Chapter 19, p.219, insert following second paragraph (that is, after ...these copies made copies of themselves.)

Some time later, an even more astounding event occurred.

We have not said much, so far, about the necessity of establishing "controls"--but when doing an experiment one must always try a variety of methods in order to check the nature and authenticity of a reaction. With regard to Kornberg's experiment just described, for example, one would assume that all four nucleotides must be present in the vessel in order for DNA synthesis to take place; but the only way to know whether this is the case is to set up a battery of test-tubes, omit one or more nucleotides from each, and observe what happens. This is what Kornberg and his associates did. They discovered that the logical assumption is correct: for a bit of natural DNA to copy itself in an artificial environment such as they had created, all four nucleotides are necessary.

In doing this experiment, Kornberg had incubated his mixes for two to three hours, then had used optical and chemical methods for measuring the increase in DNA. In 1957, however, he and his colleagues decided to try a new measurement technique. Would the increase in DNA correlate with an increase in the viscosity of the solution in which the DNA was replicating? Again, they set up the same controls that had been used previously; but this time, in addition, they took measurements for longer than the two to three hours that had been the cut-off point before.

The investigators were happy to discover that viscosity did correlate with increase in DNA. They had indeed found a useful

new method of measurement. But they found something else, too-something much more important. In one of the control test-tubes, a solution from which guanine nucleotide had been omitted--and in which, therefore, no natural DNA could have been synthesized--an investigator noted, at the fourth hour, that a very rapid increase in viscosity was taking place. This continued until the sixth hour. If increase in viscosity correlated with the formation of DNA, DNA must have formed in that test-tube--but how could it have, without one of the nucleotides?

That evening, Kornberg and his associates considered their several possible sources of error. Perhaps someone had mistakenly put into the mix the guanine that should have been omitted. Perhaps the control test-tube had been contaminated by bacteria. Perhaps there was something wrong with the equipment that measured viscosity. Therefore, they re-ran the experiment the next day, being sure to eliminate each possible source of error. The same rapid increase in viscosity, at the same time-interval after incubation, again occurred.

Controls were again set up, each omitting various of the ingredients known to be essential for laboratory synthesis of makerat DNA. It was found that, given enough time, rapid increase in viscosity occured even in the test-tube from which natural DNA -- the model, or "primer", in previous experiments--had been omitted. This particular vessel produced an unusual kind of DNA, with the following sequence:

TATATATATA A TAFA : ATAT Subsequently, another experimental mix produced another unusual DNA. It had this sequence:

Both types, once made, produced copies of themselves--and without the four-to-six hour lag period.

Note that Kornberg's original intention was not to find out whether DNA synthesis would take place without a bit of natural DNA as the model; he and has his colleagues were simply running a routine check on the raw-material requirements of natural DNA when replicating in an artificial environment.

What they found is a scientific example of serendipity.

Here, then, at a more advanced level of life, was reinforcement for the findings of experiments that had recreated a supposed

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