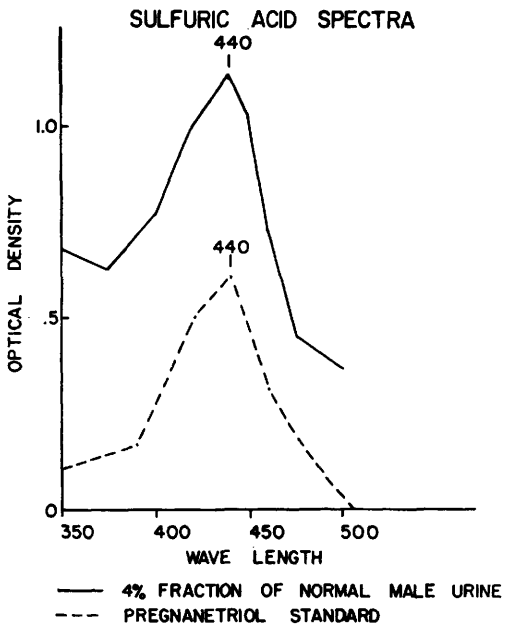

FIG. 1.

oxidized sample showed brown color with the Zimmermann reagent and gave a linear absorption curve.

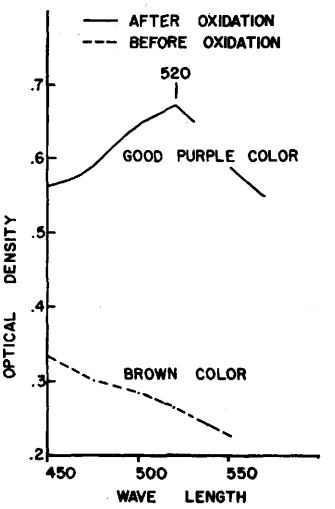

FIG. 2. Spectrum of oxidized and unoxidized 4% fraction following Zimmermann reaction (normal male urine).

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Blood 5-Hydroxytryptamine (Serotonin) Levels after Reserpine and Electroshock Therapy.* (22966)

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Recent evidence appears to lend credence to the postulate of Gaddum(1) and Woolley and Shaw(2) that 5-hydroxytryptamine (5-HT, serotonin) is involved in the function of the nervous system. Shore, Silver, and Brodie have shown that animals treated with the tranquilizing drug, reserpine, excrete large quantities of 5-HT metabolite, 5-hydroxyindoleacetic acid(3), and that brain and other body stores of such animals become depleted of their 5-HT(4,5). They have demonstrated further that this 5-HT-releasing activity is limited only to those Rauwolfia alkaloids with tranquilizing action(6).

It seemed of interest to determine blood levels of 5-HT in human subjects after treatment with reserpine; at the same time we

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studied the effect of electro-convulsive therapy on blood levels of 5-HT. Since permeability of the so-called blood-brain barrier is increased (at least in certain respects) after electroshock(7), it was conceivable that a change in concentration of 5-HT in the brain might be reflected by concentrations in blood. Blood levels of 5-HT were chosen rather than urinary levels of 5-hydroxyindoleacetic acid because the latter do not always reflect alterations in blood levels(8).

Methods. All patients were white males in a neuropsychiatric ward. Blood, usually 3 cc, was obtained from the antecubital vein, mixed with sodium citrate and extracted for one hour with 20 volumes of 99% acetone, according to the method of Amin *et al.*(9). The mixture was filtered, the acetone extract brought to dryness *in vacuo* and kept overnight below 0°C if not analyzed immediately. 5-HT was determined on the isolated heart of *Venus mercenaria*‡(10). The nutrient fluid for the heart contained (g/l): NaCl, 23.0; Na_2SO_4, 4.0; KCl, 0.65; $MgCl_2 \cdot 6H_2O$, 5.0; and $NaHCO_3$, 0.2(11). Benzoquinonium chloride ("Mytolon," Sterling-Winthrop) was always present in concentration of 6 mg/l to block the effect of any acetylcholine present in the extract. In our hands this method of extraction and assay has yielded reliable and reproducible estimates of serotonin levels in a number of biological tissues. Recoveries of added quantities of serotonin have ranged from 75% to 102%. However, insofar as whole blood is concerned, the amounts of 5-HT obtained by our extraction procedure must now be considered of relative and not of absolute significance, since Hardesty and Stacey have shown that erythrocytes interfere with the total extraction of serotonin from blood(12). Reliability of the bioassay is demonstrated in part by the fact that the extracts made in this work produced dose-response curves on the heart of *Venus mercenaria* identical to those produced by known quantities of serotonin. This bioassay preparation is highly sensitive to and specific for the stimulatory action of serotonin, since other cardio-excitatory amines like epinephrine, nor-epinephrine and histamine fail to stimulate it. Control studies with chlorpromazine (in concentrations up to 1 μg/ml) and reserpine (up to 10 μg/ml) indicated that these substances are without effect upon contractility and rate of the Venus heart and without influence upon its response to serotonin. Of 10 patients given reserpine, 4 were taking the drug when the experiments began. They were taken off reserpine for 3 weeks during which time all other medications were continued. To 6 other patients, reserpine was added to their previous medications. Three collections of blood were made on patients receiving electro-shock therapy: one immediately before and one immediately after administration of pentothal and succinylcholine; the third immediately after electro-shock. Since platelets carry blood 5-HT(12), platelet counts were done, but these did not vary significantly among patients or over the course of the experiment.

Results. The first 6 patients listed in Table I were not on reserpine at beginning of experiment. Their blood levels of 5-HT varied from 3.5 to 14 μg/100 ml. After 3 weeks on reserpine, 5-HT was minimal or not detectable in their blood.

The 5-HT levels in these patients before reserpine administration were within the wide range observed in this and other laboratories (13) in normal males and non-psychiatric patients with the exception of the value of 14 μg/100 ml observed in number 4, a patient with peripheral vascular disease. Three other patients with schizophrenia also fell within the range 2.3-8.5 μg/100 ml.

The last 4 patients listed in Table I were taking reserpine as well as other drugs when the experiments were begun. 5-HT was not detectable in their blood at this time. Three weeks after reserpine was withdrawn 5-HT levels had reached 1.7-2.5 μg/100 ml, values still appreciably below the normal range.

The concentration of 5-HT in the blood of 3 patients under electro-shock therapy was determined. In none did the initial treatment

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TABLE I.

Age	Diagnosis	Initial therapy (daily)	5-HT levels, μg/100 ml	Therapy for 3-wk interval (daily)	5-HT levels, μg/100 ml
		mg		mg	
60	Schizophrenia, hebephrenic	0	2.8	3.0 reserpine	<.11
34	Schizophrenia, unclassified	300 thorazine	5.0	300 thorazine 1.5 reserpine	.11
29	Schizophrenia, hebephrenic	450 "	4.0	450 thorazine 1.5 reserpine	<.11
40	Schizophrenia, paranoid	300 "	14.0	300 thorazine 3.0 reserpine	"
67	Meningoencephalitic syphilis	0	8.3	3.0 "	.14
70	Paresis	300 dilantin	3.5	300 dilantin 3.0 reserpine	<.17
35	Schizophrenia, unclassified	150 thorazine .75 reserpine	< .25	150 thorazine	2.5
41	Schizo-affective disorder with depression	75 thorazine 1.5 reserpine	<1.0	75 "	2.4
32	Schizophrenia, hebephrenic	450 thorazine 2.25 reserpine	< .4	450 "	1.7
59	Paresis	300 dilantin 6.0 reserpine	< .45	300 dilantin	2.2

affect the level of 5-HT in the blood. One 40-year-old patient with a reactive depression was followed for a 2-week period during which electro-shock was administered 6 times; there was no significant change in blood 5-HT levels over this period. Another patient on reserpine therapy (T.G. in Table I) was followed for 3 weeks, (9 electro-shock treatments) with no detectable change in concentration of 5-HT in the blood.

Summary. Blood 5-HT fell to non-detectable levels after administration of reserpine to patients during a 3 week period. Three weeks after withdrawal of the drug, 5-HT levels had risen but had not yet reached normal values. Electro-shock therapy did not alter the levels of 5-HT in the blood.

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