PRIMORDIAL ORGANIC CHEMISTRY AND THE ORIGIN OF LIFE

The Space Science Board of the National Academy of Sciences in an authoritative statement declared that the search for extra-terrestrial life was the prime goal of Space Biology. "It is not since Darwin and, before him, Copernicus, that science has had the opportunity for so great an impact on the understanding of man. The scientific question at stake in Exobiology is the most exciting, challenging, and profound issue not only of the century, but of the entire naturalistic movement which has characterized the history of western thought for over 300 years. If there is life on Mars, and if we can demonstrate its independent origin, then we shall have a heartening answer to the question of unprobability and uniqueness in the origin of life. Arising twice in a single planetary system, it must surely occur abundantly elsewhere in the staggering number of comparable planetary systems".[1]

There is a distinct possibility of our finding an answer to the question of the existence of life in our own planetary system by an inspection of the planets with our immediate or remote sensors. Life detection devices to be landed on Mars are already in preparation. A manned-mission to Mars is a subject of intense discussion today.

For systems outside our own planetary system, one way of answering the question is by radio contact. Although in the long run listening for evidence of intelligent life may be a profitable and exciting pursuit, the difficulties encountered may be literally astronomical.

We have, however, another possible approach to this question. The recapitulation in the laboratory of the path by which life appeared on earth would give strong support to the theory of its existence elsewhere in the universe. Laboratory experiments on earth can reveal which material and conditions available in the universe might give rise to chemical components and structural attributes of life as we know it.

Three factors have made the scientific approach to this question possible, not only theoretically but also experimentally: Astronomical advances, recent progress in biochemistry, and the triumph of Darwinian evolution. Present day telescopes reveal that there are more than 10^{20} stars. Therefore, there are more than 10^{20} opportunities for the existence of life. A conservative estimate made by Harlow Shapley suggests that of these at least 10^{8} are suitable for life.[2] Su-Shu Huang was less rigorous in the restrictions he imposed, and he suggested at least 10^{18} possible sites for the existence of life.[3] In a very recent paper, Harrison Brown has concluded that in our galaxy alone there must be at least 10^{11} planetary systems; and that of these, at least 4.3% would be in the right range of size and distance from the star to support life.[4]

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Biochemical research during the last decade has established the remarkable unity of biochemistry. We are thus led to the inescapable conclusion that all life must have had some common chemical origin. The two molecules, the nucleic acids and the proteins, are basic in all living organism whether one considers the smallest microbe or the most complex intelligent human being. (Figure 1 and Figure 2)

The Darwinian Theory of Evolution has postulated the unity of the entire biosphere. The higher forms of life are believed to be evolved from the lower over a very extended period in the life of this planet.

The scientific thinking of this problem was crystallized during the first half of this century, especially through the efforts of Oparin,[5] Haldane,[6] and Bernal.[7] Oparin postulated a primitive reducing atmosphere in which a large amount of organic material accumulated before the origin of life and a long chemical evolution as a necessary preamble to the origin of life. Haldane suggested the idea of the "primordial soup" which consisted of an ocean of organic matter which gradually gave rise to replicating systems. Bernal described the methods by which small molecules that may have been synthesized could have concentrated in lagoons or clay deposits by the sea. Air accumulation of organic matter was a necessary prerequisite for chemical evolution.

During the last decade, several experiments in this field have established the possible synthesis of molecules of biological significance under simulated primitive earth conditions. Notable among this work is the classical experiment of Stanley Miller,[8] who, in 1953, exposed a mixture of methane, ammonia, water and hydrogen to an electric discharge and obtained amino acids and organic compounds like urea, formic acid, etc.

The work I am about to describe concerns recent investigation conducted in the Exobiology Division of the Ames Research Center, Moffett Field, California.[9] The simple working hypothesis which we have adopted is that the molecules which are fundamental now were fundamental at the time of the origin of life. We are investigating the synthesis of the constituents of the nucleic acid molecule and the protein molecule. We simulate primitive earth conditions, prepare the "primordial soup" described by Haldane, and then we proceed to analyze it.

A starting point for any such experimental work must center around cosmic abundances. Astronomical spectroscopy reveals that the most abundant elements in our galaxy are in the order of rank: hydrogen, helium, oxygen, nitrogen and carbon. Hydrogen, oxygen, nitrogen and carbon are indeed the basic elementary constituents of all living organisms. We know from chemical equilibria, that in the presence of hydrogen, carbon, nitrogen, and oxygen must exist in their reduced forms as methane, ammonia, and water. The equilibrium constants for these reactions at 25°C are all of considerable magnitude. It is this atmosphere of methane, ammonia, water vapor, and small amounts of hydrogen which we shall consider as the primitive atmosphere of the earth.

The energies available for the synthesis of organic compounds under primitive earth conditions are ultraviolet light from the sun, electric discharges, ionizing radiation, and heat. While it is evident that sunlight is the principal source of energy, only a small fraction of this was in the wavelength below 2000Å, which could have been absorbed by the methane, ammonia, and water. However, the photodissociation products of these molecules could absorb energy of higher wavelengths. Next in importance as a source of energy are electric discharges such as lightning and corona discharges from pointed objects. They occur close to the earth's surface and, hence, would more efficiently transfer the reaction products to the primitive oceans. A certain amount of energy was also available from the disintegration of uranium, thorium, and potassium 40. While some of this energy may have been expended on the solid material such as rocks, a certain proportion of it was available in the oceans and the atmosphere. Heat from volcanoes was another form of energy that may have been effective, but in comparison to the energy from the sun this was only a small portion and perhaps not widely distributed.

In our experiments with ionizing radiation, we have found that the electron beam from a linear accelerator at Lawrence Radiation Laboratory of the University of California, Berkeley, provided us with a convenient source of electrons simulating K^{40} on the primitive earth. (Figure 3) When a mixture of methane, ammonia and water was irradiated with 4 1/2 mev electrons for a period of about one hour, resulting in a total dose of approximately 7×10^{10} ergs, and the resulting material analyzed, the largest single non-volatile compound formed was adenine.[10] The production of adenine in this experiment was significant in the light of the multiple role played by adenine in biological systems. Not only is it a constituent of both DNA and RNA, but it is also a unit of many important cofactors.

In our experiments with electric discharges, we employed a modified version of the apparatus used by Stanley Miller in 1953 (Figure 4). In a typical experiment lasting 160 hours, 65% of the methane could be recovered as organic compounds both in the water soluble and ether soluble fractions. About 30% of this material was in the water extract. In this solution, some of the constituents of the nucleic acid molecule have been identified.

When a mixture of methane and ammonia in the presence of water vapor is passed through a heated vycor tube at about 1000°C, and the effluent gased absorbed in water, amino acids are formed. This result has recently been reported by Fox, who identified 14 of the amino acids commonly present in protein, in a single experiment.[11] Analysis of the gas fraction has shown that a great portion of the methane is converted into higher hydrocarbons, including ring compounds such as benzene, toluene, and anthracene.

Chemosynthesis by meteorite impact on planetary atmospheres has been suggested as a possible pathway for primordial organic synthesis.[12] The reaction is probably a result of the intense heat generated momentarily in the wake of the shock wave following the impact. In a very preliminary experiment simulating these conditions, by firing a ballistic missile into a mixture of methane, ammonia and water vapor, we have been able to identify some amino acids and a few uv absorbing compounds which may be of biological significance.

In all the experiments just described, whether using uv ionizing radiation, electric discharges, or heat, one of the primary products appears to be hydrogen cyanide. Gas analysis has shown that the major constituent of these simulated primitive atmospheres even after a brief exposure to one or the other of these forms of energy is hydrogen cyanide. The second product in the gas phase is formaldehyde. Miller and Urey identified both these compounds in their early work.[13] Palm and Calvin recorded similar results.[14] Our own experiments point to the same conclusion. In subsequent experiments, we have, therefore, used hydrogen cyanide and formaldehyde as our starting materials.

When an aqueous solution of hydrogen cyanide, approximately 10^{-3} molar in concentration, is exposed to uv, a wide variety of organic compounds can be formed. Among these have been identified adenine, guanine, and urea. Adenine and guanine are the two purines in RNA and DNA. Urea is an important chemical intermediate. The reaction with hydrogen cyanide may proceed even without a source of energy. When an aqueous solution of hydrogen cyanide is left standing at -10°C, it appears to be converted spontaneously into more complex organic compounds.

In experiments starting with formaldehyde in a very dilute aqueous solution, the two sugars, ribose and deoxyribose, have been identified. These two are the only sugars in RNA and DNA.

The same forms of energy that have been instrumental in the production of the sugars and of the purines have now been demonstrated to be responsible for the synthesis of nucleosides, nucleotides, and peptides. When a solution of adenine and deoxyribose in the presence of CN^- is exposed to heat or uv, the nucleoside deoxyadenosine is rapidly formed.[16] It has even been demonstrated that when the mixture is allowed to stand at room temperature, the nucleoside is spontaneously formed. This result, therefore, confers a unique role on hydrogen cyanide. Hydrogen cyanide is a pathway for the purines. Together with formaldehyde, it undergoes the Strecker synthesis to give rise to amino acids. And in the synthesis of nucleosides, it performs the role of a catalyst.

The synthesis of peptides under abiological aqueous conditions has been considered to be a matter of great difficulty. Previous syntheses available have generally postulated anhydrous conditions, as for example, the high molecular weight proteinoids prepared by Fox.[17] In our laboratory, however, we have recently found that when an aqueous solution of glycine and leucine was exposed to uv in the presence of cyanamide, the dipeptides glycyl-glycine, glycyl-leucine, leucyl-glycine, and leucyl-leucine were formed. The action of cyanamide may be analogous to that of dicyclohexylcarbodiimide, which has been extensively used by Khorana and his co-workers for the synthesis of nucleotides.

These results show that under simulated primitive earth conditions, molecules of biological significance can be synthesized. These results lend support to the hypothesis of chemical evolution as

1) the conditions are aqueous
2) the concentrations of materials used are very small
3) the sources of energy used are those that are most likely to have existed under primitive earth conditions.

As the laws of chemistry and physics are universal laws, these laboratory experiments point out that whereever the right conditions exist, those molecules which can act as precursors of biological systems will arise anywhere in the universe. The experiments in the laboratories thus lend support to the Oparin-Haldane hypothesis of chemical evolution and our belief in the existence of extraterrestrial life.

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PHOTOGRAPHS

A-30446-26	Figure 1	"A Section of a Protein Molecule"
MU-16096	Figure 2	"A Section of a DNA Molecule"
A-31716	Figure 3	"Apparatus for Electron Irradiation of Primitive Gases"
A-32587	Figure 4	"Electric Discharge Apparatus"

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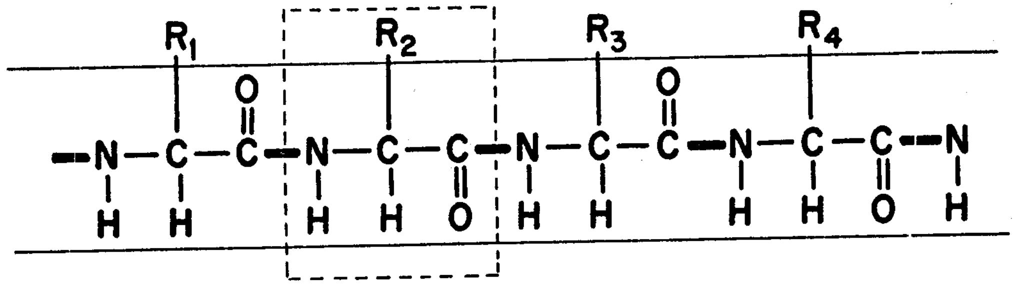

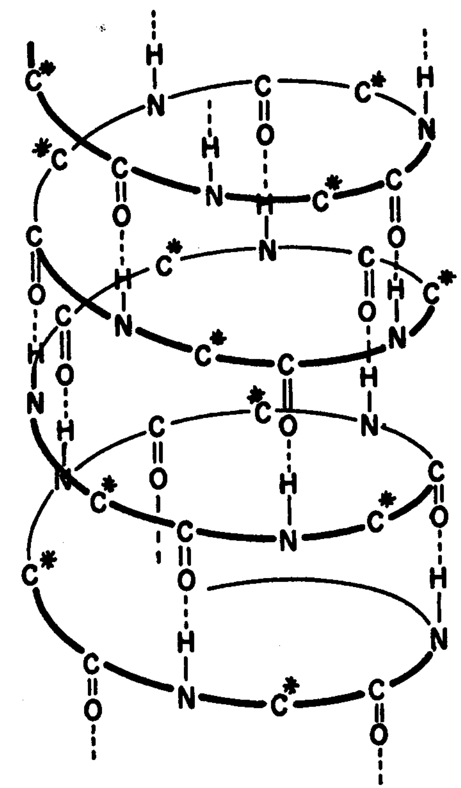

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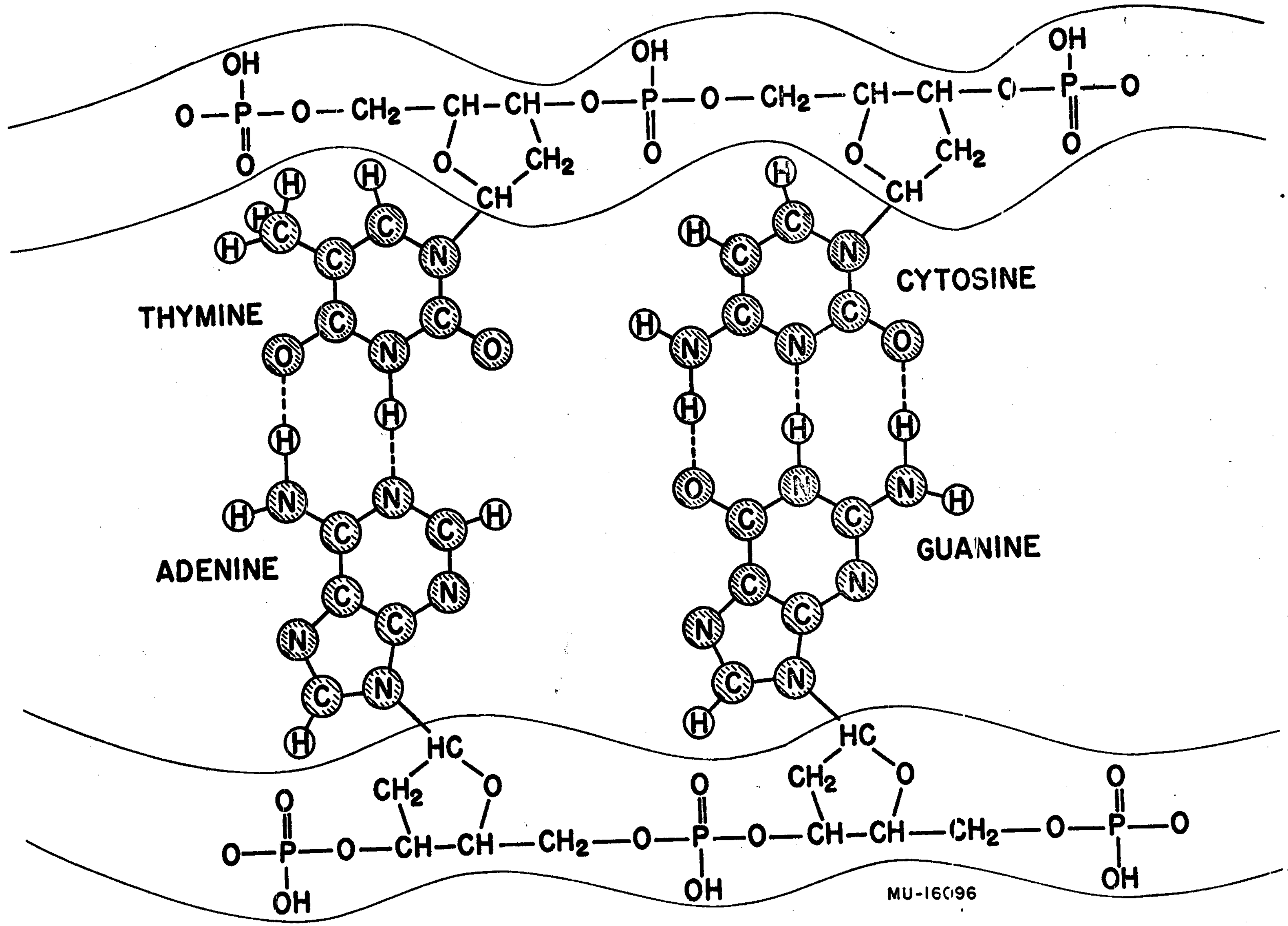

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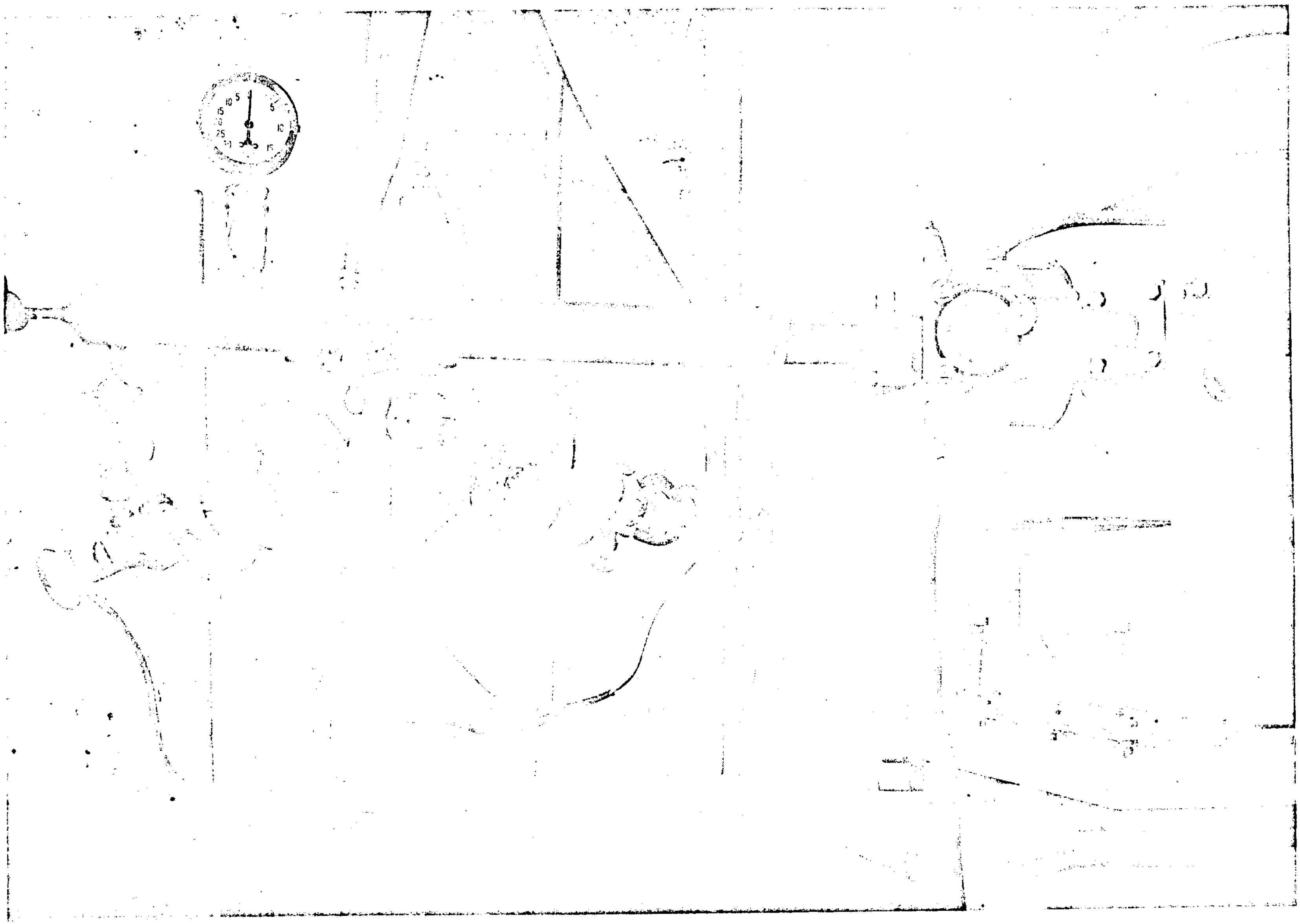

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