Copy of a printed molecular diagram referenced as "Structure of amino acids"

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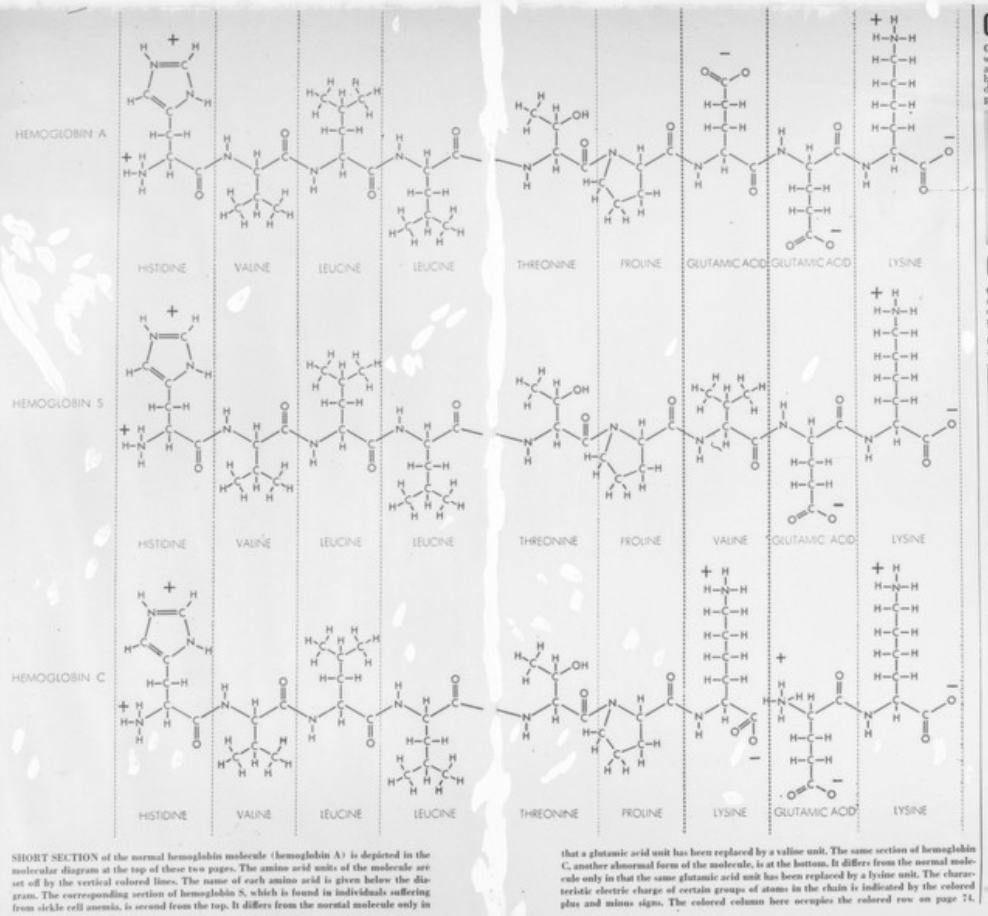
liarity in sickle cell hemoglobin. We now had to analyze the peptide, both in the normal and in the sickle cell molecule, to see what amino acids it was made of in each case. This was a very tedious business. We first had to purify the peptide, which involved cutting out the No. 4 spot on the paper, washing it off and running it again through the separation process of paper electrophoresis or chromatography. To get enough material for analysis we had to fingerprint dozens of batches of broken-down hemoglobin and purify their No. 4 peptides. Fortunately, with the very delicate methods of chemical analysis available nowadays a few thousandths of a gram of purified material was sufficient.

What did the analysis finally show? Both the normal and the sickle cell peptides turned out to contain the same types of amino acids: glutamic acid, valine, histidine, leucine, threonine, proline and lysine. But there was a difference in amount. The normal peptide had two glutamic acid units and a single valine, whereas the abnormal version had a single glutamic acid and a double dose of valine. In other words, in the sickle cell peptide a valine unit replaces a glutamic acid.

The next step was to find the order of arrangement of the amino acids in the peptide—a short chain of nine units. We broke the peptide down (this time with hydrochloric acid) into fragments consisting of from two to five amino acids. Step by step, sometimes peeling off one amino acid at a time, we determined the order of the amino acids in each fragment, and then we were able to fit the pieces together like a jigsaw puzzle to learn the sequence in the whole peptide. Thus we established that in the sickle cell peptide a valine unit occupies the place of the usual glutamic acid in the seventh position of the nine-unit sequence [*see diagrams at the right*]. A glutamic acid unit has an electrical charge; a valine unit has none. This explains the difference in the electrical charges on the two peptides.

Thus it appears that we have tracked down the difference between the sickle cell hemoglobin molecule and the normal one. According to all our evidence,



SHORT SECTION of the normal hemoglobin molecule (hemoglobin A) is depicted in the molecular diagram at the top of these two pages. The amino acid units of the molecule are set off by the vertical colored lines. The name of each amino acid is given below the diagram. The corresponding section of hemoglobin S, which is found in individuals suffering from sickle cell anemia, is second from the top. It differs from the normal molecule only in that a glutamic acid unit has been replaced by a valine unit. The same section of hemoglobin C, another abnormal form of the molecule, is at the bottom. It differs from the normal molecule only in that the same glutamic acid unit has been replaced by a lysine unit. The characteristic electric charge of certain groups of atoms in the chain is indicated by the colored plus and minus signs. The colored column here occupies the colored row on page 74.