THE SYNTHESIS OF BACTERIAL VIRUSES*

I. THE SYNTHESIS OF NUCLEIC ACID AND PROTEIN IN ESCHERICHIA COLI B INFECTED WITH T\textsuperscript{\textalpha} BACTERIOPHAGE

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The T\textsuperscript{\textalpha} and T\textalpha\textsuperscript{+} viruses are tadpole-shaped bacteriophages (1, 2) whose biological properties and relations to other bacteriophages have been reviewed by Delbrück (3). The viruses have been isolated by differential centrifugation from bacterial lysates (2, 4, 5) and some chemical and physical properties of the concentrates have been studied (6–8).

About 40 per cent of desoxyribonucleic acid (DNA) has been found in preparations of the viruses (4, 7) and a salt of polymeric DNA has been isolated from active or irradiated T\textalpha\textsuperscript{+} and T\textalpha\textsuperscript{+} in high yield (9). Taylor has claimed that ribonucleic acid (RNA) is also present in variable amounts in T\textalpha\textsuperscript{+} (7). This report has been analyzed elsewhere (9). We have been unable to find evidence for the existence of RNA in preparations of T\textalpha\textsuperscript{+} and T\textalpha\textsuperscript{+}; at least 99 per cent of the P content of the viruses can be accounted for as DNA (4, 5, 9). The data in this and the following study (5) show that cells infected with T\textalpha\textsuperscript{+} do not appear to synthesize or metabolize RNA, despite a rapid synthesis of DNA in these cells. It appears unlikely, therefore, that RNA is a constituent of either virus.

It has been observed in the Escherichia coli–T\textsubscript{2} systems that (1) the normal host cells synthesized far more RNA than DNA (7), (2) the virus contained large amounts of DNA and no RNA, and (3) during the multiplication of the virus, bacterial multiplication was inhibited without affecting the rate of O\textsubscript{2} consumption or the r.q. of the bacteria (4). The following questions were posed: (1) Which, if any, of the nucleic acids was synthesized after infection? (2) What happened to phosphorus and nitrogen assimilation during infection?

Materials and Methods

In the bacteriophage systems, independent host cells may be simultaneously infected with several virus particles. Large numbers of infected host cells may thereby be studied, all in approximately the same phase of virus

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production. The multiple infection technique provides a method of study of a single generation of virus multiplication.

The \( r^+ \) Factor—According to Hershey (10) and Doermann (personal communication) these viruses possess the hereditary property termed \( r^+ \) which affects lysis as follows: In a dilute suspension of infected cells, essentially maximal liberation occurs in about 30 to 40 minutes. In a concentrated suspension, the first small percentage of infected cells that lyse liberate \( r^+ \) virus particles which are rapidly readsoorbed to the other non-lysed cells. The adsorption of \( r^+ \) virus to a cell which already has \( r^+ \) virus within it inhibits the lysis of the cell for 60 to 90 minutes more, permitting continuing virus multiplication within the lysis-inhibited cell. The phenomenon is of assistance technically, because larger amounts of new substance can accumulate in the extended period of multiplication within the host. The \( r^+ \) characteristic may be lost by spontaneous mutation to produce an \( r \) virus which is not lysis-inhibitory.

Preparation of Virus—The purification of \( T_2r^+ \) from lysates in the ammonium lactate medium \( (F) \) and nutrient broth \( (N) \) by differential centrifugation has been described (4). Most virus concentrates used in this study, whether derived from \( F \) or \( N \), \( i.e. \) \( T_2-F \) or \( T_2-N \), were purified by the differential centrifugation procedure from lysates resulting from a single generation of virus production under conditions of multiple infection (5). Variations in the preparation of infecting virus did not appear to affect the course of the phenomena described below. Virus concentrates were suspended in 0.85 per cent NaCl. Their assay has been described (8).

Preparation of Ultraviolet-Irradiated Virus—Purified virus concentrates in 0.85 per cent NaCl were irradiated in the apparatus described and kindly loaned by Dr. W. Henle of this Hospital (11). The agitated virus solution was kept 2 inches from the lamp for 20 to 30 second periods to reduce the titer of active virus by a factor of \( 10^5 \) to \( 10^6 \).

Preparation of Normal and Infected Bacteria—The growth, assay, and turbidimetric standardization of the bacteria, \( Escherichia coli \) \( B \), from \( F \) medium and broth \( (N) \) have been described (8, 12). In aerated \( F \) and \( N \) at 37°, the division times in the logarithmic phase were 60 and close to 30 minutes, respectively. In most experiments, the concentration of bacteria was about \( 2 \times 10^8 \) per cc.; in studies involving protein synthesis, bacteria were grown to a concentration of \( 2 \times 10^8 \) per cc., centrifuged, and resuspended at a concentration of \( 10^9 \) per cc. At the desired bacterial concentrations, virus was added to produce multiple infection; \( i.e. \) three to five virus particles per cell. Infected cultures were vigorously aerated. The experiments were done in \( F \) medium unless otherwise stated.

Analysis—Aliquots of the cultures were precipitated by the addition of 50 per cent trichloroacetic acid (TCA) to give a final TCA concentration of
5 per cent. The mixture was chilled 15 to 30 minutes and centrifuged 10 minutes at 4000 r.p.m. The supernatant fluids were poured off and the tubes were drained. Two additional washings with cold 5 per cent TCA were used if the end-product was to be analyzed for phosphorus or nitrogen.

Phosphorus was determined by the King procedure (13). Nitrogen was estimated by the micro-Kjeldahl method, with a 1 hour digestion in a H₂SO₄-Κ₂SO₄ mixture with CuSO₄ catalyst. 2 drops of 30 per cent H₂O₂ were then added and the digestion was continued for 1 hour.

DNA was determined on the drained sediments by the diphenylamine procedure (14) in Klett colorimeter tubes. With bacterial substance corresponding to 1 to 2 × 10⁹ bacteria, the heated mixtures gave colorimeter readings with a No. 540 filter of about 20 before infection to >100 near the end of virus synthesis. The values of DNA are given in terms of free acid, since the standard sample of the neutralized DNA was standardized by its P content, the free acid (DNA) being considered to have 10.0 per cent P. The theoretical P content of a polymeric DNA consisting of repeated tetranucleotides is 9.97 per cent.

Pentose was determined by the Mejbaum modification of the Bial reaction (15) on TCA precipitates. The pentose in pyrimidine nucleotides is not estimated by this procedure. The standard for these estimations was D-ribose and the color was read in a Klett-Summerson photoelectric colorimeter with a No. 660 filter. Determinations on unsedimented samples rich in lactate developed green colors slightly modified by brown; nevertheless the relative constancy of these values indicated that pentose, including any non-RNA pentose, did not accumulate. The absence of a change in pentose during synthesis is considered to signify the constancy of RNA. The RNA content of Escherichia coli B was about 3 times the DNA content (7).

Substances—The preparation of DNA has been described (8). D-Ribose had been prepared by the late Dr. P. A. Levene of the Rockefeller Institute. 5-Methyltryptophan was generously supplied by the Winthrop Chemical Company. Parenamine is an acid hydrolysate of casein, supplemented by tryptophan, and was obtained from Frederick Stearns and Company. It was neutralized before use. L-Glutamic acid was a Merck product.

EXPERIMENTAL

Synthesis of DNA in Injected Cells—A bacterial culture (200 cc. at 3.5 × 10⁸ cells per cc.) was divided into two portions, to one of which was added 0.32 cc. of a T₂r+ concentrate with a titer of 3.1 × 10¹⁴ per cc. The turbidities and the virus and bacterial contents of the suspensions were determined; DNA was estimated in 8 cc. aliquots. The data on this experiment are presented in Fig. 1.
In the uninfected culture the viable bacterial count, turbidity, and DNA increased exponentially for 3 hours. In other experiments of this type, the slope of the log turbidity-time curve was frequently less than that of the log viable count-time curve, indicating a decrease of the size of individual bacteria during this period. In the infected culture, the count of bacteria capable of forming colonies fell to a very small value as virus was adsorbed. The number of infectious centers fell to the level of infected bacteria, i.e. to about one-third of the original virus added, and remained constant for a period. At 2 hours, virus appeared, becoming maximal at 5 hours (5). Despite the liberation of virus concomitant with the lysis of the host, turbidity remained roughly constant. A possible explanation appears to be that lysis of r+ virus-infected cells, under the conditions given, begins without considerable fragmentation and, proteolysis being relatively weak, large fragments of cellular débris remain for many hours and scatter light.

In the uninfected culture the turbidity and DNA almost doubled in the 1st hour. In the infected culture, during the same time period, there was no significant increase in turbidity, since only a few per cent of bacteria were...
lysed, but the DNA content had more than tripled. The rate of DNA synthesis per infected cell in the 1st hour of the experiment was about 4 times that of normal dividing cells. Therefore, despite the inhibition of bacterial multiplication, the synthesis of this virus constituent was markedly increased. It will be shown in Paper II that much of this newly synthesized DNA can be isolated in the virus (5).

**Effect of 5-Methyltryptophan on Nucleic Acid Synthesis**—5-Methyltryptophan (5-MT) will inhibit T₃ or T₄ multiplication in this system without any effect on O₂ consumption (16). The compound is inhibitory because of its competition with tryptophan at sites of protein synthesis (17). The inhibitory effect of 5-MT on virus synthesis is completely reversible on addition of tryptophan (18).

At low bacterial concentration, 5 × 10⁻⁴ M 5-MT in F medium was invariably inhibitory in the absence of added tryptophan. At about 2 × 10⁸ bacteria per cc., the effect of 5-MT was more variable. Virus multiplication after infection in the presence of 5-MT was inhibited for only 1 to 3 hours. Furthermore, interruption of virus synthesis after it had begun was not always successful at these concentrations, and, when it occurred, seldom lasted more than 1 ½ hour. Nevertheless, since 5-MT was a specific antimetabolite for an essential protein constituent, it was of interest to determine whether the inhibition of protein synthesis affected DNA synthesis. It was found that bacteria infected with T₃ in the presence of 5-MT were incapable of synthesizing protein-bound DNA for several hours. A typical experiment is given in the following section.

**Absence of Synthesis of RNA in Infected Cells**—Both DNA and RNA were followed in infected cells in the presence and absence of 5-MT. 1 minute before addition of virus 10 cc. of 5 × 10⁻³ M 5-MT in F medium were added to a 100 cc. aliquot of a bacterial culture. After infection, the turbidities were determined as well as the DNA and pentose contents of the TCA precipitates. The results are given in Fig. 2.

In normal cells, RNA was synthesized at a rapid rate (see pentose in Fig. 3). However, throughout infection RNA was constant, in contrast to the stimulated synthesis of DNA. RNA was not synthesized in 5-MT-treated infected cells, even when there was inhibition of both virus multiplication and DNA synthesis.

**Nucleic Acid Synthesis in Cells Treated with Ultraviolet-Inactivated Virus**—Ultraviolet-irradiated virus inhibited bacterial multiplication without change in the rate of O₂ consumption or R.Q., although virus was not being synthesized (4). It was of interest to know whether nucleic acid was synthesized under these conditions. To one of three aliquots of a bacterial culture was added a T₂ concentrate containing 5.6 × 10¹⁰ active virus per cc. To another was added the same amount of previously irradiated concen-
trate (active virus content of $10^3$ per cc.). The data on the turbidity, DNA, and total pentose contents of the cultures are presented in Fig. 3. Aliquots of 8 and 2 cc. were used for the DNA and pentose determinations respectively.

Fig. 2. DNA and pentose synthesis in T2r+ infected Escherichia coli B in F medium in the absence and presence of $5 \times 10^{-4}$ M 5-methyltryptophan.

Fig. 3. DNA synthesis in a normal bacterial culture and in bacteria treated with active or irradiated T2r+.

In the normal bacteria, turbidity, DNA, and RNA increased throughout the experiment. In the bacteria infected with active virus, DNA increased markedly, while pentose remained low. In bacteria treated with irradiated virus, DNA synthesis was completely inhibited over a 2 hour period, during which time total pentose increased slightly. The nature of the late DNA increment in this experiment with irradiated virus is not understood.
Phosphorus Assimilation and DNA Synthesis—Phosphate assimilation in the protein-bound phosphate fraction in normal and infected bacteria was examined to see whether phosphorus-containing compounds besides DNA were being synthesized. Infected and normal cultures at $2 \times 10^8$ bacteria and $10^9 \Phi_2$ per cc. were incubated for 2 hours. In this interval the turbidity of the infected culture increased only 10 per cent. The DNA, nitrogen, and phosphorus contents of protein-bound constituents are presented in Table I.

In the normal bacteria, one-quarter of the protein-bound phosphorus was DNA-P; the remainder was for the most part RNA-P, but also included small amounts of phospholipides (7). As the bacteria approached the end of their logarithmic phase after 2 hours, a slight decrease was observed in the proportion of phosphorus appearing in DNA. Nevertheless, the molar

<table>
<thead>
<tr>
<th>TABLE I</th>
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<tr>
<td>Synthesis in Normal and $\Phi_2$-Infected Escherichia coli B</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Culture</th>
<th>N per 50 cc.</th>
<th>P per 50 cc.</th>
<th>DNA per 50 cc.</th>
<th>DNA-P</th>
<th>Total P</th>
<th>Molar ratios, N:P</th>
</tr>
</thead>
<tbody>
<tr>
<td>B at 0 hr.</td>
<td>0.333</td>
<td>0.0602</td>
<td>0.154</td>
<td>0.26</td>
<td>12.2</td>
<td></td>
</tr>
<tr>
<td>&quot; &quot; 2 hrs.</td>
<td>1.229</td>
<td>0.2219</td>
<td>0.422</td>
<td>0.19</td>
<td>12.2</td>
<td></td>
</tr>
<tr>
<td>$B_2 - B_0$</td>
<td>0.896</td>
<td>0.1617</td>
<td>0.268</td>
<td>0.17</td>
<td>12.2</td>
<td></td>
</tr>
<tr>
<td>B-$\Phi_2$ at 0 hr.</td>
<td>0.307</td>
<td>0.0655</td>
<td>0.179</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&quot; &quot; 2 hrs.</td>
<td>0.430</td>
<td>0.1053</td>
<td>0.545</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(B-$\Phi_2$)$_2 - (B-$\Phi_2$)$_0$</td>
<td>0.123</td>
<td>0.0368</td>
<td>0.366</td>
<td>0.99</td>
<td>7.38</td>
<td></td>
</tr>
</tbody>
</table>

N:P ratio was essentially unchanged in the culture throughout this period. Grossly, then, normal bacteria synthesized normal bacterial constituents in nearly the same proportions in which they were originally present.

In infected bacteria, the increments of nitrogen and phosphorus were far less than in the normal dividing bacteria. However, the amount of DNA formed in infected cells was greater than that formed in 2 hours in the normal culture. The DNA in infected cells almost exactly accounted for the phosphorus assimilated by those cells.

In this experiment the N:P ratio of the increment in the infected cells was 7.4, in contrast to 12.2 for normal cells. The former figure is the ratio characteristic of $\Phi_2$ which has been found to be 7.2 to 7.6 when isolated from F or N lysates. Thus the material synthesized in infected cells in a 2 hour interval had the N:P and DNA-P:P ratio characteristic of $\Phi_2$ bacteriophage.

Rates of DNA and Protein Synthesis—It appeared that virus-infected cells synthesized virus or virus components alone, in contrast to normal bacteria which synthesized several types of substances, such as nucleic acid, proteins,
and enzymes. Studies were undertaken to determine whether exponential increase of these constituents or some other types of growth curve characterize virus reproduction in infected cells. The former, as described in Fig. 1, is characteristic of DNA in cells in a normal culture under the conditions employed.

Synthesis was first studied in the normal period of virus synthesis, the non-lysis-inhibited period. In a typical experiment, bacteria were concentrated by centrifugation and resuspended in F medium. After infection with five virus particles per cell aliquots for total N and DNA analyses were removed at 5 minute intervals. The DNA increments were converted to nucleic acid N by multiplying by the factor 0.169. Protein N was considered to be total N minus DNA-N. The increments of both protein N and DNA-N are presented in Fig. 4. The following points were observed: (1) The curves of synthesis of DNA and protein in infected cells were linear and not exponential; (2) protein synthesis started at the beginning of infection; (3) the increment in DNA appeared from 7 to 10 minutes after protein synthesis began; (4) if the increment in DNA were converted to an increment in P, the ratio of the rates of increment of N to P in the experiment in Fig. 4 was found to be 12.4, the value for normal bacteria.

The most active concentrate of T2 studied had $1.6 \times 10^9$ infectious units per microgram of DNA. In five experiments, DNA increments of 2.2 to 2.6 were obtained by $2 \times 10^8$ cells in 25 minutes, yielding an equivalent of seventeen to twenty T2 particles per cell in that interval. Since our most active T2 preparation probably contained some inactive virus, this represents a minimal figure. Nevertheless, this agrees with the amount of T2.
liberated from Escherichia coli B in F medium; i.e., about twenty virus particles per cell (18).

In four experiments of this type the following ratios of the rates of increment of N to P were obtained: 13.2, 12.6, 11.7, and 12.4. Therefore, in the non-lysis-inhibited system, i.e. before 30 minutes, the ratio of the rates of utilization of N and P was approximately the same as in the normal cells. However, in four of five experiments in which these rates were determined over a 2 hour period in infected cells, it was observed that the rate of protein synthesis was sharply reduced between 30 and 50 minutes, while the rate of DNA synthesis was unchanged, as in Fig. 5. This effect was possibly due to lysis inhibition appearing soon after the first liberation of and readsoption of r+ virus. Thus, after 30 minutes, the ratio of N to P continually decreased until it approached that of virus. At this point, occurring at about 2 hours, synthesis of DNA abruptly stopped. At this time virus began to appear and a rapid decrease in TCA-precipitable N ensued, indicative of proteolysis accompanying bacteriolysis.

Inhibition of Protein Synthesis by Irradiated Virus—Ultraviolet irradiation reduced the activity of T2 by a factor of 8.5 X 104. Fully active T2 or irradiated virus was added to bacterial cultures concentrated to 108 per cc. Aliquots were removed for N and DNA analysis at 0 and 120 minutes. Data on the N and DNA increments after 2 hours are presented in Table II. In the bacteria infected with active T2, synthesis of DNA and protein occurred in the ratio approximating that of virus. On the other hand, the bacteria which adsorbed ultraviolet-inactivated virus did not increase their protein-bound N content after a 2 hour interval.

Initiation of DNA Synthesis—It has been demonstrated that DNA does not increase for 7 to 10 minutes after infection. Four lines of evidence sug-
suggest that this represented the time necessary for the synthesis of virus peptides as a prerequisite for DNA synthesis. (1) Protein was synthesized from the beginning of infection. That this was indeed virus protein was suggested by the viral ratio of N to P at the end of the lysis-inhibited multiplication. (2) DNA synthesis stopped when the excess of protein was markedly depleted as the final ratio approached that of virus. (3) 5-Methyltryptophan prevented protein synthesis and thereby prevented DNA synthesis. (4) It was possible to reduce the time for the beginning of DNA synthesis and increase the rate of DNA synthesis by increasing the rate of peptide synthesis. This was most clearly demonstrated by the following method. *Escherichia coli* B was grown in broth, instead of in F medium. When this organism was transferred to F medium and washed in F, its synthetic abilities were much slower than F-grown organisms. Under these

### Table II

**Inhibition of Protein Synthesis by Irradiated Virus x**

<table>
<thead>
<tr>
<th>Culture</th>
<th>Time</th>
<th>DNA-P per cc.</th>
<th>Total protein-bound N per cc.</th>
<th>Molar ratio, N:P</th>
</tr>
</thead>
<tbody>
<tr>
<td>B-T₂</td>
<td>0</td>
<td>1.45</td>
<td>40.2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>6.00</td>
<td>56.5</td>
<td></td>
</tr>
<tr>
<td>Increment</td>
<td></td>
<td>4.55</td>
<td>16.3</td>
<td></td>
</tr>
<tr>
<td>B-irradiated T₂</td>
<td>0</td>
<td>1.56</td>
<td>40.4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>1.96</td>
<td>40.4</td>
<td></td>
</tr>
<tr>
<td>Increment</td>
<td></td>
<td>0.40</td>
<td>0.0</td>
<td></td>
</tr>
</tbody>
</table>

![Fig. 6. DNA synthesis in *Escherichia coli* B of the same origin infected in different media by T₂x. The ordinate presents increments over initial values.](http://www.jbc.org/)

![Fig. 6. DNA synthesis in *Escherichia coli* B of the same origin infected in different media by T₂x. The ordinate presents increments over initial values.](http://www.jbc.org/)
conditions, infection in F medium resulted in an extended latent period of virus synthesis and DNA synthesis, with a low yield of virus, as compared to these functions in broth (19).

Bacteria were grown in broth to $1.5 \times 10^8$ per cc., centrifuged, and washed twice with F medium. The washed bacteria were suspended at their original concentration in broth, F, F + casein hydrolysate (1 mg. per cc.), or in F + glutamic acid at 200 $\gamma$ per cc., respectively, and infected with T$_2$. From the DNA analyses presented in Fig. 6, it may be seen that the nutrient broth and amino acid-fortified F medium markedly stimulated DNA synthesis. Some of the difference in the rate of virus and DNA synthesis in these two media can be reduced by further supplementation with purines and pyrimidines (19). Glutamic acid was the most active single amino acid supplement. However, a mixture of amino acids was more efficacious in stimulating virus synthesis and DNA synthesis.

Finally, a complete medium has been developed which supported a rate and amount of virus multiplication closely approximating that in nutrient broth (19). Omission of any one of eight amino acids from the complete defined medium consisting of F, L-amino acids, purines, and pyrimidines resulted in an extended latent period of DNA synthesis. This procedure has been used to detect nutritional requirements for virus multiplication (12).

**DISCUSSION**

After infection, phosphate was apparently channeled into the formation of only that nucleic acid characteristic of virus, namely DNA. The site of the shunt in the pathways of nucleic acid synthesis producing this effect is clearly of utmost importance in understanding the precise nature of the parasitic process in this system. If ribose-5-phosphate was the precursor to both ribose-3-phosphate of RNA and desoxyribose phosphate of DNA, it is conceivable that inhibition of the formation of the ribose-3-phosphate could result in the increased formation of desoxyribose phosphate. Furthermore, since RNA is a common constituent of cellular structures such as mitochondria and microsomes, which are the sites of numerous enzymes, the inhibition of the formation of one element (RNA) of these complex structures may prevent the synthesis of the remaining components.

In infected cells, the rates of synthesis of protein and DNA were constant regardless of the number of virus particles formed within the cell. It would therefore appear that the virus does not contain the enzymes for DNA or protein synthesis and that new enzymes have not been synthesized or, if synthesized, were not being used for virus synthesis. Thus the metabolic equipment which synthesizes the most complex virus components are the enzymes of *Escherichia coli* B, presumably according to the new models
supplied by the infecting virus particles. That this manner of virus synthesis may be general is supported by the fact of the intracellular character of virus multiplication and the data on the composition of various viruses infecting plants, animals, and bacteria, indicating limited structural and enzymatic equipment in these parasites (4, 9).

A constant rate of synthesis in itself may merely indicate some limiting factor in the duplication process and does not eliminate the possibility of a "doubling" process. The limiting factor may be of the character of limitation of substrate, energy supply, or enzyme sites or combination of these. Regardless of the reason for the constant rate, three types of evidence suggest that the curve of the synthesis of protein-bound DNA is indeed a measure of the rate of virus synthesis. (1) Luria and Latarjet have shown that a single hit ultraviolet inactivation curve is obtained for singly infected cells for the first 7 minutes after infection (20). After this time, which coincides closely with the beginning of an increase in DNA, there occurs a slight deformation in the curve which they interpret as "probably an indication that some multiplication has started by this time." (2) The amount of DNA synthesized by infected bacteria in F medium in 25 minutes approximates the amount contained in the virus liberated from the bacteria at about this time. Similar correlations have been found for Escherichia coli-T2 in other media (12). (3) The data of Doermann (personal communication) indicate that, in lysis-inhibited systems of varying latent periods, the burst size is roughly proportional to the length of the latent period. This suggests linear virus synthesis during these periods. His data are consistent with the continued linear synthesis of DNA during lysis inhibition noted above.

The methods described in this paper have strongly suggested that (1) virus is synthesized from the components of the medium assimilated after infection, and (2) RNA is not synthesized in infected cells. Since by the methods described the possible turnover in compounds such as RNA cannot be measured, isotope techniques were employed to confirm these conclusions. Studies with radioactive phosphorus are presented in Paper II (5).

SUMMARY

1. The synthesis of nucleic acid and protein has been studied in T2 bacteriophage-infected Escherichia coli B in simple medium, F. Ultraviolet-irradiated T2 inhibited the synthesis of these components, in contrast to the action of active virus.

2. In infected cells, only the nucleic acid found in T2, DNA, was synthesized in contrast to normal cells which synthesized about 3 times as much RNA as DNA. In infected cells, essentially all the phosphorus going to form protein-bound constituents appears in DNA.

3. 5-Methyltryptophan inhibited DNA synthesis in infected cells.
4. In infected cells, protein and DNA were synthesized at a constant rate in the period of normal virus multiplication, prior to the establishment of lysis inhibition. Protein synthesis was apparent from the beginning of infection; DNA began 7 to 10 minutes later. The ratio of the rates of increment of N and P utilization was similar to that of normal cells.

5. The rate of protein synthesis decreased during the period of lysis inhibition in most of the experiments. At the onset of the final lysis, the ratio of the increments in N and P approached that of virus.

6. The length of the period of onset of DNA synthesis was determined by the rate of synthesis of virus peptides.

7. Some aspects of these phenomena have been discussed.

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