The preparation of fibrinolysin and additional details will be described in another paper.

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Minimal Electroencephalographic Response to Metrazol as a Method for Measuring the Convulsive Threshold for Use in Human Beings

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Measurement of the convulsant threshold by direct means (induction of seizures) has been performed, chiefly on animals. The harshness of the procedure precludes or limits its use in human beings. If a method were available to measure this response indirectly in man, it might have many practical applications. It therefore occurred to one of us (E. Z.) that perhaps the first, or at least an early, minimal response to the injection of a convulsant drug, such as metrazol, indicated by the electroencephalograph might be an indirect measure of the convulsive threshold. Dr. Sjaardema assisted in the electroencephalographic recordings and interpretations at first, but later this was continued by Dr. Bercel.

The method consists of the usual electroencephalographic recording. The subject is then given an intravenous injection of metrazol of given concentration at a uniform rate, and the time at which the first recognizable change occurs in the EEG is recorded. In the rabbit we have used the first appearance of high-voltage slow waves, usually a 1- to 2-second run of waves of 4–5 cycles per second of increased amplitude. This repeats itself shortly and tends to become "established" as a recurring paroxysmal episode of increasing frequency. The injection may or may not be continued on to the point of a convulsion.

The purpose of this communication is chiefly to record the method. However, certain observations have already been noted.

In our experiments with rabbits the minimal EEG response was always obtained, and always preceded the convulsion.

When the convulsive threshold was altered in rabbits as a result of drugs, the minimal EEG response was altered in the same direction. In rabbits, phenobarbital retarded the appearance of the minimal EEG response and of the convulsion. The following is an example of such a test run:

Injection of 0.5% Solution of Metrazol (1 cc./min.)

	Minimal EEG Response	Convulsion
Before phenobarbital	0.6 cc.	1.4 cc.
2½ hr. after phenobarbital	1.2 cc.	5.4 cc.
Phenobarbital: 50 mg./kg. by stomach tube		

Dilantin did not have the anticipated effect of raising the convulsive threshold. At times a convulsion appeared more rapidly after the dilantin than before. However, the minimal EEG response also showed a lowered threshold. The following experiment is an example:

Injection of 1% Solution of Metrazol (1 cc./min.)

	Minimal EEG Response	Convulsion
Before dilantin	0.9 cc.	6.2 cc.
2 hr. after dilantin	0.5 cc.	2.3 cc.
Dilantin: 60 mg./kg. by stomach tube		

Diluting the metrazol gave a rise in the convulsive threshold and also a rise in the threshold for the minimal EEG response.

Rabbit #68	Minimal EEG Response	Convulsion
1.0% metrazol solution	3.1 cc.	5.5 cc.
0.5% " "	6.1 cc.	15.8 cc.
0.25% " "	12.7 cc.	31.3 cc.

In a few patients who were tested the threshold for the minimal EEG response was raised by the administration of phenobarbital and dilantin. The following is an example:

Injection of 10% Solution of Metrazol (1 cc./min.)

Patient With Epilepsy	Minimal EEG Response
Without medication 11 hr.	0.4 cc.
Dilantin gr. iss. 5 and 2 hr. before	1.1 cc.

It may be concluded, therefore, that metrazol and possibly other convulsant drugs and other convulsive agents produce a minimal response on the EEG before the occurrence of the seizure. The data reported tend to support the thesis that this minimal EEG response fluctuates in the same direction as the convulsive threshold under different conditions of excitation.

[1] The authors are indebted to Bilhuber-Knoll Company for contributing the metrazol used in this study.

It is suggested that the minimal EEG response can therefore be used as a method for studying convulsive threshold in human beings, thereby avoiding drastic aspects of the seizures themselves.

Utility of Sulfa Drugs for the Inhibition of Mold Respiration in Grain [1]

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Recent studies (*3*) have indicated that the carbon dioxide evolved from normal grain, held over time intervals of several days at moisture levels in hygroscopic equilibrium with air relative humidities in excess of 75 per cent, is due principally to the respiration of an indigenous mold population growing on the seeds. Under such conditions, the respiration of the seeds themselves is completely obscured. The respiratory activity of a freshly dampened seed sample increases continuously over time periods of several days and then tends to level off, the respiration-time curve thus assuming the form of a microbiological population-growth curve. On the other hand, at moisture levels in equilibrium with relative humidities below 75 per cent, where mold growth is not involved, seed respiration shows an extremely low and virtually constant rate with time.

With the object of obtaining data on the characteristics of true seed respiration at humidity values where it is normally obscured by mold respiration, a large number of organic compounds have been tested on wheat for fungistatic activity. The criterion of a suitable compound is that it must be fungistatic or fungicidal, but it must not adversely affect seed respiration or viability. Among the compounds which have been proposed for the suppression of mold respiration in grain are carbon tetrachloride (*2*) and trichloroethylene, quinosol, diacetyl, and phenothiazine (*1*). In the present studies search is being made for fungistatic compounds which are dry, relatively insoluble powders of low toxicity to animals and humans, and which would be odorless and tasteless. Among those investigated were 11 common sulfa drugs. Snow and Watts (*4*) have recently observed fungistatic activity by certain sulfa drugs when these were incorporated into nutrient agar media on which were cultured several mold species isolated from feeding stuffs.

TABLE 1

EFFECT OF SULFA DRUGS ON THE INCREASE OF ACIDITY DUE TO MOLD GROWTH ON REGENT WHEAT

Compound	Acidity*
Control	67.8
Sulfanilamide	22.6
Sulfapyridine	34.5
Sulfapyrazine	50.6
Sulfathiazole	33.3
Sulfaguanidine	52.2
Sulfadiazine	52.2
Sulfamerazine	53.8
Sulfaquinoxaline	50.1
Sulfasuxidine	29.6
Phthalyl sulfathiazole	56.3
Sulfamethazine	57.1

* Milligrams KOH required to neutralize benzene extract of 100 grams ground sample, air dry basis.

In the present studies the sulfonamides were finely ground and dusted onto the damp grain. Relative fungistatic activity was estimated from the increases in the acidity of benzene extracts of Regent wheat dampened with water to 20 per cent moisture (equilibrium relative humidity, 90 per cent) and stored for one month at room temperature. The results of this experiment are shown in Table 1. The effect of dry, powdered sulfanilamide in concentrations of from 1/2,000 to 1/250 (ratio of weight of sulfanilamide to weight of damp seed) on the respiration of Regent wheat containing 20 per cent moisture is shown in Fig. 1. Germination data for these wheat samples after the 11-day respiration trial are given in Table 2.

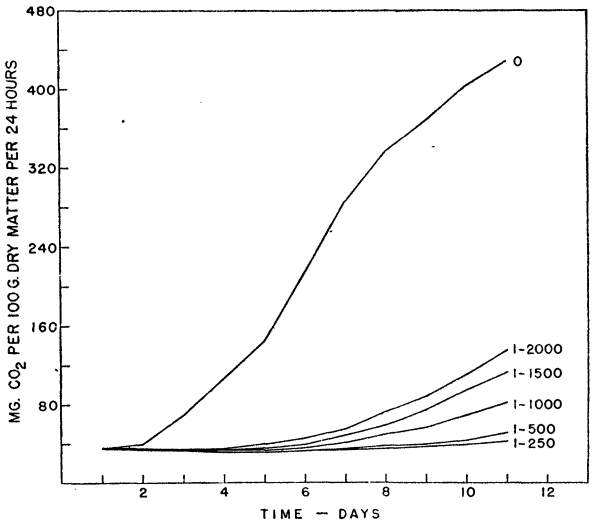

FIG. 1. Influence of various concentrations of powdered sulfanilamide on the respiratory behavior of wheat at 20 per cent moisture (relative humidity, 90 per cent).

Sulfanilamide showed the greatest fungistatic activity of the 11 sulfa drugs tested. It would appear that substitution in the amino group attached to the sulfonyl radical reduces the inhibitory effect of sulfa drugs toward the particular mold types which proliferate on wheat at this humidity level.

In the respiration trial the control sample showed respiratory increases analogous to the form of a

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