jected into the jugular vein. Quantitative comparison of rises induced by serotonin and by LSD-25 as a pressor agent showed that the LSD-25 was 1 to 3 times as active as serotonin (on a weight basis).

The pressor action of LSD-25 could be prevented by prior treatment of the dog with the new and powerful antimetabolite of serotonin—namely, 1-benzyl-2,5-dimethylserotonin, or BAS (*10, 11*). BAS has been shown to be quite specific, in that dogs protected against serotonin with it are not protected against the pressor effects of adrenaline. The curves will show that BAS protected the dogs against the pressor effects of LSD-25 (*12*).

A third type of experiment in which LSD-25 showed an action similar to that of serotonin has been described by Marrazzi and Hart (*13*). This was the inhibition of synaptic transmission in the optic cortex of the cat. It is therefore clear that one can find both serotoninlike and antiserotonin actions of LSD-25. In fact, both types of effect may be seen in one preparation. Thus, dogs given LSD-25, as in the afore-described experiment, were found to be partially protected against the pressor action of serotonin when it was subsequently injected. In thinking about these facts one should not forget that dogs, as well as isolated organs, can be protected against the effects of serotonin by serotonin itself (*10, 14*).

Although this possession of both serotoninlike and antiserotonin action may seem perplexing in the extreme, it need not be so. One may picture serotonin as acting on tissues by combination with a receptor specifically designed to react with it. One may also picture these receptors as not all of one kind but varying slightly from tissue to tissue (*15–17*). Serotonin combines with these receptors and, in so doing, causes a contraction of the tissue, just as acetylcholine is believed to do when it combines with its specific receptors (*18*). An antimetabolite such as BAS combines with the serotonin receptors in such a way that serotonin cannot reach them, but still, because the "fit" is not perfect, the BAS does not cause the contraction. It thus blocks the action of serotonin but at the same time does not fulfill the function of the hormone. LSD-25 also because of its structural analogy to the hormone combines with these receptors. From some kinds—for example, those in isolated segments of carotid arteries or in rat uterus—it acts like BAS and blocks the action of serotonin without at the same time causing a serotoninlike contraction. For other kinds of serotonin receptors—for example, those in *V. mercenaria* hearts—the LSD-25 not only combines with the receptors but is able to induce a serotoninlike effect, presumably because the "fit" is good enough. The antiserotonin action of serotonin itself then may be pictured merely as the combination of two or more molecules of serotonin with one receptor site. This site is then blocked because it has not combined with a single molecule of serotonin but rather with several. As was pointed out earlier (*10*), this is the classical picture of inhibition of an enzyme by an excess of its substrate and seems applicable here as well.

Do these findings of a serotoninlike action of LSD-25 mean that we can decide between the alternate explanations of an excess and a deficiency of serotonin in the causation of mental disease as pictured in references 1 and 6? It seems unwarranted to answer this question now. In the first place, the concept does not depend on the hallucinogenic effects of LSD-25 alone but rather on the central actions of a variety of analogs of serotonin—namely, harmine, yohimbine, medmain, and so on. It will be necessary to demonstrate that all of these analogs have serotoninlike activities if the theory of excess is to prevail (*19*). Furthermore, the abnormal (psychotic?) behavior induced in mice by LSD-25 has been prevented by serotonin (*20*). This might argue in favor of the hallucinations being manifestations of deficiency. Nevertheless the antiserotonin action of excess serotonin itself may obscure this conclusion. It would seem that both possibilities (excess and deficiency) must be kept in mind until a more crucial means of testing becomes available.

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* With the technical assistance of E. Van Winkle and M. DeLucia.

26 March 1956

Gamma-ray Activity of Contemporary Man

Measurements of the natural gamma-ray radioactivity of the human body have been reported recently by several workers who made use of large ionization chambers (*1*) or liquid scintillation counters (*2*) surrounding the subject to be investigated. These apparatus, however, do not have adequate spectrometric properties to permit identification of the radioelements involved.

In our laboratory, following successful reduction of the background radiation by shielding and choice of crystal canning material (*3, 4*), we have availed ourselves of a NaI scintillation crystal (10.8 cm in diameter and 3.8 cm thick) mounted on a DuMont 6364 phototube connected to a Marconi 24-channel pulse analyzer (5). Whole body radiation was measured by placing the face of this crystal 8 cm from the back of a seated person at the height of the twelfth thoracic vertebra (*6*). Background readings were obtained with a similarly placed mockup consisting of distilled water in steel cans. As a standard of K^{40} activity, 2 lb of KOH (C.P.) in sealed bottles was used at a distance of 40 cm. Geometric and scattering parameters *in vivo* were determined experimentally by the use of a few microcuries of K^{42}, the gamma ray of which has sensibly the same energy as that of K^{40}. The short-lived isotope solution was divided into two equal parts, one of which was administered to the subject and the other of which was retained as an intermediate radioactive standard after dilution in a mass of water of electron content equivalent to the 2 lb of KOH. Comparisons were made *in vivo* 10 hours or more after ingestion in order to attain equilibrium between K^{42} and K^{40}.

Preliminary pulse-height spectra of the radiation emitted by uncontaminated members of our staff were obtained in early 1955 (*7*). They disclosed potassium as essentially the only radioelement, in amounts corresponding to 0.22 percent of body weight in men and 0.16 percent in women. Inasmuch as this activity represents about 10^{-8} c of gamma radiation,

the activity of Ra, expected in amounts of 0.5×10^{-10} c (*8*), could not be measured in its presence despite the fact that the probable average deviation of a 2-hour reading of background was equivalent to only 4×10^{-11} g of Ra in the body.

Subsequent observations on members of our staff, a few visitors from various parts of the country and from overseas, local medical students, and foreign student members of the reactor school have disclosed the presence of a photopeak around 660 kev (*9*) in the scintillation spectra of all our test subjects (see Fig. 1) and its gradual increase in three individuals who were available for long-term study. No correlation was noted between net photopeak height and geographic origin of the subject. This type of radiation was detected also in various samples of urine, where the presence of the suspected element, Cs^{137}, was confirmed through chemical separation (*10*) of the activity by the addition of carrier to the ashed urine and double precipitations of cesium silicowolframate and perchlorate (*11*). The amounts involved *in vivo* ($\sim 10^{-9}$ c) are several orders of magnitude lower than accepted permissible levels (*12*).

In order to reconcile the persistence of the photopeak with the relatively short biological life of cesium (*13*), a few tests were performed to identify the contaminating sources. Of the foods, some, but not all, of the meats and milk powders were positive, whereas drinking water, vegetables, and sea scallops proved to be negative. Filter-collected dust of laboratory air and sweepings from house carpets from Chicago, Cleveland, and Tucson failed to disclose the Cs^{137} photopeak in the presence of overriding activities at 150, 500, and 750 kev. These energies indicate the presence of other fission products in the atmosphere—namely Ce, Zr-Nb, and Rh-Ru—and their absence from the spectra of human beings and cattle products is suggestive of low retention on the part of the intact mammal. In general, these findings are consistent with the known abundance of fission products of nuclear detonations and with their metabolic properties (*13*). Moreover, they suggest that Cs^{137} might be gaining access into the human body by its continual deposition on grazing lands and following thereafter much the same pathways described in the case of Sr^{90} (*14*).

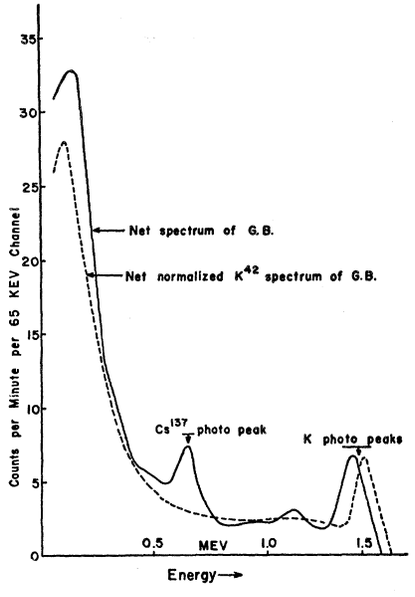

Fig. 1. (Solid curve) Typical scintillation spectrum of a human being (1955). (Dashed curve) Scintillation spectrum of the same individual after administration of K^{42} with its own natural spectrum subtracted. Ordinates are normalized to equal photopeak values.

Despite these difficulties, estimates of total body potassium remained feasible by restricting analysis to the 700-kev-to-1.6 Mev pulse-height band. For 12 male subjects (22 to 34 years old) who were studied, the average amount of potassium as percentage of body weight was 0.188 ± 0.006; for three women (22 to 29 years old), it was 0.154 ± 0.003.

Our figures appear somewhat lower than those based on body activity measurements and in better agreement with those obtained by radioisotope dilution techniques (*15*). Although the averages quoted here possess statistical uncertainties considerably lower than those of previous reports, they cannot be assumed to demonstrate either the existence or absence of nonexchangeable potassium in human beings of the much larger variations in individual potassium content. Clarification of the issue will require application of both techniques to the same subject, with accuracies higher than those reported heretofore (*16*) and with due attention paid to the existence of exogenous contaminants (*17*).

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27 March 1956

Mitochondrial Self-Duplication Observed in vitro

Two mechanisms of genesis of mitochondria have been suggested. Lindberg and Ernster (*1*) have concluded that the microsomal fraction of cytoplasm is gradually and continually converted into mitochondria by retention of synthesized protein. On the other hand, Ephrussi (*2*) and others advocate cytoplasmic genetic continuity, thus requiring autoduplication of these cytoplasmic elements. Such a process was reported for mitochondria in 1910 by Faure-Fremiet (*3*). In the course of some studies we performed on the morphology of mitochondria, this phenomenon of self-duplication was also found to occur *in vitro*.

In these experiments (*4*) mitochondria from fasted rat liver were used (Long-Evans, 200 g). They were prepared and examined in either 0.25*M* or 0.60*M* sucrose (*5*).

The mitochondria in the "fluffy layer," which is usually discarded, was found to contain a high percentage of limbus or club forms (*6*). Examination with the phase microscope (× 1455) at room temperature showed that many of this type had a slight constriction in the transverse plane. The larger rod forms found in the fluffy layer were also similarly constricted. If these types were watched over a period of time, they were seen to constrict actively, thus eventually forming two fragments. At least one of these