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## **DNA Replication & S Phase**

**Study Guide — DNA Replication**

Comprehensive Pre-med style questions on DNA replication, S phase, enzymes, directionality, and regulation

**30 items — Study Guide with Answers**

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Generated February 20, 2026

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1 Which event defines the S phase of the eukaryotic cell cycle?

- A Separation of sister chromatids
- B Synthesis and complete replication of the nuclear DNA ✓**
- C Rapid cell growth without DNA synthesis
- D Formation of the mitotic spindle
- E Partition of cytoplasm during cytokinesis

► **Explanation:** During S phase, the entire nuclear genome is replicated so that each chromosome consists of two sister chromatids; chromatid separation occurs later in mitosis.



2 DNA replication in cells is described as 'semi-conservative'. What does this mean?

- A Each daughter DNA molecule contains two newly synthesised strands
- B Each daughter DNA molecule contains two parental (old) strands
- C Each daughter DNA molecule contains one parental strand and one newly synthesised strand ✓**
- D Only half of the genome is replicated in each cell cycle
- E Only some bases are copied accurately

► **Explanation:** In semi-conservative replication, the two parental strands separate and each serves as a template for a new complementary strand, producing hybrids of one old and one new strand.



3 During DNA replication, in which direction are new DNA strands synthesised by DNA polymerases?

- A 5' → 3' only ✓**





- B 3' → 5' only
- C Either 5' → 3' or 3' → 5', depending on the strand
- D Randomly in both directions
- E Direction is not relevant for DNA synthesis

► **Explanation:** All known DNA polymerases add nucleotides to a pre-existing 3' OH, so synthesis proceeds in the 5' → 3' direction along the growing strand while reading the template 3' → 5'.

4 Which statement about DNA polymerase is **CORRECT**?



- A It can initiate DNA synthesis de novo without a primer
- B It requires a free 3' OH group to extend a pre-existing strand ✓
- C It synthesises RNA primers for DNA replication
- D It unwinds the DNA double helix ahead of the replication fork
- E It forms phosphodiester bonds only between ribonucleotides

► **Explanation:** DNA polymerases cannot start synthesis de novo; they extend from a free 3' OH (usually supplied by an RNA primer) and add deoxyribonucleotides.

5 What is the main role of DNA helicase at the replication fork?



- A Relieving torsional strain by cutting and rejoining DNA
- B Synthesising short RNA primers
- C Unwinding the parental double helix by breaking hydrogen bonds between base pairs ✓
- D Sealing nicks between Okazaki fragments
- E Holding single-stranded DNA in an extended conformation





► **Explanation:** Helicase uses ATP to separate the two parental DNA strands ahead of the replication fork, allowing each to be used as a template.

**6** Single-strand DNA-binding proteins (SSBs) are essential during replication because they:



- A Cut and rejoin DNA to relieve supercoiling
- B Stabilise unwound DNA strands and prevent them from reannealing or forming secondary structures ✓
- C Create RNA primers for DNA polymerase
- D Proofread newly synthesised DNA and remove mismatches
- E Ligate Okazaki fragments together

► **Explanation:** SSBs bind exposed single-stranded DNA and keep it from re-pairing or forming hairpins before replication can occur.

**7** Which enzyme synthesises the short RNA stretches that provide 3' ends for DNA polymerase to begin replication?



- A DNA polymerase III
- B DNA ligase
- C Primase ✓
- D Topoisomerase
- E Helicase

► **Explanation:** Primase is an RNA polymerase that synthesises short RNA primers de novo, providing the 3' OH required by DNA polymerases.





8 What is the role of DNA ligase in replication?



- A Extending RNA primers with DNA
- B Joining Okazaki fragments by forming phosphodiester bonds between adjacent DNA fragments ✓**
- C Removing RNA primers from lagging strands
- D Unwinding the DNA helix
- E Adding methyl groups to newly synthesised DNA

► **Explanation:** DNA ligase seals nicks in the sugar-phosphate backbone, particularly between adjacent Okazaki fragments on the lagging strand.

9 Topoisomerases are crucial for DNA replication primarily because they:



- A Add nucleotides to the growing DNA strand
- B Cut one or both DNA strands to relieve supercoiling ahead of the replication fork ✓**
- C Create RNA primers at the origin of replication
- D Protect single-stranded DNA from nucleases
- E Initiate transcription at promoters

► **Explanation:** Helicase unwinding introduces positive supercoils; topoisomerases transiently break DNA strands, allowing the helix to relax and preventing fork stalling.

10 Which statement correctly distinguishes leading and lagging strand synthesis at a replication fork?



- A The leading strand is synthesised  $3' \rightarrow 5'$ , the lagging strand  $5' \rightarrow 3'$





**B The leading strand is synthesised continuously towards the replication fork; the lagging strand is synthesised discontinuously away from the fork ✓**

- C** Both leading and lagging strands are synthesised continuously
- D** Both leading and lagging strands require only one RNA primer
- E** The leading strand does not need a primer, but the lagging strand does

► **Explanation:** Because DNA polymerase can only add nucleotides  $5' \rightarrow 3'$ , one new strand (leading) is continuous, whereas the other (lagging) is made in Okazaki fragments laid down away from the fork.

**11 Okazaki fragments are:**



- A** Short RNA pieces made on the leading strand
- B Short DNA fragments synthesised on the lagging strand ✓**
- C** Regions of DNA enriched in guanine and cytosine
- D** Sections of DNA that are not replicated in S phase
- E** Short RNA-DNA hybrids found only in prokaryotes

► **Explanation:** On the lagging strand, DNA is synthesised in short  $5' \rightarrow 3'$  stretches called Okazaki fragments that are later joined by ligase.

**12 Why are multiple RNA primers required specifically on the lagging strand during replication?**



- A** The lagging strand DNA polymerase is unable to bind DNA directly
- B The lagging strand is synthesised discontinuously, so each Okazaki fragment must be initiated by its own primer ✓**
- C** The lagging strand is synthesised  $3' \rightarrow 5'$ , requiring primers at both ends
- D** Primers on the lagging strand are not later removed





- E Primers on the leading strand are unnecessary because synthesis starts at a telomere

► **Explanation:** Each Okazaki fragment on the lagging strand requires a new starting point for DNA polymerase, supplied by a fresh RNA primer.

**13** In bacteria (e.g. *E. coli*), which DNA polymerase is primarily responsible for bulk synthesis of new DNA on both leading and lagging strands?



- A DNA polymerase I
- B DNA polymerase III ✓
- C DNA polymerase
- D DNA polymerase
- E Reverse transcriptase

► **Explanation:** In bacteria, DNA polymerase III is the main replicative polymerase; DNA polymerase I removes RNA primers and fills short gaps.

**14** Which is the primary function of bacterial DNA polymerase I during DNA replication?



- A Initiating DNA synthesis at replication origins
- B Removing RNA primers with its 5' → 3' exonuclease activity and replacing them with DNA ✓
- C Synthesising the leading strand continuously
- D Unwinding DNA at the replication fork
- E Joining Okazaki fragments with phosphodiester bonds

► **Explanation:** DNA polymerase I in bacteria uses its 5' → 3' exonuclease to remove RNA primers and then fills in the resulting gaps with DNA.





**15** In eukaryotes, which combination of DNA polymerases is most closely associated with replication of nuclear DNA on the leading and lagging strands?



- A Pol  $\alpha$  for both strands
- B Pol  $\alpha$  as the main replicative polymerase and Pol  $\delta$  as primase
- C Pol  $\alpha$ –primase to start synthesis, then Pol  $\delta$  mainly on the leading strand and Pol  $\epsilon$  mainly on the lagging strand ✓**
- D Pol  $\delta$  on both strands in the nucleus
- E Pol  $\delta$  for mitochondrial DNA and Pol  $\alpha$  for nuclear DNA

► **Explanation:** Eukaryotic replication typically uses the Pol  $\alpha$ –primase complex to lay down RNA–DNA primers, Pol  $\delta$  for continuous leading-strand synthesis, and Pol  $\epsilon$  for lagging-strand Okazaki fragments.

**16** What is the function of the sliding clamp (  $\beta$  clamp in bacteria, PCNA in eukaryotes) in DNA replication?



- A It unwinds the DNA double helix
- B It loads RNA primers onto the DNA template
- C It holds DNA polymerase tightly to DNA, greatly increasing processivity ✓**
- D It seals nicks between DNA fragments
- E It cuts and rejoins DNA to relieve supercoiling

► **Explanation:** Sliding clamps encircle DNA and tether DNA polymerases, allowing long stretches of synthesis without dissociating.





**17** Many replicative DNA polymerases possess a 3' → 5' exonuclease activity. What is its main role?

- A** Removing RNA primers from Okazaki fragments
- B** Proofreading: removing incorrectly paired nucleotides from the 3' end of the growing strand ✓
- C** Extending the DNA chain beyond the 3' end
- D** Repairing double-strand breaks
- E** Adding telomeric repeats to chromosome ends

► **Explanation:** 3' → 5' exonuclease activity allows polymerases to remove misincorporated nucleotides immediately, increasing fidelity.



**18** Telomerase helps solve which specific problem in DNA replication?

- A** Replication of circular bacterial chromosomes
- B** Replication of the very ends of linear chromosomes on the lagging strand ✓
- C** Removal of RNA primers from Okazaki fragments
- D** Unwinding of the double helix
- E** Random introduction of mutations into telomeric DNA

► **Explanation:** Because lagging-strand synthesis cannot fully replicate the 5' ends of linear chromosomes, telomerase extends the 3' overhang with repeats so that no essential genetic information is lost.



**19** Which cells typically show the highest telomerase activity in humans under normal physiological conditions?

- A** Most differentiated somatic cells (e.g. neurons)





- B Germ-line cells and many stem cells ✓**
- C Red blood cells
- D All cells in G0 phase only
- E Only cancer cells

► **Explanation:** High telomerase activity is typical in germ-line cells and some stem cells, maintaining telomere length; many cancer cells also reactivate telomerase.

**20 Which statement correctly compares DNA replication origins in prokaryotes and eukaryotes?**



- A Both typically have a single origin per chromosome
- B Prokaryotic chromosomes have many origins; eukaryotic chromosomes have only one
- C Circular bacterial chromosomes usually have one main origin, whereas linear eukaryotic chromosomes have many origins ✓**
- D Only eukaryotes use origins; prokaryotic replication starts randomly
- E Origins are required only for lagging-strand synthesis

► **Explanation:** Bacteria like *E. coli* typically initiate replication at a single *oriC*, while large eukaryotic chromosomes use multiple origins to complete replication efficiently.

**21 In a eukaryotic cell, how is it ensured that each origin of replication fires (is used) only once per cell cycle?**



- A By continuous synthesis of new origins during S phase
- B By licensing origins with specific proteins in G1, then preventing relicensing once S-phase CDK activity rises ✓**
- C By destroying all replication enzymes at the end of S phase
- D By limiting the availability of dNTPs to a single replication round





- E By allowing replication only at telomeres

► **Explanation:** Origins are 'licensed' in G1 by assembly of pre-replication complexes; activation in S phase requires CDKs, which also prevent new pre-RCs from forming until the next G1.

**22** A diploid human cell ( $2n$ ) in G1 has a DNA content of  $2C$ . Immediately after S phase, but before mitosis begins, what are its ploidy and DNA content?



- A  $n$  and  $2C$
- B  $2n$  and  $2C$
- C  $4n$  and  $4C$
- D  **$2n$  and  $4C$**  ✓
- E  $n$  and  $4C$

► **Explanation:** S phase doubles the DNA content but not the chromosome number. The cell remains diploid ( $2n$ ) but now has two sister chromatids per chromosome ( $4C$ ).

**23** A drug blocks topoisomerase activity but leaves helicase and DNA polymerase intact. Which immediate effect on replication is most likely?



- A RNA primer synthesis is abolished
- B **Supercoiling ahead of the fork increases, causing replication forks to stall and DNA breaks to accumulate** ✓
- C DNA ligase cannot seal Okazaki fragments
- D DNA polymerase begins synthesising DNA in the  $3' \rightarrow 5'$  direction
- E Origins of replication cannot be recognised by initiator proteins

► **Explanation:** Without topoisomerase, helicase-induced unwinding creates excessive supercoiling, mechanically blocking fork progression and potentially causing DNA breaks.





**24** A nucleotide analogue used in chemotherapy lacks a 3' OH group on its deoxyribose. When incorporated into DNA by a polymerase, what is the most direct consequence?



- A** DNA becomes resistant to nuclease digestion
- B** DNA synthesis continues normally with increased speed
- C** DNA synthesis stops because no further nucleotides can be added to that chain (chain termination) ✓
- D** The DNA strand is rapidly proofread and repaired
- E** The analogue is removed by primase before ligation

► **Explanation:** DNA polymerase requires a 3' OH to form the next phosphodiester bond; a chain lacking this group cannot be extended, so replication stalls.

**25** If DNA ligase activity is inhibited in a replicating eukaryotic cell, which outcome is most likely on the lagging strand?



- A** Okazaki fragments remain unjoined, leaving many nicks in the sugar-phosphate backbone ✓
- B** RNA primers cannot be synthesised
- C** Helicase cannot unwind double-stranded DNA
- D** Leading-strand synthesis stops, but the lagging strand is unaffected
- E** Supercoils cannot be relaxed ahead of the replication fork

► **Explanation:** Without ligase, RNA primers may be removed and replaced by DNA, but the remaining nicks between Okazaki fragments cannot be sealed.





**26** Replication forks originate at an origin of replication and move in which way along a typical eukaryotic chromosome?



- A** In a single direction, producing a single replication fork per origin
- B** Bidirectionally, producing two replication forks that move away from the origin in opposite directions ✓
- C** Randomly jumping between chromosomes
- D** Only towards the telomeres
- E** Only towards the centromere

► **Explanation:** In most organisms, replication is bidirectional from each origin, generating two forks that move in opposite directions, forming a replication bubble.

**27** Which statement best distinguishes DNA replication from transcription in eukaryotic cells?



- A** Replication uses ribonucleotides, while transcription uses deoxyribonucleotides
- B** Replication requires RNA primers and copies the entire genome; transcription does not need a primer and copies specific genes ✓
- C** Replication occurs only in the nucleus; transcription occurs only in the cytosol
- D** Replication synthesises RNA; transcription synthesises DNA
- E** Replication proceeds only  $3' \rightarrow 5'$ ; transcription only  $5' \rightarrow 3'$

► **Explanation:** DNA replication copies all DNA once per cycle, needs RNA primers, and uses DNA polymerases; transcription copies particular genes into RNA without primers using RNA polymerases.

**28** During DNA replication, the template strand is read in which direction by DNA polymerase?





- A  $5' \rightarrow 3'$ , the same direction in which the new strand is synthesised
- B  $3' \rightarrow 5'$ , opposite the direction of new strand synthesis ✓**
- C Randomly in both directions
- D Direction is irrelevant, as nucleotides are added independently
- E  $5' \rightarrow 5'$

► **Explanation:** DNA polymerase moves along the template  $3' \rightarrow 5'$  while synthesising the new complementary strand  $5' \rightarrow 3'$ .

29 Which statement about DNA replication in bacteria is **CORRECT**?



- A Replication starts from multiple origins on the circular chromosome
- B Replication initiates at a single origin, and two replication forks progress in opposite directions around the chromosome ✓**
- C Replication proceeds only in one direction around the chromosome
- D Replication is independent of helicase activity
- E Replication requires telomerase to complete the ends of the chromosome

► **Explanation:** Most bacteria have a single circular chromosome that is replicated bidirectionally from one origin until the forks meet on the opposite side.

30 A mutation abolishes the  $3' \rightarrow 5'$  exonuclease (proofreading) activity of a DNA polymerase but leaves its polymerisation activity intact. Which consequence is most likely?



- A Replication speed increases with no change in accuracy
- B Replication cannot initiate at origins of replication
- C Replication continues, but the mutation rate during DNA synthesis increases ✓**





- D** Replication is impossible because primers cannot be removed
- E** The direction of DNA synthesis reverses to  $3' \rightarrow 5'$

► **Explanation:** Without proofreading, misincorporated nucleotides cannot be efficiently removed during replication, leading to higher error rates.

