3.4 ESTABLISHMENT OF DNA AS GENETIC MATERIAL (1944)

While the experiment of Griffith described above, already provided a hint that there is a transforming principle that is responsible for the transfer of genetic information. However the key biomolecule which forms this transforming principle remained obscured until the evidence provided by a set of experiments. Two important experiments were performed one by Avery, MacLeod and McCarty and another by Hershey and Chase. Bacteriologists suspected that the transforming factor was some kind of protein. The transforming principle could be precipitated with alcohol, which showed that it was not a carbohydrate like the polysaccharide coat itself. But Avery and McCarty observed that proteases, enzymes that degrade proteins, did not destroy the transforming principle. Neither did lipases enzymes that digest lipids. They found that the transforming substance was rich in nucleic acids, but ribonuclease, which digests RNA, did not inactivate the substance. They also found that the transforming principle had a high molecular weight. They had isolated DNA. This was the agent that could produce an enduring, heritable change in an organism. This was an epoch-making experiment, but the three men did not get the Nobel Prize. The Nobel laureate Arne Tiselius said that Avery was

the most deserving scientist not to receive the Nobel Prize Later, further evidence was provided by Alfred Hershey and Martha Chase in 1952 through seminal work. In their experiments, the scientists used bacteriophages to demonstrate that DNA, not protein, is the genetic material. They labelled the DNA of T2 bacteriophages with radioactive phosphorus-32 and the protein coat with radioactive sulfur-35. When these labelled phages infected bacteria, only the progeny containing radioactive DNA retained the label, indicating that DNA, not protein, was transmitted into the bacterial cells. Further experiments confirmed that DNA was protected from degradation by enzymes, and the labelled DNA entered the bacterial cells upon infection, leading to the conclusion that DNA, rather than protein, carries genetic information. This landmark experiment provided crucial evidence supporting the role of DNA as the hereditary material. **Hershey** shared the 1969 Nobel Prize in Physiology or Medicine with **Max Delbrück** and **Salvador Luria** for their "discoveries concerning the genetic structure of viruses.

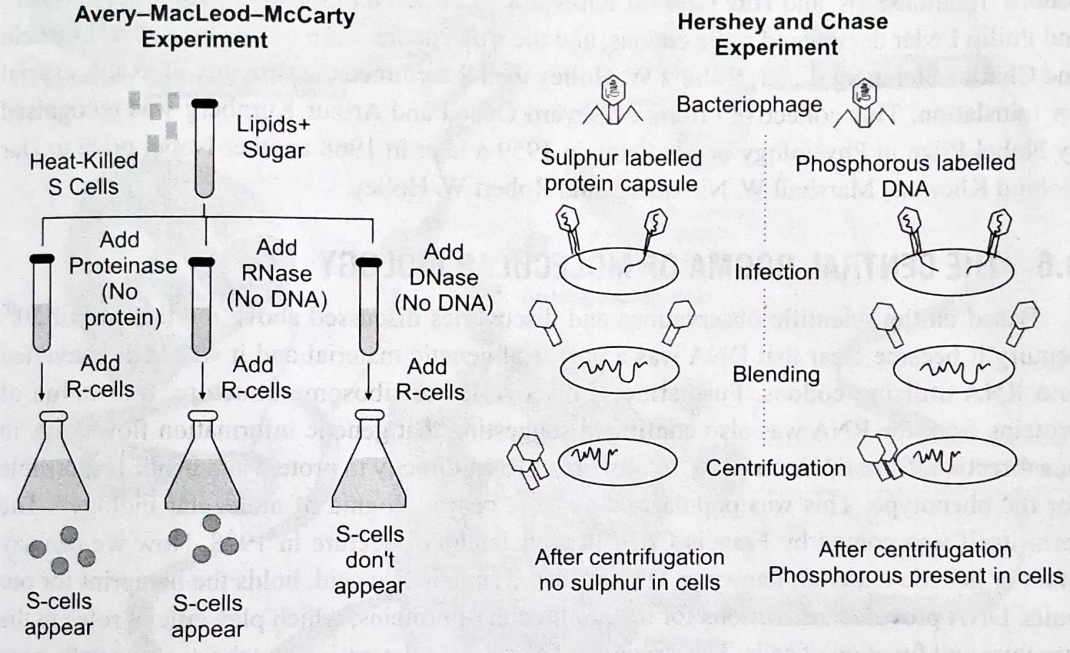

Fig. 3.3. *Two landmark experiments which established DNA as genetic material. A. Avery, MacLeod and McCarty's experiment and B. Hershey and Chase Experiment.*

3.5 THE GENETIC CODE

While the nature of genetic material was established in late 1952, the ongoing work on elucidating the structure of DNA was also accompanying at that time by another group of researchers in UK. With the classical Fiber X-ray diffraction approach of Rosalind Franklin and Maurice Willkins, James Watson and Francis Crick along with the Erwin Chargaff were able to delineate the double helical model of DNA, which represented an antiparallel series of nucleotides connected through phosphodiester linkage and strengthened by base pairing of nitrogenous bases. However, despite this, it remains unclear that how DNA is responsible for phenotype and transforming the information. This puzzle was solved by efforts of several research. The discovery of the genetic code was a collaborative effort that unfolded over several decades. Soviet-American physicist **George Gamow** proposed the idea of a triplet code, where

sets of three DNA bases (triplets) would encode the 20 amino acids used by living cells to build proteins. He named this interaction the "diamond code." In 1954, Gamow formed the RNA Tie Club, an informal organisation aimed at understanding protein synthesis. The club's pivotal contribution came from Francis Crick, who proposed the **adaptor hypothesis**, suggesting that the triplet code was carried by a molecule called tRNA, rather than directly to amino acids. In 1956 **Arthur Kornberg** isolated the first DNA polymerising enzyme, now known as DNA polymerase I and along with **Severo Ochoa** elucidated the mechanism of biological synthesis of DNA. Simultaneously, **Marshall Nirenberg** and **J. Heinrich Matthaei's** experiments in 1961 revealed the first codon, linking the RNA sequence UUU to the amino acid phenylalanine. They used artificial mRNA molecules with known sequences to identify specific nucleotide triplets that correspond to specific amino acids. For example, they showed that the RNA sequence UUU codes for the amino acid phenylalanine. Severo Ochoa's lab further elucidated other codons' relationships, and **Har Gobind Khorana** identified the remaining codons. Nirenberg and Philip Leder deciphered more codons, and the stop codons were named by Richard Epstein and Charles Steinberg. Later, **Robert W. Holley** then determined the structure of tRNA, crucial for translation. This collective efforts of Severo Ochoa and Arthur Kornberg was recognised by Nobel Prize in Physiology or Medicine in 1959 a later in 1968 another Nobel prize to Har Gobind Khorana, Marshall W. Nirenberg, and Robert W. Holley.