travel in straight lines, but diffuse through the interstellar magnetic field. Similar objections have been raised by P. Morrison and others in private communications (*2*). It is our contention that enough of the radiation arrives in a sudden burst concentrated in a few days or less to produce an acute dose of radiation.

In our report we took the optimistic point of view that most of the high-energy flux was received in a short period; we avoided discussion of such factors as the effects of long-term chronic radiation, which is very difficult to estimate, and the dynamics of the expansion of a relativistic gas in the interstellar magnetic field. Concerning this latter point, it would appear that the expansion cannot be described in terms of the diffusion of individual particles. For distances less than about 100 light-years, the pressure in the cosmic ray gas is much greater than the pressure in the interstellar magnetic field, so the field is strongly modified by the cosmic ray gas and has little effect on its motion. The gas would push its way through the field and would arrive at the earth spread out over a period of only the order of a few light-days. However, if the interstellar matter in front of the gas were ionized, the situation would be more complicated. Current theories of collisionless shock waves in ionized gases indicate that the ions would be "snow-plowed" in front of the expanding gas, in which case the expansion must stop in a few light-years. The state of ionization in the interstellar medium surrounding a star before and just after a supernova explosion are not known; it depends on the density of circumstellar gas and on the radiation spectrum. However, the important point for our consideration is that, even if diffusion approximation holds, some flux will arrive from the radiations that travel in straight lines—cosmic rays with energies $\gtrsim 10^{17}$ ev and high-energy gamma rays. These particles will initiate extensive air showers of secondary particles that produce ionization at sea level and hence radiation doses. Here we will discuss only the gamma ray component.

During the early stages following a supernova explosion, a large number of gamma rays will be produced by the inverse Compton effect, bremsstrahlung and π^0 decay following proton-proton collisions. The exact number depends on the early radiation field, the density of the interstellar medium around the supernova, and the number of relativistic protons and electrons produced by the explosion, but it is reasonable to estimate that between 10^{48} and 10^{50} gamma rays with energies of about 10^{12} ev are emitted. The extensive air showers initiated by these photons will result in doses between 10 and 1000 rads, for an explosion 100 light-years away. Taking a number intermediate between these limits shows that doses of the order of 100 rads are to be expected from the high-energy gammas produced by explosions 100 light-years distant, a factor of 3 less than we had previously used for discussing the biologic effects. The numbers involved are uncertain, of course, but we feel that our basic hypothesis, namely, the amount of energy from a nearby supernova explosion that arrives at the earth in the form of a concentrated blast of high-energy radiation is sufficient to cause very dramatic biologic effects, remains quite plausible (*3*).

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21 March 1968

Displacement Pattern of the Basilar Membrane: A Comparison of Experimental Data

Johnstone and Boyle (*1*) presented a new set of experimental data on the vibratory displacement of the basilar membrane in the guinea pig cochlea. Their measurements were obtained by application of the Mössbauer technique, and their results are the first of their kind since Békésy's classical observations (*2*). Furthermore, they presented a tuning curve for a place in the cochlear base, 1.4 mm from the stapes (*1*, Fig. 1), whereas all of Békésy's measurements were limited to the apical cochlear turn for technical reasons.

Johnstone and Boyle (*1*, p. 389) stated that before their study "no absolute values of these amplitudes of the basilar membrane were presented. . . ." Although many of Békésy's measurements were given without reference, he presented absolute values on several occasions (*2*, Fig. 6-43, pp. 464 and 481; *3*, Fig. 6). For instance, for a sound pressure level of 140 db he measured a displacement value of 7×10^{-5} cm in a human cadaver specimen.

In reference to their Fig. 1, Johnstone and Boyle further state (*4*, p. 390) that their own "tuning curves . . . resemble those obtained by Békésy but are more sharply peaked with a Q . . . of 2.5 (most of Békésy's curves have a Q [of] around 1.6 or less)."

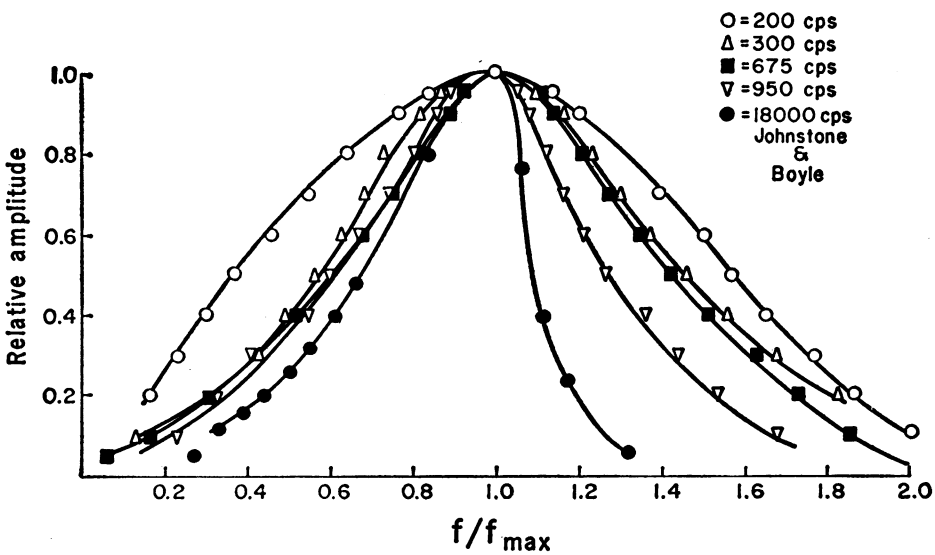

Fig. 1. Normalized tuning curves for the displacement of the basilar membrane in guinea pigs [Data from Békésy (*2*) and Johnstone and Boyle (*1*)].

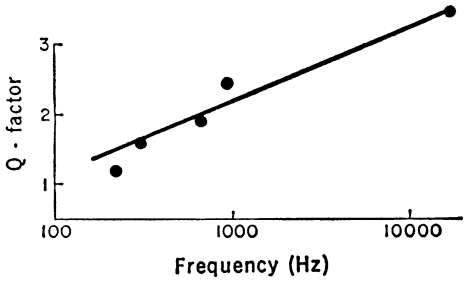

Fig. 2. Relation of Q-factor and frequency calculated from the curves of Fig. 1.

When one plots the data Békésy obtained in human cochlear specimen (*2*, Fig. 11-49) in a normalized manner with respect to frequency (*4*), then indeed it might appear as though Johnstone and Boyle were correct. Although there is some nonsystematic spread of individual data, the Q-factor, for the frequency range studied, does not appear to vary with frequency and it has a value of approximately 1.7.

However, Fig. 1 presents the data Békésy obtained in guinea pigs (*2*, Fig. 12-23) in a normalized manner with respect to frequency and the curve of Johnstone and Boyle (*1*), also obtained for guinea pigs, is appropriately entered. There is a systematic change of the Q-factor with frequency. For better illustration, the latter change is presented in Fig. 2. The relation follows, in first approximation, a straight-line function, and the value of Johnstone and Boyle, also included in this figure, represents a reasonable extension of Békésy's low-frequency data. [There is a numerical discrepancy between the Q-factors as computed by Johnstone and Boyle from their data (2.5) and that calculated here (3.56). Since we had to take the data from the graph in (*1*), we are not sure whether the discrepancy is genuine.]

It is gratifying that the new data of Johnstone and Boyle (*1*) fit those of Békésy (*2*) rather well. In fact, we find the agreement remarkable.

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6 March 1968

Tonndorf and Khanna's method of plotting the tuning curve is interesting, as is their graph of the relationship between Q and frequency. We had also noticed the trend in Q (*1*). As to the question of absolute values, our statement was that no absolute values had been given for the tuning curves, and this statement is correct as far as we know. We acknowledged that Békésy did present some absolute values, and we quoted them (400 Å at 90 db SPL); however, the relationship of this figure to the tuning curves is obscure.

Our results are in some aspects different from Békésy's, almost certainly because they were measured at a different place and with different frequencies; however, our measurements are in no way inconsistent with his observations.

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25 March 1968

Cancerostatic Action of Methylglyoxal

Several years ago, experiments on a cancerostatic agent found in normal tissues (*1*) indicated that it might be methylglyoxal, a keto-aldehyde, or a derivative thereof (*2*). Several α-keto-aldehydes were therefore synthesized and studied (*3*), and were found to have a specific inhibitory effect on cell proliferation by inhibiting protein synthesis (*4*, *5*). Bacteria, germinating seeds, flagellates, fertilized eggs of sea urchins, and cells in tissue culture were used as test material (*5*). Some of our findings were corroborated by others (*6*). We found that cancer cells in tissue cultures were more sensitive to methylglyoxal than normal ones were, a finding of possible significance for cancer therapy (*3*, *7*).

Swiss albino mice were injected intraperitoneally with 20 million ascites sarcoma 180 cells, and were then treated with an intraperitoneal injection of methylglyoxal (*8*) for 9 consecutive days. The mice were divided into four groups of 20 animals each. In the first group, treatment began 1 hour after inoculation; in the second, 4 hours; in the third, 24 hours; and in the fourth, 48 hours after inoculation. Each animal received 18 injections (four 2-mg injections followed by fourteen 1-mg injections) twice daily, 12 hours apart. Control animals received the same volume of physiological saline. The mice were observed for 10 months. In the first group, 15 animals remained free from ascites; in the second group there were 13; in the third group, 7; and in the fourth group, 4. The rest showed varied lengths of survival. All the control animals died in the first 26 to 34 days of the experiment. The cured animals had normal-sized, healthy litters.

Our experiments show that mice inoculated intraperitoneally with sarcoma 180 can be cured by intraperitoneal injections of methylglyoxal.

These experiments, performed in the winter of 1966 to 1967, were not published because we doubted the value of local treatment of cancer, and no therapeutic effect was obtained with solid tumors of sarcoma 180 on intraperitoneal or subcutaneous injection of methylglyoxal. Our experiments were preliminary, and we planned to extend and improve them. We report them here in response to the paper in which Apple and Greenberg (*9*) described similar results. These authors seem not to have been fully acquainted with our work on methylglyoxal, whose derivative, Kethoxal (Upjohn), is used as a cancerostatic agent.

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Displacement Pattern of the Basilar Membrane: A Comparison of Experimental Data

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