gleichzeitig laufen lassen kann, trennen 14 von den 19 PTH-Aminosäuren der Tabelle IV. Mit Hilfe einer einfachen Oxydationstechnik (Fig. 7) und durch saure Hydrolyse mit anschliessender dünnschichtchromatographischer Identifizierung der freigesetzten Aminosäure, die hier in jedem Fall hydrolysebeständig ist, werden die noch fehlenden 5 Substanzen mit wenig zusätzlichem Aufwand ebenfalls nachweisbar (Fig. 8 und [24]). Zum Sichtbarmachen der PTH-Aminosäuren bewährt sich ein modifizierter Chlor-Tolidin-Test; die Erfassungsgrenze liegt bei etwa $3 \cdot 10^{-4}\,\mu M$, das heisst zum Beispiel bei 0,05 μg PTH-Pro (!).

Summary. Methods for the identification of DNP- and PTH-amino acids are improved by application of thin-layer chromatography using Kieselgel G. The advantages over paperchromatography are better resolution, increased sensitivity and time-saving.

Cell Metabolism and Virus[1]

By E. Kovács[2]

Viral infection is a cellular phenomenon. The virus, as a particle of macromolecular organization – or one part of it, the nucleic acid moiety – adsorbed on the external barrier of the cell, penetrates into it, takes over command of various physiological functions and determines or provocates its own reproduction by the host-cell. Thus, one might assume *a priori* a profound alteration, almost a metamorphosis of the cellular metabolism as the consequence of infection *with* and biosynthesis *of* the virus. As a matter of fact, experimental data accumulated up-to-date support the rightness of such ideas[3,4], in spite of many difficulties for the technical approach. For instance, up to about the last one and half decades, living experimental animals were almost exclusively used, which fact means a heterogeneous cell population regarding morphology and function, or viral sensitivity. With the use of chorio-allantoic membranes (CAM) of embryonated eggs[5], and later the tissue cultures of mammalian cells, for virus research[6], it became possible to study the sequence of events at the cellular level, also in viral diseases of animals. By this way, our actual concept of Virology was born: a biochemical and molecular one, quite different from the orthodox, bacteriological, and microbiological ideology. Thus the virus disease is a novel chapter of the Cell Physiology and Cell Pathology; 'a chemical infection' caused by invading *macromolecules*.

After this preamble, we want to limit this broad subject almost exclusively to the discussion of data regarding the metabolism of mammalian cells. Especially findings obtained in cultivated cells will be reviewed for the characteristic alterations caused by various viruses. Two great categories will be excluded from the beginning, namely that of the bacteriophage and plant viruses. These limitations allow us to list in this relation pertinent findings with the animal viruses, including human ones. However, this domain is so extremely rich, that only the most important experimental facts can be presented and discussed.

Cell respiration and virus. From the historical angle, we quote experiments intended to demonstrate, without success, changes in O_2 consumption of brain slices derived from animals infected with poliomyelitis virus[7]. On the other hand, a slight increase of respiration was described in western equine encephalitis virus infected tissue cultures[8]. However, brain homogenates of mice paralyzed with human or murine poliomyelitis did not differ from the normal controls regarding respiration[9,10]. Later PARODI[11] and others[12–14] observed, with more refined special techniques, an increase, respectively the decrease of oxygen consump-

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tion in fowls eggs inoculated with the virus of influenza, WEE, and Newcastle Disease, but no change with mixoma virus[14]. More recently, the group of SYVERTON investigated systematically this problem in HeLa cell cultures[15–17]. They did not find significant differences between those infected with poliovirus and the non-infected cells, so long as drastic morphological changes did not occur. In contrast to earlier work[16], these authors recently described the propagation of poliovirus under anaerobic conditions[17], although the latent period became somewhat prolonged. The results of DEKEGEL[18], however, are at variance with the above findings, although obtained under not comparable circumstances. Other works also emphasize the importance of oxidative energetic processes, employing different techniques and host-virus systems[19–22]. With the use of 2,4-Dinitrophenol (DNP) THOMPSON[23] and later ACKERMANN et al.[24] revealed the dependence of virus production on the oxidative phosphorylation in connection with vaccinia infected Maitland Type tissue cultures, and influenza infection of CAM *in vitro*. Similary GIFFORD et al. claimed more recently greatly reduced yield of poliovirus in HeLa cells treated with non-toxic doses of DNP[25]. In conclusion, we may say, that there is large variation in experimental results obtained by different systems regarding the gas exchange of virus infected cells. However, in general *the normal respiratory quotient of the cell suffice* for the biosynthesis of a virus. The alterations of respiration are perhaps of secondary nature, due to morphological changes of degenerative character. This was evidenced by the classical experiments of HOWE et al.[26] on the cytochromeoxidase and succinic dehydrogenase of anterior horn neurons in monkeys paralyzed following experimental poliomyelitis infection. Similar works should be repeated in tissue culture, where the sequence of the pathological and biochemical changes could perhaps be followed with less difficulty.

Glucose utilization in infected cells. This is a very intensively worked field of cell biochemistry and pathology, but the literature shows many contradictory results. The experiments of RACKER et al.[27,28] will be more extensively quoted; first of all because they illustrate the hidden difficulties of such work and for the possible theoretical significance of their findings. RACKER et al.[27] have observed the diminution of glycolysis in brain homogenates of mice infected with murine or human poliovirus (of Theiler's respectively Lansing strains). Such homogenates proved inhibitory to glycolysis also, when added to normal cell suspensions[28]. After time consuming laborious work, a complicated biochemical mechanism was revealed: a typical example of pathological changes on the molecular level. One abnormally high iron content of the infected homogenates was detected[29] which enhanced some proteolytic enzymes. This Cathepsin-type of biocatalyst, on the other hand, destroyed the hexosediphosphate-dehydrogenase, disturbing in this way the regeneration of ATP, thus *interferring* with the normal functioning of the glycolytic cycle. We have to say at once that perhaps here also it is a secondary phenomenon revealed and the experimental set-up was not adequate to discover the basic cause, but only the vitious circle of the metabolism. Hence it remained the privilege of other, especially tissue-culture workers to demonstrate the initial increase of glycolysis in a very early stage of the infection, as evidenced by decrease of glucose concentration or enhanced lactic acid production[14, 30–33]. It seems that the glucose is the fuel of the virus synthesis[18,34]. However, the production of influenza virus in cells maintained on simple physiological salt mixture (Tyrode's solution), containing low concentrations of glucose[35], and that of poliovirus on salt solution alone[36,37], or only with 0.5 g/l glucose[38], substantiate the conclusion that the intracellular stock of nutrients suffice for virus reproduction in certain cases.

Toxic metabolites and other inhibiting substances may interfere with various phases of the glycolytic cycle[29,31,39]. It is pertinent to quote the claim of ISAACS[40] on the hyper-glycolytic effect of the 'interferon', a not fully defined biological product of virus-

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host interaction[41], claimed to be the cause of interference with influenza virus infection. In concluding our discussion, it is sufficient to say that certain chemicals, for instance certain antiglycolytic substances, suppress the biosynthesis of various viruses[18, 23, 42–44]. Unfortunately, the practical application of this theoretical approach is frustated by many factors actually not within the grasp of clinical medicine, although encouraging experimental results were reported recently[41].

Krebs-cycle and viral infection. Thus the normal functioning of the tricarboxylic cycle of the host cell is necessary for virus propagation. This is almost an axiome of modern Virology, as demonstrated by many workers in different systems[42–48]. As a matter of fact, inhibitors of the Krebs-cycle reduce the multiplication of influenza, polio, mumps, EEM, PVM, virus extensively, *in vitro* and partly *in vivo* experiments also. The viruses so far investigated *do not possess Krebs-cycle or other metabolic enzymes*, thus the above fact may be additional strong evidence for the complete *metabolic dependence* of the virus on the biochemical organization of the host-cell. Being, however, of highly cytotoxic nature, these inhibitors were not yet successfully applied in clinical or veterinary medicine.

Lipid metabolism of virus infected cells. The metabolism of fats in connection with virus infections was investigated only recently, general attention being orientated towards other sectors, e.g. the carbohydrate utilization. Biochemical analyses, and especially radiophosphorus studies, demonstrated the marked enhancement of the turnover rate of the lipidic fraction of cells infected with GD VII strain of murine poliovirus[49] or with human poliovirus[50, 51]. We might take these findings as the indication of a general activation of the cell-metabolism and may be not of a specific nature, because the above viruses do not contain lipids as integral structural constituents, at least in their final mature forms[52]. However, infections with other lipid containing viruses (e.g. lipoid membranes) should be more intensively studied from this angle[53]. We might justly conclude that the fat metabolism may also be activated in virus-infected cells and the lipids may be utilized as a source of energy or as building stones for the virus particles.

Inorganic salts in infected cells. We mentioned before the enzymatic anomalies caused by increased iron concentrations in nerve tissue of mice infected with Theiler virus[28, 29]. Other results on record regard changes in inorganic phosphorus concentrations[32, 54, 55] magnesium[56] and, naturally, potassium and sodium [57–59], the much preferred ions of physiologists[59]. The primary nature of these alterations, however, is open to question, because the intra- and extra-cellular concentration of such ions is the function of permeability of the cell membrane to inorganic salts: in other words, it depends on the active and passive transport of such elements. These factors, on the other hand, govern the hydration state of the colloids and macromolecules, which form complexes with the various anions[59, 60]. An important feature has to be discussed in spite of the limitation of space: namely, the rôle of bicarbonate. The presence of this salt seems to be an essential factor not only for the physiology of cultivated cells, but for the biosynthesis of various particles, such as herpes, polio- and Coxsackie viruses[61]. The opinion of CHANG, who stipulates the precursor rôle of bicarbonate in nucleic acid synthesis, and not merely a regulator of the Hydrogen ion concentration of the internal 'Milieu' of the cells[59, 60] will be discussed later. Similarly, the inhibitor or activator effect of some metabolic ions, and of trace elements in general, is deeply connected with the physiological function of various enzyme systems. However, as was recently showed by KOVÁCS et al.[38], poliovirus propagation may take place even in media *lacking* inorganic salts, with the exception of bicarbonate. The inoculum however has to be suspended in complete media, containing inorganic ions. In isotonic sucrose alone, the virus will not be adsorbed to the cells[62], because the process requires optimum Calcium and Magnesium concentrations[63], a fact more extensively studied in

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connection with bacteriophage[64]. On the other hand, the virus already penetrated into the cell may determine its own reduplication *even if the external medium is lacking in salts or nutrients.* This is a conclusion which has to be underlined, because it is another solid argument in favour of the *autarchy* of the host-cell during the biosynthesis of the virus.

Metabolism of nucleic acid of virus infected cells. Abnormalities of general cell activities were listed in the preceding sections, which are more the signs than the essence of the primary pathology. With the study of nucleic acid changes, however, we reach the real cause of the alterations mentioned before: namely, the invasion of a cell by a specific type of macromolecule, which is not, or need not be, too different from the host material. This fact enables the cell to resynthetize it on the order, or on the *cytochemical stimulation* of the newly emerged 'model' substance. Now enough experimental evidence has been accumulated proving the identity of the genetic material with the infectious nucleic acid of various viruses[65–78]. Thus the metabolic studies of nucleic acids during virus infection are of capital importance. This is further emphasized by the rôle assigned to nucleic acids (especially RNA) in protein biosynthesis in general and the protein moiety of the virus in particular. The latter determines the physical form, shape, and serological specificity of a virus[79]. Thus protein metabolism has also to be understood and recapitulated briefly in order to draw an integrated picture of the behaviour of host-cells following infection with virus.

The 'classical' genetic material, the DNA seems to possess more physicochemical and biological stability than the RNA, at least during the interphase of the mitotic cycle or in nondividing cells. However, as we shall see in connection with DNA containing viruses, the general behaviour of this nucleic acid may be similar to that of the RNA. Many experimental results are available showing a quantitative decrease of RNA concentration in organs of animals infected with various viruses. For instance, SOURANDER demonstrated the decrease of RNA by ultraspectrophotometric techniques in spinal ganglions of chick embryos infected with rabbic virus[80]. This reduction occurred long before any inflammatory reaction; thus it may reflect a primary host-virus interaction. Others[81–83], by similar methods, were able to reveal increase in nuclear or cytoplasmic nucleic acids at an early stage of the infection. Thus, we may conclude, especially on grounds of the biophysical and biochemical investigations of the group of ACKERMANN of Ann Arbor[84,85], that the virus multiplication is preceded by a highly increased RNA, necessary for the biosynthesis of the virus and host nucleic acid, or nucleo-protein. With the progression of the infection with poliovirus, *in vitro*, or polioencephalomyelitis virus, *in vivo*, the RNA concentration decreases to levels below those of the normal controls[86,87] or remains constant in others[88,89]. This descripton, however, is an over-simplification, because others demonstrated large periodical fluctuations in the RNA and protein levels of non-infected HeLa cells, which findings cast much doubt on some of the above results[90–92]. Furthermore, there are additional data revealing a subnormal incorporation of P^{32} into the DNA of HeLa cells infected with poliovirus[86]. There is more agreement in the 'turnover' studies regarding the incorporation of radioactive phosphorus in the RNA of infected cells[48,54,84–86,89,90]. Technical difficulties inherent in biological assays may be responsible for the discrepancies, even in less complex experimental set-ups, such as tissue cultures. The drop of RNA of cortisone-treated and influenza virus-infected CAM was described years ago by WOMACK et al.[93], but all these works have to be repeated with more refined techniques.

GINSBERG et al.[94] confirmed the increase of DNA during adenovirus infection, and other workers did

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the same with polyhedrosis virus of insects[95]. These observations bear some analogies with the above findings[85,86] because they demonstrate DNA-increase of the host-cell in infections with DNA viruses[94–99].

Besides quantitative differences in nucleic acid and protein content between non-infected and infected cells, there have been many attempts to demonstrate qualitative differences between the viral and host nucleic acids. *In vivo* experiments of SIEGEL and KUUSI[100] with MEF-I strain of poliovirus, and those of ADA and PERRY[101] with influenza, REDDI[102] with plant viruses, or SCHWERDT et al. using crystalline poliovirus, did reveal variations between different virus strains[102], or host and virus NA[103]. However, the striking differences found by WYATT and COHEN[104] with the discovery of 5-methylcytosine in *E. coli* phage were not yet reduplicated in other sections of Virology. Even the above findings need confirmation in view of the marked heterogenity of cellular RNA from various sources, or regarding purine and pyrimidine ratios[105–107], which may depend upon the functional state of the cells. We ignore the mechanism of polynucleotide-synthesis in infected animal cells; notwithstanding, phosphorylases analogous to those isolated by the group of OCHOA[108] and KORNBERG are present also in animal cells[109,110] and the effect of phage infection on bacterial phosphorylases was studied by BESSMAN[111].

The influence of depolymerization of nucleic acids on virus propagation was studied by pretreatment of the cells with crystalline RNAse, prior to infection. The enzyme enters the cells and degrades cellular RNA[112] so that at the time of the subsequent inoculation with virus there may be a diminished concentration of highly polymerized RNA available intracellularly. LECLERC found in CAM, prepared as said before, a blockage of influenza virus multiplication. It seems that the presence of cellular macromolecular RNA is necessary for virus production[113,114]. Similar but less suggestive results were obtained by BARSKI with poliovirus in Rhesus kidney cells[115].

Aspects of the protein metabolism and virus infection. Any classification in a period of transition has its pitfalls. Therefore it may be possible that protein metabolism is more important for virus production than is supposed nowadays, or it may be at least of equal biological importance with that of the nucleic acids, which stands in the focus of today's experimental and theoretical research. There may be time-sequence differences also. It seems that the infection is transmitted by the nucleic acid part. However, by this induction mainly complete virus will be produced, unless the 'normal' cycle of reproduction is not interferred with. Finally there are *experimental* results[72,116] showing a simultaneous presence or production of infectious NA and virus particles. Thus the protein metabolism has its significance and needs at least equal attention to that of the NA. As a matter of fact, many of the writers quoted above[85,94] demonstrated increased protein synthesis in an early stage of virus infection *in vitro*. However, contrasting findings were reported by LEVY et al.[30,31] and the criticism of SALZMAN[90–92] is valid for this field also. Therefore, no definite assessment of this problem can yet be made. It seems that, in contrast to the nucleic acid synthesis, the intracellular 'metabolic' pool of amino acids and that of the medium can also be utilized for the *de novo* production of virus proteins[117]. Protein synthesis and turnover are inhibited after $^1/_2$ to 2 h of infection[118]. The mechanism may not differ from the physiological one, which process has been reviewed recently by various workers[119–124]. The problem of amino acid activation, and their attachment to the polynucleotides-chain in terminal position, seems to be the mechanism of nucleoprotein synthesis[124,125], but these questions were not investigated in connection with viral diseases.

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In this section, we may quote the work of KILBOURNE[126,127] on the effect of cortisone, this strong protein-catabolic steroid, which may act through the carbohydrate metabolism of the cells[128]. The auto-interference of the infective particles, an explanation offered by this author for the diminished virus production under the influence of cortisone, calls for a biochemical interpretation. The exact evaluation of the point of attack of the hormone in these particular cases, needs further investigation.

Enzyme-changes in cells infected with animal viruses. The reasons for treating this subject in a separate chapter are various. First of all, although so many intracellular enzymes are known, their exact rôle in the metabolism of the cells is not always clear. Nevertheless, the importance of biocatalysts in the biosynthesis of the virus is so great that it may be said, in analogy with the claim of VAN POTTER[129] regarding cell biology and the cancer field, that the great majority of the phenomena observed in virus-host interaction are due to enzymic processes. The virus in general being devoid of metabolic enzymes[56], it depends on the biocatalytic activities of the host cells. Thus the study of changes in these systems during virus infection is fully justified. Finally, being especially interested in the field, one may take the occasion to recapitulate briefly personal contribution, and ideas which may be helpful for a classification and stimulating in pursuing this laborious experimental approach.

First of all, we should like to speak of the work of DERITIS and his group[130–132], who demonstrated the decreased activity of some enzymes, especially of transaminases of the liver in mice infected with hepatitis virus and an increase of this and other enzymes in the plasma due to the alterations of the liver cells. These changes occurred a few hours after systemic infection; thus before secondary (inflammatory) reaction had occurred. Therefore some of their findings may reflect a basic phenomenon, namely the primary interaction between liver cell and virus.

We ourselves working on clinical material between 1949 and 1954, found in the cerebrospinal fluid (CSF) an increased RNase activity, the absence of DNase and the inhibition of crystalline pancreatic DNase with CSF of paralytic poliomyelitis patients[133,134]. This inhibition was reproduced later with infected tissue culture fluid, suggesting the presence of a *toxic factor*, described for the first time in connection with this infection[135–137]. This observation was extended to other biocatalysts and interpreted as a toxic action, derived from the cell metabolism vitiated by the virus, or a direct effect of the distorted viral macromolecules on intracellular enzyme systems *in situ*[138–142]. A series of papers published between 1954 and 1960 described the various aspects of an irreversible transformation of the enzymic activities of the host cell[143–147]. This process leads through an initial stimulation of nucleolytic enzymes to the destruction of the microcosmic harmony of the cell. The kinetics of the enzymes goes through maxima and minima, and recently we were able to demonstrate, with some microsomal (glucose-6-phosphatase), lysosomal or mitochondrial and nucleolar biocatalysts (RNases)[148], a very early activation period[149]. This is perhaps the first biochemical sign of the infection in a preparative phase of the biosynthesis of infective particles (Fig. 1 and 2). This stimulation was detected in some instances within 30 min after the first contact of HeLa cells with poliomyelitis virus (Fig. 2). In contrast with this, some of the biocatalytic functions may be inhibited or unchanged[149] at the same time, causing an imbalance in the physiology of the cell. The above observations are in agreement with the findings of others in connection with different other viruses[150,151].

Effect of the 'milieu' on virus infection. The influence of environmental medium and temperature on cellular metabolism, or the infection with virus, has been extensively studied. The reaction of the internal milieu in the great majority of animal cells, is around neutrality[59,60]. The optimum of the metabolism is near to this pH, and one may affirm, speaking mainly about cultivated cells or living animals, the constancy of the internal milieu[59,60]. As a matter of fact, only

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drastic changes of the pH influence the virus production[38], perhaps through altered cell metabolism. It is known, for instance, that below pH 6 there is no poliovirus synthesis in HeLa cells[16] or in hyperalcaline or acid medium, variants and mutants of the virus are generated[152]. However, it seems to us that the optimal intracellular hydrogen-ion concentration is far from the optimum for isolated, purified, concentrated, or crystallized enzymes *in vitro*. The exact explanation of this discrepancy is not known at the present time.

The effect of under- and over-optimal temperature on virus infection interested many research workers. This physical environmental factor may exert its influence through the kinetics of various enzyme systems which are temperature-dependent, and, in this way, indirectly, through the metabolism of the cell. In animals, the body temperature is regulated by hormon-governed processes, first of all by thyroxine. Thus the effect of various endocrine factors was intensively studied in connection with viral infection[153]. The influence of hibernation caused by hypothermia (and drugs) was explored by CRISALLI[154]. The hopes attached to similar approach were not realized, because the animals in general were protected while hibernating, but when returned to normal temperatures, the virosis followed its usual course. *In vitro* assays indicate that moderate hyperthermia increases the virus yield[155], high fever counters it[156], while hypothermia delays the liberation of poliovirus into the supernatant fluid; at 4°C there is no virus synthesis[157]. For the thermolabile non-neurotrop poliovirus see the excellent review of LWOFF[156]. Similar findings were reported with other viruses also[158]. The phenomenon of synchronization of the mitosis by intermittent temperatures, well known in bacteriology, may prove the interdependence of cellular metabolism and optimal temperature. Unfortunately, similar experiments are more difficult with adult animal cells[159]; thus no successful application to virological problems has yet been reported.

Discussions and conclusions. Summarizing the experimental data, the following biochemical concept could be delineated to explain the effect of virus on various functions of the cell and, above all, on its metabolism. The virus is adsorbed to the host-cell, if it is adapted: i.e., if biologically and biochemically, it is not too different from the cellular components. This adaptation is the result of passages, during which manipulation some 'marker' molecules of the original virus may survive and others will be attached to it by the host organism, by means of its own metabolism. When this grade of tolerance is not established, the virus particle becomes digested and assimilated, possibly during or shortly after its attachment and penetration. However, in case of an adapted strain, the intrusion of the viral nucleic acid into the cell will be accomplished[160], possibly in highly polymerized form.

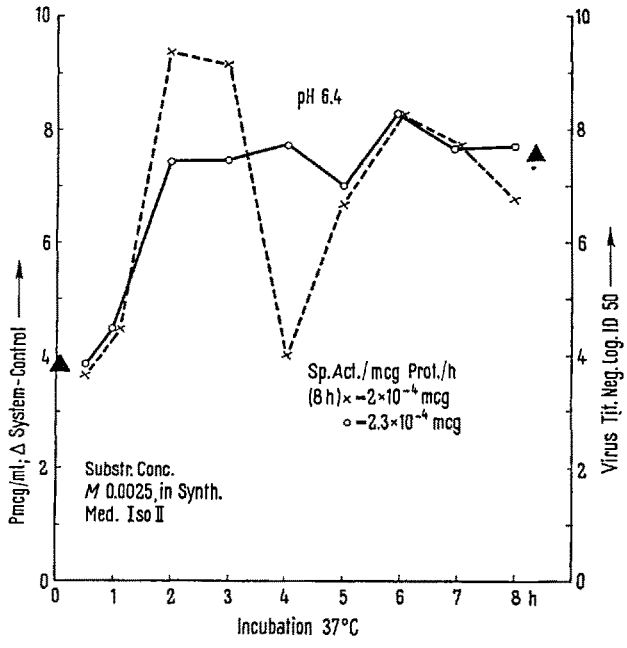

Fig. 1. Relative activity. Glucose-6-Phosphatase in HeLa culture.
×---× Infection 1 ml Type. I. Poliovirus, no dilution, 10 min adsorption.
○——○ Control +normal supernatant medium, 10 min adsorption.

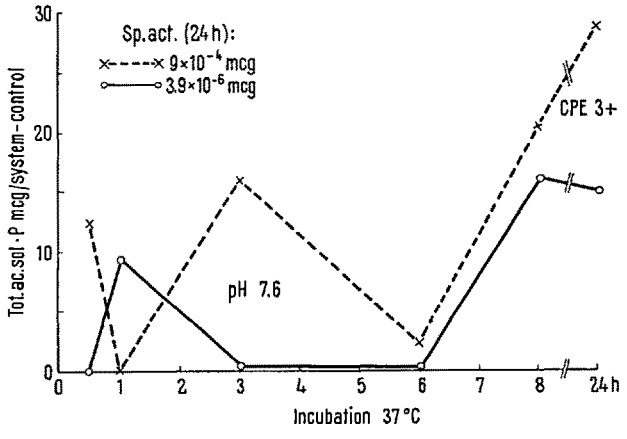

Fig. 2. Relative activity. RNase in HeLa culture.
× ---× Infection 2 ml Type. 1. poliovirus, 10° dilution, 5 min adsorption.
○——○ Control + normal supernatant medium, 10° dilution, 5 min adsorption.
Substrate 0·01% RNA in Medium Iso II + Hanks'.

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This is a decisive moment because in normal cells there should be no *free* nucleic acid present in similar macromolecular state and with some configurational differences[103]. Thus the appearance of virus nucleic acid, provokes an intense metabolic activity, for the mobilization or synthesis of new proteins to combine with and *neutralize* the invading nucleic acid (toward which they may possess great chemical affinity[161,162], in the form of a nucleoprotein. This combination with the close packing of the molecule protects the newly formed particle from hydrolases[163] and thus its survival is ensured. However, the synthesis of protein molecules requires new RNA molecules[123] and this need will be satisfied through the induction of nucleic acid synthesis, carried out at first partially, later exclusively, on the template of the infectious macromolecules. The model substance may be highly polymerized NA, or (in case of RNA-viruses) the 'core' indigestible by RNases consisting of di- and tri-nucleotides. This nucleic acid rest could be completed and rebuilt by adding mono- and oligo-nucleotides to it from the intracellular pool[92] of these substances. The small amount of surviving protein or peptides carried with the infective nucleic acid[65], may serve as a model for the protein-moiety of the virus. The other possibility might be that the physicochemical architecture of the nucleic acid determines the attachment of amino acids[124,125]; thus a *de novo* synthesis of protein is possible without a special template. This is however a theoretical possibility only at the present time. Any way, the play proceeds up and down until the synthesis of some of the consistituents becomes insufficient for a stochiometric combination. This mechanism may be one explanation for the appearance of incomplete or non-infectious particles, lacking, for instance, sufficient amounts of nucleic acid[162]. These forms are perhaps more vulnerable by the enzymic defense mechanism of the cell[164]. The specificity of the genetic material may survive only, if at least the 'core' is saved, serving as a frame in the reconstruction of RNA-molecule. For instance, when non-specific diesterases of the cells are absent or inhibited, the complete hydrolysis of the nucleic acid will be prevented[165,166] and the 'core' may be used as template of the resynthesis of the macromolecule. The experimental proof for these ideas of the writer is however still lacking[167], and they are mentioned mainly as a working hypothesis for the time being.

In conclusion we may underline again the extreme importance of the physiological state of the cell and its metabolism for the initiation and course of viral infections. However, a direct comparison between the various viruses and experimental systems is a condition forced upon us by the physical limitations of a short review. As a matter of fact, such comparison is permitted in certain cases only, and in exercising the greatest care and criticism. To draw an integrated picture, we have given preference to experimental data with certain viruses where our knowledge is more advanced. But this choice is made for the sake of convenience only and not for scientific reasons, or in an effort at premature generalization.

Zusammenfassung. Es werden die wichtigsten experimentellen Ergebnisse über Sauerstoffverbrauch, Zukker- und Fettumsatz, Funktion des Citronensäurecyclus und die Wirkung von Salzen und Milieufaktoren auf die Virusinfektion der tierischen Zelle referiert. Die Änderungen haben sehr verschiedene Bedeutung für die Physiologie der Zelle. Irreversible Schädigungen entstehen nur durch Änderung der Nukleinsäure- und Proteinsynthese, durch die virusbildende Einheiten entstehen.

Der zeitliche Ablauf der Prozesse wird am besten bei gezüchteten Zellen untersucht. Es zeigt sich deutlich die besondere Bedeutung der biochemischen Veränderungen, vor allem an den Enzymen, die den strukturellen Störungen vorausgehen. Der Autor weist darauf hin, dass die makromolekulare Schädigung, die das Wesentliche der Virusinfektion darstellt, chemisch interpretiert werden muss.

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