necrotic reaction. Fractions from peak II had a significantly higher antitoxic activity than fractions from peak I; no fraction tested had less antitoxic activity than untreated γ-globulin.

Table 1 shows the average antitoxic and hemagglutination inhibitory activity of fractions from peaks I and II and the ratios of these activities in the six serums studied. Current evidence indicates that digestion of a single antibody molecule will yield either fragments I and III or fragments II and III (*6*). Antibody of one specificity may reside in fragment I and of another specificity in fragment II (*6*). Our data support these concepts; the difference in the ratios for peaks I and II may reflect a similar difference in the distribution of antibody specific for the toxic site as opposed to that directed against other antigenic sites on the toxin molecule.

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Daily Rhythmicity of Corpus Allatum and Neurosecretory Cells in Drosophila melanogaster (Meig)

Abstract. *Adult females of* Drosophila melanogaster *show a bimodal daily rhythmicity in the function of neurosecretory and corpus allatum cells. This result was obtained by measuring the size of the nuclei and determining the pattern of neurohormone secretion.*

Previous experiments with insects seemed to indicate that neurosecretory and corpus allatum cells undergo cyclic changes during 24 hours (*1*). This has been shown either by measuring the nuclear volume by using a biological test or by just observing the amount of neurosecretory material in the cell. For further investigations it seemed desirable to measure also the amount of neurosecretion quantitatively and to work with genetically defined material under standardized conditions, which can be realized rather easily with *Drosophila*.

For these experiments I used highly inbred stocks of *D. melanogaster* and kept them at 25°C under a cycle of 12 hours of light and 12 hours of darkness. Flies, 3 to 5 days old, were killed every 3 hours and treated either according to methods of Gabe (*2*) or Gomori (*3*) for neurosecretory material, or Flax and Himes (*4*) for RNA. Sections of 2-μ or 4-μ thickness were cut with a cooled microtome knife; these sections had to be dried for 3 days on the albumin-coated slides before staining. After being embedded, the long and short diameters of the nucleus were measured by means of a camera lucida; the values were multiplied with each other, because the product gives a less arbitrary indication of the nuclear size than the attempt to calculate the volume.

The amount of neurosecretory material was determined from the absorption in the neurosecretory cells of the pars intercerebralis (*5*) after staining with paraldehyde fuchsin (PAF) or chromehematoxylin phloxine. The absorption spectrum of PAF-stained protein has its maximum at 550 mμ so that the green emission from a mercury vapor lamp could be used as an appropriate light source. The slide was projected by a microscope on a screen with a 0.0625-cm diameter hole opening to a photoelectric element. The absorption was measured once near the nucleus ("circumnuclear"), then toward the axon at the periphery of each cell. By calculating the ratio of these two values some variations in the amount of staining are eliminated, while a good indication is given of the secretory process.

The size of the nucleus of the neurosecretory cells of the pars intercerebralis stained with paraldehyde fuchsin (Fig. 1*a*) shows two peaks during 24 hours: a rather steep peak 3 hours before dawn and another, somewhat smaller but broader, 3 hours before dusk. The curve for the corpus allatum nuclei stained with Azure B (Fig. 1*b*) appears to be similar in the general

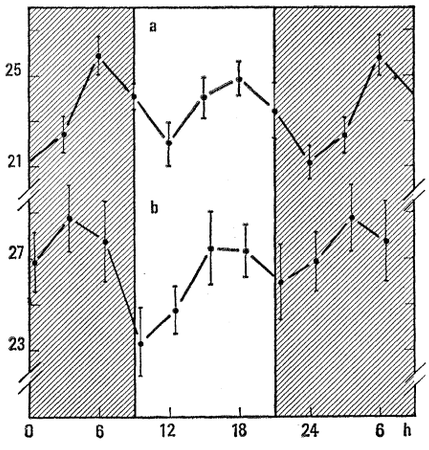

Fig. 1. Nuclear size of neurosecretory cells (*a*) and corpus allatum cells (*b*). Ordinate: product of longer and shorter diameter; abscissa: time in hours. Every point is the mean obtained from measurements on ten female flies, from each of which 15 to 20 nuclei were measured. Points of the dark phase are plotted twice on the same curve; vertical lines indicate the standard error.

shape, except that maxima and minima are occurring 3 hours earlier. The rather high variance in the corpus allatum curve may be due to individual differences in body size, slight differences in the conditions of development, and differences in the phase of the oscillation.

The distribution of neurosecretory

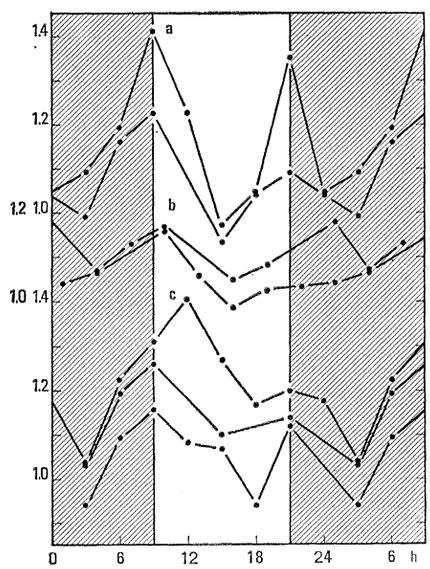

Fig. 2. Absorption of stained neurosecretory material. (*a*, *b*) Stock No. 103; *a* stained after Gabe (*2*), *b* after Gomori (*3*); (*c*) Stock No. 101, stained after Gabe. Ordinate: ratio between circumnuclear and peripheral absorption; abscissa: time in hours. Points of the dark phase are plotted twice on the same curve.

material exhibits changes which follow a bimodal pattern (Fig. 2), the higher values indicating a relatively high absorption by PAF-stained material around the nucleus, the lower values a relatively high absorption toward the axon. Again the variance in the position of a maximum or minimum between individuals, between strains, or between different staining techniques is up to 3 hours; the highest value, however, for the ratio of "circumnuclear" to peripheral absorption remains consistently at dawn. These bimodal changes in the distribution of neurosecretory material suggest a flow from the nucleus to the axon, the release of these granules into the neural pathway occurring at the middle or end of every light and dark phase. This can be confirmed by the observation that neurosecretory granules appear in the corpus cardiacum mainly 3 hours before dawn and dusk, whereas no granules can be detected shortly after the transition from light to dark.

The bimodal pattern of activity in neurosecretory cells, and in the corpus allatum has its parallel in the pattern of the locomotory activity (*6*) and oxygen consumption (*7*) which show peaks around dawn and dusk, so that neuro- and corpus allatum hormones may be a part of the activity controlling mechanism. The phase relation of corpus allatum cells to neurosecretory cells may suggest an activating influence from the corpus allatum hormone on neurosecretion as well as an inhibition in the opposite direction, which would amount to a negative feedback control (*8*). The transport of neurosecretory granules to the corpus cardiacum, the release, and the effect seem to occur within a few hours.

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Human Bone Marrow Distribution Shown in vivo by Iron-52 and the Positron Scintillation Camera

Abstract. *Radioactive iron, which concentrates in erythropoietic marrow, is given intravenously, and 16 hours later pictures of its distribution are taken with the positron camera. The instrument is an imaging device that produces pictures of the distribution of positron-emitting nuclides without scanning. Wide variations in the distribution of marrow are found in various diseases.*

The positron scintillation camera is a sensitive electronic instrument for producing pictures of the distribution of positron-emitting isotopes in vivo. Iron-52 is a cyclotron-produced positron-emitting isotope with a half-life of 8.2 hours. With this new instrument and isotope, we are taking relatively clear pictures of the distribution of erythropoietic marrow in living subjects; we use a dose of Fe^{52} that is within the limit permissible for diagnostic purposes. Less clear pictures of the distribution of marrow in the skeleton have been obtained in the past by the use of Fe^{59} and special scanning devices (*1*), but the positron camera and Fe^{52} provide information previously obtainable only by laborious postmortem examination.

Study of a number of cases has begun to yield characteristic patterns of bone marrow distribution for various disease states. In addition to being of potential diagnostic value, it is expected that these studies will aid our understanding of the pathogenesis of diseases of the bone marrow (*2*). This report deals with the technique and initial clinical results.

The positron scintillation camera has already been described (*3, 4*). It is being used to localize brain tumors with Ga^{68} EDTA (*5*), to study the deposition of F^{18} in bones and teeth of human subjects, and to determine the distribution of positron-emitting tracer compounds in small animals as a function of time after administration.

A diagram of the instrument is shown in Fig. 1. Immediately above the subject is an image detector consisting of a single sodium iodide crystal, 29 cm in diameter and 12 mm thick, activated by thallium—viewed by an array of multiplier phototubes. Below the subject is a focal detector consisting of an array of 19 scintillation counters with separate crystals. Both detectors remain stationary during the time a picture is being taken.

When a positron is emitted in tissue, it travels a few millimeters, and then combines with an electron. Two simultaneous annihilation gamma rays (0.51 Mev) are produced that travel away from the point of origin in opposite directions. The mean variation from 180 deg is 1/137 radian or ± 0.4 deg (*6*).

By use of a coincidence circuit and analog computing techniques, a two-dimensional readout of the distribution of the positron emitter is displayed as a series of position-oriented flashes of light on an oscilloscope. They are recorded on Polaroid film and an image of the distribution of the positron emitter results.

In the image detector, the phototubes are spaced about 7 cm from the crystal so that they view overlapping regions. When a scintillation occurs, the light divides among the tubes. The computing circuits sense the position of the scintillation and determine its x and y coordinates so that the scintillation can be displayed as a point of light on the oscilloscope if coincidence and pulse-height requirements are met. When scintillations occur at intermediate points between the phototubes, their position is still accurately determined because of the proportionate division of light among the tubes. The useful diameter of the crystal, over which an essentially undistorted image is obtained, is about 24 cm.

By summing the outputs from the phototubes, a signal is obtained that is proportional to the brightness of the scintillation without regard to where it occurred. This signal is sent to a pulse-height selector tuned to the photopeak of the 0.51-Mev gamma ray. Gamma rays that have lost an appreciable amount of energy by scattering are rejected. The same image detector is used with pinhole and multichannel collimators to display the distribution of nuclides that emit gamma rays (*4*).

For positron emitters, however, the focal detector and coincidence circuits are used because of the higher sensitivity achieved. Imagine a simplified version of the focal detector with only a single counter located at the center of the array shown in Fig. 1. When one gamma ray hits the counter, the other