is the trademark of the Wm. S. Merrell Co., Cincinnati, Ohio, for alpha-4-piperidyl benzhydrol hydrochloride.
9. F. Rinaldi *et al.*, in preparation.
10. F. Rinaldi and H. E. Himwich, *Diseases of Nervous System* 16, 45 (1955).
11. ———, *Am. J. Physiol.* 179, 665 (1954).

* Fulbright fellow on leave from the Clinic for the Diseases of the Nervous System, University of Cagliari, Cagliari, Italy.

21 January 1955

Influence of Calcium on Mobility of the Electrophoretic Components of Chicken Blood Serums

The increase in the amount of nondiffusible calcium present in the blood serums of the laying hen has been confirmed many times (*1*). The same relationship has been shown to hold for young hens and cockerels under the influence of the female sex hormones. It has been demonstrated that the serum proteins of the laying hens or hormone-treated birds contain electrophoretic components not present in the serums of the nonlaying birds (*2–4*). Evidence indicating that the variations in the nondiffusible calcium of chicken serums can be associated with the change in concentration of these electrophoretic components has been reported (*5*). A method for measuring P^{32} distribution in the electrophoretic components of protein mixtures has been reported (*6*), and by means of this method it has been shown that the leading component of laying-hen serums and of hormone-injected cockerel serums was extremely rich in phosphorus (*7*).

The high phosphorus content of this leading fraction makes possible the determination of the position of this component under different conditions, even though it may be masked by the fact that it is migrating at the same rate as other components of the serum. By employing the afore-mentioned electrophoretic-radiochemical technique, the effect of increasing concentrations of calcium upon the mobility of this component has been determined (*8*).

The blood serum was prepared from the blood of 8-wk old cockerels injected with 2.0 mg of diethylstilbestrol per day for 5 days. Each chick was fed 0.5 mc of P^{32} daily for 5 days. The electrophoretic (*2*) and radiochemical (*6, 7*) techniques have been described elsewhere. The electrophoreses and previous dialyses were carried out with a borate buffer that contained graded amounts of calcium. The concentrations of calcium employed are indicated in Fig. 1.

When the leading protein fraction was not apparent in the electrophoretic picture but the P^{32} activity associated with it was found to be present in some other fraction, it was assumed that the two fractions were migrating at the same rate. In addition, the areas associated with the electrophoretic components were also determined; when the component containing the extra P^{32} activity had increased in area, the afore-mentioned assumption was considered valid. By this method the mobility associated with this high-phosphorus leading protein component and the other protein components was determined in buffer solutions containing various levels of calcium.

Results of this experiment (Fig. 1) show that the mobility of fraction I, the fastest moving component in buffer containing no calicum, was drastically changed by the addition of calicum to the buffer. The mobilities of the other five

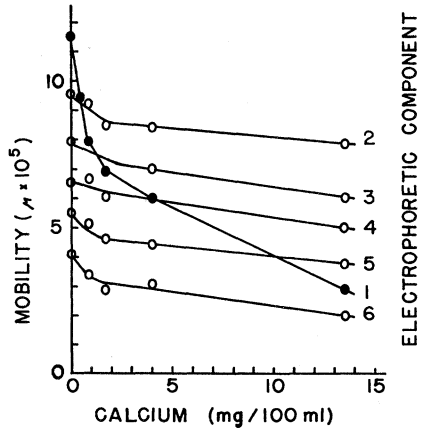

Fig. 1. Mobilities of the electrophoretic components in the serums of diethylstilbestrol-treated cockerels in a borate buffer, *p*H 8.6, containing graded amounts of calcium.

protein fractions were changed but slightly by the presence of calcium in the buffer. This change in mobility of the leading component can be explained by assuming that calcium combined with this component and thus changed the charge of the protein molecule. The result was a marked reduction in the mobility of component 1.

Previous evidence has shown that the rise in the nondiffusible calcium of chicken serum caused by the administration of diethylstilbestrol was paralleled by a rise in two of the electrophoretic components (*5*). This extra binding ability may be attributed to the leading, phosphorus-rich component. Utilizing buffer solutions containing Ca^{45} and an electrophoretic cell modified to determine its activity, we are now investigating the distribution of calcium in the various electrophoretic components of chicken blood serums. A more detailed discussion of this investigation is in preparation.

A. T. ERICSON
R. E. CLEGG
R. E. HEIN
Kansas State College, Manhattan

References and Notes

1. J. T. Correll, and J. S. Hughes, *J. Biol. Chem.* 103, 511 (1933).
2. L. W. Brandt, R. E. Clegg, A. C. Andrews, *ibid.* 191, 105 (1951).
3. R. E. Clegg *et al.*, *Science*, 114, 437 (1951).
4. D. H. Moore, *Endocrinology* 42, 38 (1948).
5. R. E. Clegg and R. E. Hein *Poultry Sci.* 32, 867 (1953).
6. R. E. Hein and R. E. Clegg, *Nucleonics*, 10, No. 10, 70 (1952).
7. R. E. Clegg and R. E. Hein, *Science*, 117, 714 (1953).
8. This work was aided by a research grant from Eli Lilly Co., Indianapolis, Ind. This paper is contribution No. 515, department of chemistry, Kansas Agricultural Experiment Station. This paper is also a portion of a dissertation to be presented by A. T. E. as partial fulfillment of the requirement for the Ph.D. degree.

25 February 1955

Agglutinating Strains of Trypanosomes Obtained with Oxophenarsine

In the course of producing oxophenarsine-resistant strains of *Trypanosoma equiperdum,* we observed the development of strains with a marked tendency to agglutinate when infected blood containing them was diluted 1:100 with physiological saline in a red-cell-counting pipette at 20° to 30°C (*1*).

The agglutinated masses of trypanosomes, which varied in size up to clumps that contained hundreds of organisms, were so firmly bound together that individual cells did not break away, although they were actively motile. When they were first seen, it was thought that the smaller agglutinated masses represented a failure of cell division, but further observations of the trypanosomes in warm saline (38°C) and in stained, dried blood films proved that the clumps were formed *in vitro*. When warm saline was used and the pipette and counting chamber were warmed to 38°C, the agglutinating tendency was greatly weakened and reliable counts could be obtained, something quite impossible at room temperature. Furthermore, the clumps were dispersed when the pipette in which they were contained was warmed in an incubator at 38°C. This behavior is reminiscent of cold hemagglutination, and cold hemagglutinins have been observed in trypanosomiasis (*2*), but there was no evidence of hemagglutination with serums from mice containing our strains, even at 4°C.

The unmodified strain from which the agglutinating strains were derived was observed in saline at 4°C, and no evidence of agglutination was found. At room temperature the unmodified strain formed evenly dispersed suspensions that were easily counted in a hemocytometer and they showed no tendency to stick together.

All the agglutinating strains have appeared in mice treated with subcurative doses of oxophenarsine when the infection was at levels of 50,000 to 1 million trypanosomes per cubic millimeter of blood. The first strain was obtained on the second day after treatment was started, and other strains developed up to 2 mo after treatment was started. During this period the dose was increased until a strain with 80-fold increased resistance to oxophenarsine was obtained.

In the first strain the agglutinating characteristic persisted in a highly developed form through at least eight passages that were made at 2- to 3-day intervals in untreated mice, but between the 8th and the 17th passages it almost disappeared, being replaced by a predominately nonagglutinating strain. It was possible, however, to recover partially the agglutinating characteristic by centrifuging diluted, infected blood and using the sediment to infect other mice.

On two out of two trials the agglutinating component was destroyed by treating infected mice with somewhat larger doses than the ones that were given just before the strains appeared; their relapse strains were nonagglutinating. Blood obtained from a mouse carrying an agglutinating strain but cleared of trypanosomes by treatment with oxophenarsine did not agglutinate the normal strain. An agglutinating strain was passed to rats, and the characteristic remained well developed in this species.

Although the agglutinating tendency seemed to be related to drug treatment, it was not difficult to obtain highly resistant strains that were completely free of the characteristic by always maintaining several substrains; this was because the incidence of the agglutinating characteristic was relatively low. Most of the mice were treated repeatedly, some as many as 10 times, without inducing any change other than a gradual increase in oxophenarsine resistance.

WILLIAM CANTRELL
Department of Pharmacology, University of Louisville School of Medicine, Louisville, Kentucky

References and Notes

1. This work was aided by a grant to the School of Medicine by the Kentucky State Medical Research Commission and by research grant G-4117 from the National Microbiological Institute of the National Institutes of Health U.S. Public Health Service.
2. *W. Yorke, Ann. Trop. Med. Parasitol.* 4, 529 (1911).

22 December 1954

Science, Population, and Arid Lands

It is becoming increasingly clear as world population soars to new heights that population pressure aggravates the struggle to maintain high living standards. The outcome of this struggle will depend not alone on available resources but also on the race between population increase and the research that makes resources more usable.

The world population is estimated to have doubled from 100 million to 200 million in the first 1000 years A.D., more than doubled from 500 million to 1200 million in the 200 years from 1650 to 1850, and again doubled from 1200 million to 2400 million in the century from 1850 to 1950. The curve of increase has been rapidly climbing, and if it is projected into the future it promises still higher increase rates.

With such increases, population pressures within densely populated areas are certain to push people into marginal, less densely populated areas. These are mainly the arid lands of the world, where lack of water is the critical factor in making them marginal or less usable in character.

It was shown at the Arid Lands Meeting in New Mexico in late April 1955 that arid zones occupy nearly one-third (32 percent) of the land surface of the earth, and that about 14 percent of the Americas was included. These lands are arid from a variety of causes but mainly because of the planetary wind patterns of the earth, which bring prevailingly dry winds to certain areas. Others lie in the rain shadow of mountains.

Rainfall on arid lands is usually inadequate to produce runoff (except quick heavy showers); hence, most water available in deserts comes in streams from distant mountains or regions of heavier precipitation. Such water, concentrated