Editor's remark: The following article treats a problem of especial interest at the present time, primarily by means of the statistical method. No experimental findings were made, and the authors emphasize that too far-reaching conclusions from their expositions probably are not justified. We are glad to publish the article of the American authors, however, because we believe in this case that we should pass on the valuable stimuli to further investigation.

Cosmic Radiation and Cancer Mortality

By P. A. MORRIS[1], Swarthmore, Pa., and W. J. NICKERSON[2], Boston, Mass.

In the light of recent investigations concerning the relationship between cosmic radiation and cancer[3], and the production of radiocarbon from cosmic radiation[4], the authors anticipate further experiments which will seek to demonstrate the existence of correlations between certain fluctuations in the intensity of cosmic radiation and cancer incidence or mortality. We have endeavored to include in the present paper a collection of data which will serve primarily as a basis for discussion and perhaps as a starting place for further investigations. Two types of variation in the total intensity of cosmic radiation come to mind immediately; the geomagnetic latitude effect and the altitude effect. The magnitude of these effects may be observed in Figs. 1 and 2, respectively.

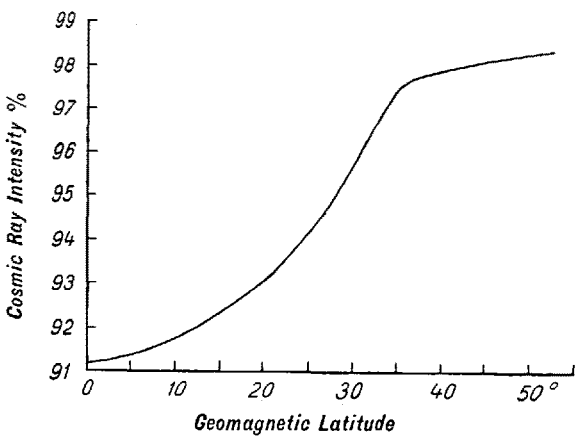

Fig. 1. – Cosmic Ray Intensity vs. Geomagnetic Latitude[5].

It will be observed in Fig. 1 that the minimum intensity occurs in the region of the geomagnetic equator and is of the order of 10% less than the total intensity incident in the high latitudes. The maximum displacement in latitude that a location on the earth's surface can undergo in conversion from geographic to geomagnetic coordinates is approximately 11·5 degrees. Even in the region of most rapid change in total intensity, this displacement in latitude would correspond to a change of less than 4% in the total intensity of cosmic radiation as observed at sea level (it should be remembered that there exists a 4% change in intensity between sea level and approximately 1,000 feet). It is doubtful, therefore, if one can distinguish between geographic and geomagnetic latitude in any variation with latitude that might exist in rates of cancer incidence or mortality as a result of the variation in total intensity of cosmic radiation.

Data on cancer mortality for countries and cities of the world have been obtained from various sources (as indicated) and plotted against the geographic and geomagnetic latitudes of the region. That the mortality rates for certain types of cancer do vary with latitude is demonstrated by Figs. 3–6, 11, 13, 15. That there is little choice between geomagnetic latitude and geographic latitude may be observed by a comparison of Figs. 3 and 4, and Figs. 5 and 6. The variation is not clearly defined, however, because of the scatter of the separate observations. The scatter may be entirely statistical, owing to the nature of the observations (including

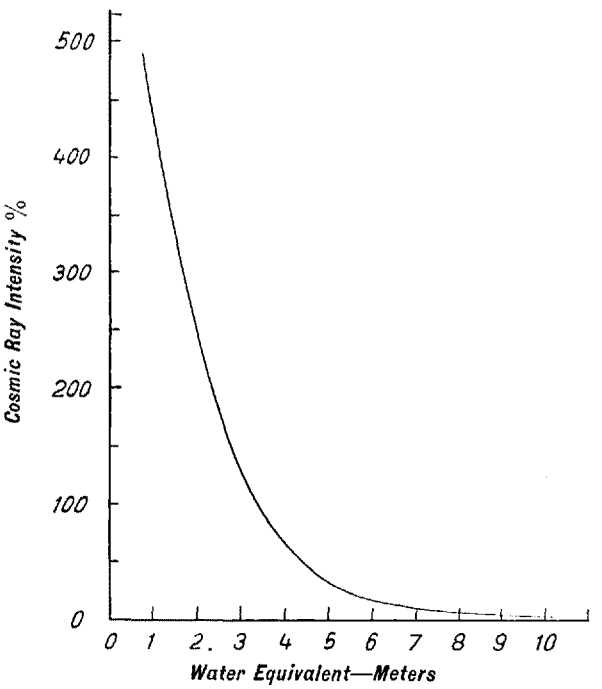

Fig. 2. – Cosmic Ray Intensity vs. Altitude[1].

[1] Bartol Research Foundation of the Franklin Institute, Swarthmore, Pa.

[2] Wheaton College, Norton, and Tufts Medical School, Boston, Mass. – Guggenheim Memorial Fellow at Carlsberg Laboratories, Copenhagen, Denmark, 1947–8.

[3] J. EUGSTER and V. F. HESS, Die Weltraumstrahlung (kosmische Strahlung) und ihre biologische Wirkung. (Orell-Füßli-Verlag, Zurich 1940). – F. H. J. FIGGE, Science *105*, 323 (1947).

[4] E. C. ANDERSON et al., Science *105*, 576 (1947).

[5] After A. H. COMPTON and R. N. TURNER, Phys. Rev. *52*, 799 (1937).

[1] After I. R. BOWEN, R. A. MILLIKAN, and H. V. NEHER, Phys. Rev. *52*, 80 (1937).

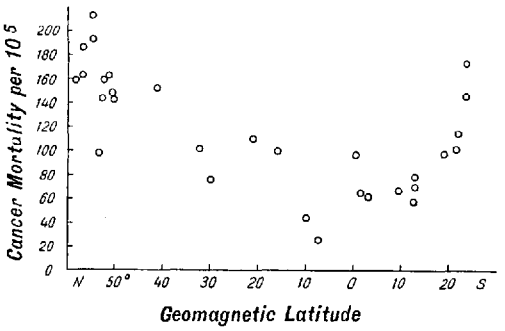

Fig. 3. – Cancer Mortality vs. Geomagnetic Latitude for Cities in the Western Hemisphere larger than 300,000[1].

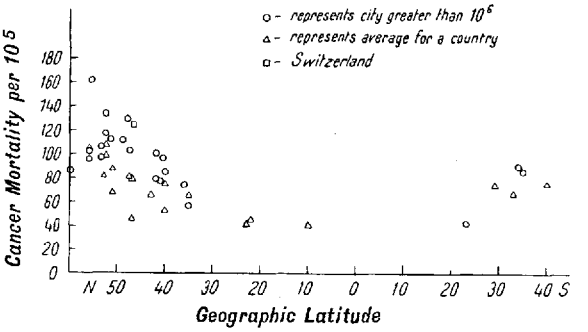

Fig. 6. – Cancer Mortality vs. Geographic Latitude throughout the world [2].

diagnosis), or may be caused by reasons unknown. It is conceivable that the entire variation may be a function of climate, or other phenomena, which vary with the latitude and which tend to favor carcinogenesis. However, in so far as the authors are aware, there does not exist at this time any known relationship between carcinogenesis and phenomena which are known to vary more or less directly with the absolute value of the latitude (as required for agreement with the relationships shown in Figs. 3 to 6), such as temperature range and extremes, humidity range and extremes, duration of daylight, etc. It has been suggested by PITTARD[2] that ethnical considerations play an important role in cancer incidence. We do not feel that the

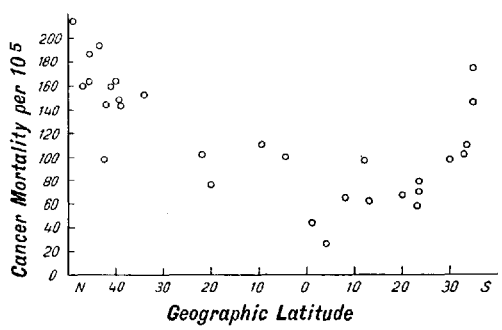

Fig. 4. – Cancer Mortality vs. Geographic Latitude for Cities in the Western Hemisphere larger than 300,000.[1]

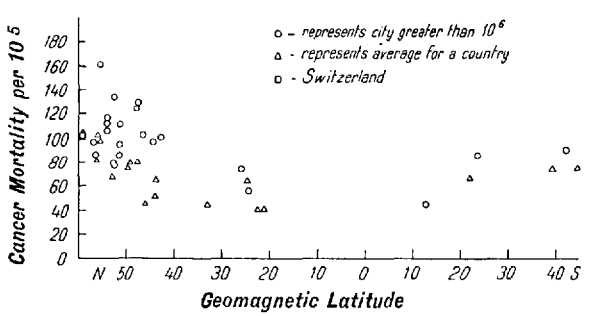

Fig. 5. – Cancer Mortality vs. Geomagnetic Latitude throughout the world[3].

data available at present are sufficient to be conclusive on this issue.

The possible importance of the factors above mentioned prohibits, at the present time, the conclusion that the latitude effects of certain types of cancer mortality are, or are not, a function of variation in cosmic radiation. In addition, it should be remembered that radiation from radioactive sources plays an important role in the amount of radiation sustained by an individual.

In an effort to compare the strengths of different radiations to which the body is subject we shall use the gram röntgen unit. The gram röntgen shall be defined as the amount of radiation which will produce $1{\cdot}6 \cdot 10^{12}$ ion pairs per gram. (This figure corresponds to one electrostatic unit of ions per cm^3 in air.) We find, then, that the equivalent radiation received from cosmic rays is of the order of 10^{-4} röntgen/day[1]. The gamma radiation from the earth's surface is also of the order of 10^{-4} röntgen/day[3], although this figure is subject to wide variations due to local conditions. In comparison with these figures, it can be shown that the radiation from the K^{40} in the body is sufficient to subject a man to the order of 10^{-4} röntgen/day. To sum up, then, we find that the primary radiation from cosmic rays is probably not different by an order of magnitude from the radiations received by natural sources to which the body is exposed. While the values given in röntgen units for gamma and for K^{40} radiation probably represent near maximal values, the secondary radiation from cosmic ray showers may subject an organism to a vastly greater intensity of ionizing radiation[4].

In addition to the radiations mentioned above, it may prove valuable to investigate further the effects of the latitudinal distribution of ultra-violet light on normal mutation production[5]. Some very interesting

[1] Data for period 1936–42 as published in Pub. No. 195 Pan American Sanitary Bureau: Biostatistical and Epidemiological Report on the Americas (R. H. MARTINEZ, 1943).

[2] E. PITTARD, Exper. 2, 306 (1946).

[3] Data for period 1908–12 as published by HOFFMAN, The Mortality from Cancer throughout the World (Prudential Press, 1915).

[1] A. H. COMPTON and I. A. GETTING, Phys. Rev. 47, 817 (1935).

[2] See footnote 3, left column.

[3] V. F. HESS, Carnegie Inst. of Wash. Year Book 43, 54 (1944).

[4] N. ARLEY, Stochastic processes and their application to the theory of cosmic radiation (Gads Forlag, Copenhagen, 1943).

[5] Experimental induction of skin cancer in mice by ultra-violet radiation has been shown by H. F. BLUM, J. Nat. Canc. Inst. 5, 89 (1944).

Fig. 7. – Cancer Mortality vs. Urban Percentage of Population for each of the United States[3].

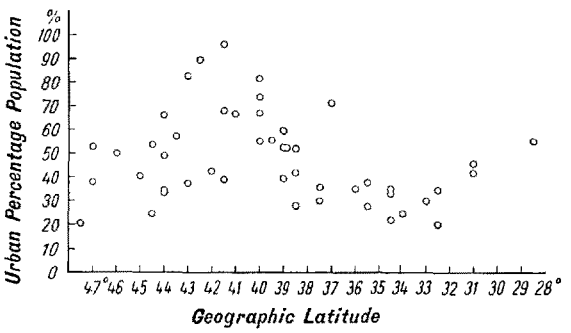

Fig. 8. – Urban Percentage of Population vs. Geographic Latitude[3].

work has already been done along these lines by HOLLANDER and EMMONS[1], for example. However, it should be remembered that the latitudinal distribution of total ultra-violet intensity is approximately the inverse of the relationship shown in Fig. 1 for cosmic radiation (note Fig. 12).

As pointed out by FIGGE[2], the cosmic ray shower producing properties of ceilings, roofs and other building materials, might lead to an increased amount of radiation sustained by persons who spend long periods of time in office buildings and the like. One must remember, however, that the low energy rays, which are the most prolific shower producers, and the low energy rays which are their progeny, are also those rays which are most readily absorbed by screening materials.

Whereas it has been known for some time[4] that cancer mortality rates are higher in urban areas than rural areas (see Fig. 7), it is impossible to conclude at this time that this indicates a correlation between cancer mortality and intensity of cosmic radiation. Fig. 7 is presented to show the good correlation between cancer mortality rates and percentage of urban population in a state. However, the criticism may arise that this conclusion is unjustified because of the higher concentration of urban areas in the northern section of the United States, where the mortality is higher, than in the southern section, generally speaking. For this reason, we show in Fig. 8 the percentage of urban population in a state plotted against the average latitude of the state. We believe that the difference in the degree of correlation between the two graphs is sufficiently large to give strong evidence for the correlation between urban percentage and cancer mortality rates. In addition, if we extrapolate the data in Fig. 7 to the 100% urban population of a city (which may or may not be justified) we find the rate of 150 per 100,000 in good agreement with the rates given for cities in the United States.

Further significance is given to this phenomenon when one considers the present trend in mortality rates at ages over 45 from all causes of death. According to WATKINS and DE SAO PAULO[2] the mortality at ages above 45 has generally been declining and the rates of decline are greater in industrialized areas than in non-industrialized ones. The increase in cancer mortality rates, therefore, appears as a counter current.

If it is assumed that a correlation between total cancer mortality and the distribution of cosmic ray intensity does exist, as indicated by Figs. 3 to 6, one might be led to consider only those functions which vary directly with latitude as being intimately related to carcinogenesis. This restriction would direct one's attention toward physical phenomena and effectively exclude all biological function. (Biological investigations have emphasized the unity in biochemical processes and the constancy of the species. These are not matters, so far as we know, that are subject to varia-

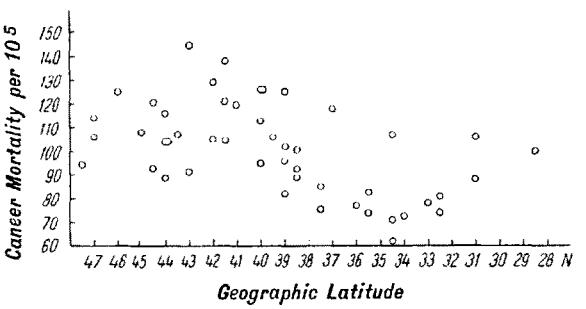

Fig. 9. – Cancer Mortality vs. Geographic Latitude for each of the United States[1].

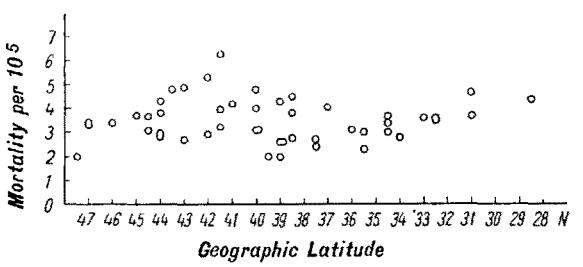

Fig. 10. – Buccal Cavity and Pharynx Cancer Mortality vs. Geographic Latitude for each of the United States[1].

[1] A. HOLLANDER and C. W. EMMONS, Symposia on Quantitative Biology (Cold Spring Harbor) *11*, 78 (1946).

[2] F. H. J. FIGGE, Science *105*, 323 (1947).

[3] Data for 1935–7, J. Nat. Canc. Inst. *6*, 251–299 (1946).

[4] F. L. HOFFMAN, The Mortality from Cancer throughout the World (Prudential Press, 1915).

[1] Data for 1935–37, J. Nat. Canc. Inst. *6*, 251–299 (1946).

[2] J. H. WATKINS and S. DE SAO PAULO, Yale J. Biol. a. Med. *19*, 443 (1947).

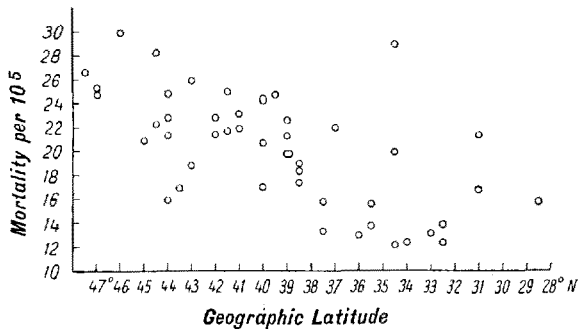

Fig. 11. – Stomach and Duodenum Cancer Mortality vs. Geographic Latitude for each of the United States[1].

tion with latitude[2].) However, there are well authenticated examples of unequal distribution of resistance and susceptibility to disease among populations within the human race. Cancer of the breast is frequently cited[3] in this connection. It might be that the distribution reflected in Figs. 3 to 6 for total cancer mortality, is related to clinical variables that vary noticeably with latitude (Fig. 11) and are sufficiently potent to control

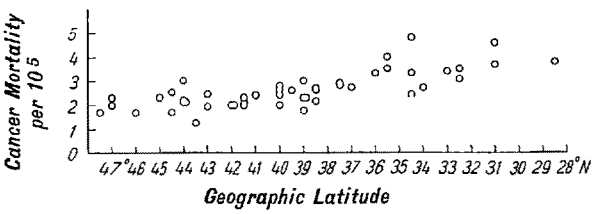

Fig. 12. – Skin Cancer Mortality vs. Geographic Latitude for each of the United States[1].

the form of the curves for the distribution of total cancer mortality (Figs. 3 to 6). Other variables, that are less potent, may be independent of latitude (Figs. 10 and 14), or may vary indirectly as the latitude (Fig. 12) and be the result of different causes.

Perhaps the most fruitful field in the endeavor to discover whether or not a significant correlation exists between cancer incidence and mortality and cosmic

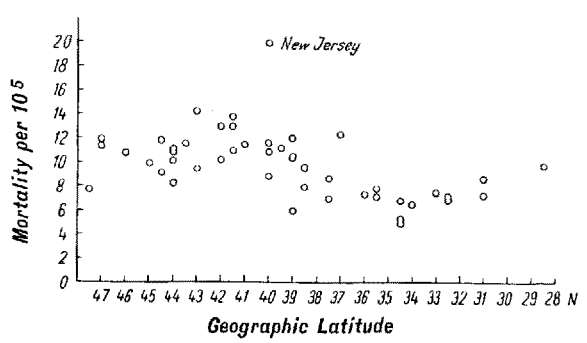

Fig. 13. – Breast Cancer Mortality vs. Geographic Latitude for each of the United States[1].

[1] Data for 1935–37, J. Nat. Canc. Inst. *6*, 251–299 (1946).

[2] Fertility has been considered to vary with latitude; it is thus of interest that J. BARNÓTHY and M. FORRÓ, Exper. *4*, 31 (1948) have demonstrated the lethal action of cosmic ray showers on the progeny of mice and of rabbits.

[3] F. L. HOFFMAN, loc. cit.

radiation, will be a study of altitude effects. The change in the total intensity of cosmic radiation from sea level to 5,000 feet is the order of a factor of two. The authors were unable to obtain sufficient data on cancer mortality with respect to altitude to present a graph. However, we should like to point out the singular position of the data for Switzerland. The mortality rate in Switzerland is approximately 1·8 times the average rate for other countries in the same latitude (see Figs. 5 and 6).

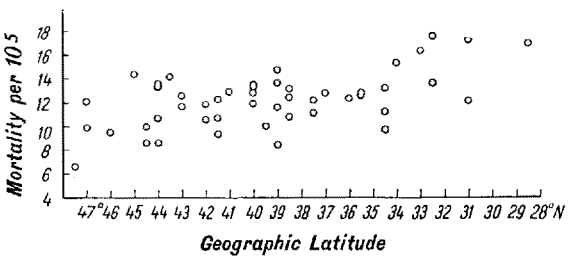

Fig. 14. – Liver and Biliary Passages Cancer Mortality vs. Geographic Latitude for each of the United States[1].

In compiling the data, the rates for cancer mortality were obtained from the sources mentioned on the graphs. The geomagnetic latitude was computed for each point from the following relationship, which assumes the earth's magnetic field as that of an eccentric dipole[2]:

$$\sin \lambda = \cos \psi \cos (\omega - \varphi) \cos L + \sin \psi \sin L$$

where

λ = Geomagnetic latitude of the place
ψ = Geographic latitude of North magnetic pole
φ = Geographic longitude of North magnetic pole
ω = Geographic longitude of the place
L = Geographic latitude of the place.

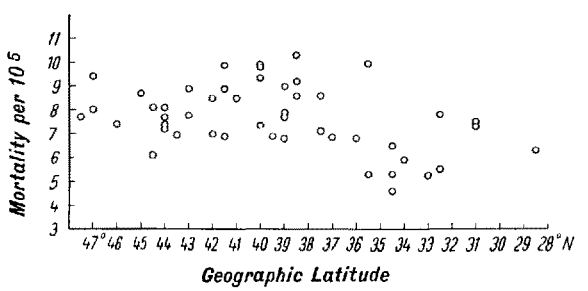

Fig. 15. – Uterus Cancer Mortality vs. Geographic Latitude for each of the United States[1].

The authors have made no correction for altitude in the data here presented, because most of the data are for sea level locations and the large scatter of these points does not warrant the application of altitude corrections to the others.

It will be noted that the authors have confined themselves, in speaking of cosmic radiation, to the

[1] Data for 1935–37, J. Nat. Canc. Inst. *6*, 251–299 (1946).

[2] L. A. BAUER, Terrestrial Magnetism *28*, 1 (1932).

total intensity. By this we mean all types of particles or rays whose origin may be traced to the incoming primary cosmic radiation. In the endeavor to establish a relationship between cosmic radiation and carcinogenesis, it may be well to keep in mind the various types of particles and rays that occur in the secondary radiation which is incident at the earth's surface, and to remember that their frequency distribution with respect to altitude, latitude, and absorbing or shower producing material may be quite different from that manifested by the total radiation.

(Vide addendum p. 284)

In conclusion, we should like to express our appreciation and gratitude to Professor G. DE HEVESY and Drs. L. J. MULLINS, J. OTTESEN, K. ZERAHN, and W. F. G. SWANN for reading the manuscript and offering advice.

Zusammenfassung

Es wird versucht, die Krebssterblichkeit in verschiedenen Orten und Ländern mit der dort vorhandenen Intensität der kosmischen Strahlen in Verbindung zu bringen. Gewisse klinische Faktoren beeinflussen allem Anschein nach die offensichtliche Abhängigkeit der Krebssterblichkeit von der geographischen Breite und damit von der Stärke der kosmischen Strahlen. Im Hinblick auf neuere experimentelle Ergebnisse (Erzeugung von kosmischen Strahlenschauern unter Blei und Krebserkrankungen) wird auf den Zusammenhang zwischen Krebssterblichkeit und «percent urbanity» hingewiesen. Die Häufigkeit bestimmter Krebsarten ist indessen, das muß betont werden, von der geographischen Breite vollkommen unabhängig. Bei der Auswertung des angeführten Materials ist einige Vorsicht notwendig; definitive Schlußfolgerungen sind noch nicht möglich. Es werden Vorschläge zum Ausbau dieser Forschungen gemacht.

Das organische Wachstum und seine Gesetzmäßigkeiten

Von LUDWIG VON BERTALANFFY[1], Wien

1. *Einleitung*

Daß Pflanzen, Tiere und Menschen wachsen, ist eine banale Tatsache; daß nicht nur die Bäume nicht in den Himmel wachsen, sondern daß das Wachstum auch bei Tier und Mensch eine Grenze findet, ebenfalls. Fragen wir in der Physiologie über das Problem des Wachstums nach, so berichtet sie uns eine Fülle von Tatsachen über *Beeinflussungen* des Wachstums, wie sie beispielsweise durch die Ernährung, die Temperatur, den Lebensraum eines Organismus, insbesondere aber durch Wirkstoffe, wie Hormone und Vitamine, bedingt sind. Aber die Physiologie ist bisher kaum der Frage nähergetreten, welches denn die Gründe des Wachstums *als solches* sind. Das Wachstum beruht auf der Fähigkeit der Assimilation durch die einzelnen Zellen und den Gesamtorganismus; aber warum hört es schließlich auf? Das kann nicht an den Zellen liegen; wir wissen ja, daß in der Gewebekultur tierische Zellen unbegrenzt leben, wachsen und sich teilen können. In der Physiologie finden wir bisher kaum eine Erklärung für das Wachstum, außer dem Hinweis auf einen recht mysteriösen «Wachstumstrieb», und in führenden Darstellungen und Lehrbüchern lesen wir Sätze wie etwa: «Ebensowenig wie wir etwas über die Ursachen des Wachstums wissen, ebenso unerklärlich bleibt uns schließlich seine Abnahme im Alter», oder: «Die innere Ursache des Wachstums ist unbekannt».

Eine recht unbefriedigende Antwort auf eine Frage, die zweifellos ein grundlegendes Phänomen des Lebens betrifft. Wir wollen ihr eine zweite, nicht weniger unbequeme Frage anschließen. Die Organismen treten uns als eine Fülle unzähliger Gestalten des Tier- und Pflanzenreichs entgegen. Mit dieser Formenfülle setzt sich die Biologie in verschiedener Weise auseinander. Sie beschreibt und ordnet sie in der Morphologie, sie untersucht diese Gestalten im Hinblick auf die Funktionen, welche sie leisten, in der physiologischen Anatomie, sie lehrt sie uns in ihrer keim- und stammesgeschichtlichen Entwicklung usw. verstehen. An einem bestimmten Punkt bleiben wir jedoch unbefriedigt. Die organischen Formen scheinen sich einer *quantitativen Analyse* zu entziehen; wir können anscheinend ihre Vielfalt nur beschreiben, nicht aber exakt faßbare Gesetzmäßigkeiten für sie aufstellen.

Wachstum und Gesetze der organischen Formen — damit sind zweifellos zwei grundlegende Probleme des Lebendigen angegeben. Ist die eben angedeutete Resignation nun notwendig, oder vermögen wir doch Wege ausfindig zu machen, diese Probleme einer gedanklichen und damit schließlich auch praktischen Beherrschung zugänglich zu machen? In der Tat vermag die Forschung den genannten Problemen auf verschiedenen Wegen, die im folgenden skizziert seien, näherzukommen. Soweit nicht anders angegeben, beruht die folgende Darstellung auf den Arbeiten des Verfassers und seiner Mitarbeiter[1].

Wir wollen mit einer ganz allgemeinen Feststellung beginnen. Die Formen, in denen uns das Lebendige gegenübertritt, sind nur äußerlich beständig und gleich-

[1] Zoologisches Institut der Universität Wien.

[1] L. v. BERTALANFFY, Roux' Arch. *131*, 613 (1934); Human Biol. *10*, 181 (1938); Roux' Arch. *140*, 81 (1940); Biol. generalis (Wien) *15*, 1 (1941); (mit M. RELLA) Roux' Arch. *141*, 33 (1941); Biol. Zbl. *61*, 510 (1941); (mit I. MÜLLER) Riv. Biol. *35*, (1943); Z. vergl. Physiol. *30*, 139 (1943); Biol. Zbl. *63*, 446 (1943); Forsch. u. Fortschr. *19*, 13 (1943); Z. Rassenkde. *13*, 277 (1943); (mit O. HOFFMANN-OSTENHOF und O. SCHREIER) Nature *158*, 948 (1946); Mh. Chem. *79* (1948); (mit O. SCHREIER) Österr. Zool. Z. (im Druck).