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HEMIN AND CHLOROPHYLL— THE TWO MOST IMPORTANT PIGMENTS FOR LIFE ON EARTH[1]

PAUL ROTHEMUND

The Ohio State University, Columbus, 10, and Muskingum College, New Concord, Ohio

Two chemical processes are the prerequisites for all life on earth: the absorption of some of the energy from the sun in the green plants and its transformation into carbon compounds on one hand, and the use of the chemical energy of these compounds by animals in controlled decomposition reactions on the other.

From the chemist's point of view the green leaf is a veritable chemical laboratory: carbon dioxide from the air, and water and inorganic salts from the soil are the raw material, the visible portion of the sun radiation furnishes the energy, and the numerous complex constituents of the plant represent the manufactured products. Some of the substances synthesized are structural matter, like cellulose in the wood, or cork in the bark, others are food reserves, as starch in the grains of corn or wheat, or in potatoes. Of the many other materials produced in the green plant only a few may be enumerated here, sugars, fats, oils and waxes, proteins and nucleic acids, fibers like cotton or hemp, vitamins, hormones, indigo and other dyes, latex for producing rubber, alkaloids like the nicotin in tobacco leaves, valuable medicinally used compounds, such as quinine, cocaine, and morphine, and—most important—the green pigment chlorophyll. "Photosynthesis", or the "assimilation of carbon dioxide" is the biochemical process, in which simply constructed and relatively inert inorganic compounds are built up into the highly complex, reactive and sensitive organic compounds, which characterize living matter. Only living, active plant cells containing chlorophyll, and exposed to light, can perform this outstanding chemical feat. The phenomenon has been studied for a long time, and much detailed information has been gathered about it. Yet, the exact mechanism is still unknown, and the chemist cannot perform in his laboratory the same reactions with the same means, which the plants use on a gigantic scale every year.

Every living cell of any plant or animal requires energy in order to carry out its ordinary life processes, and it secures this energy from some organic material within the cell. This food material is in the last analysis always a product of photosynthesis. In the process of metabolism the oxygen of the air is used to oxidize the food, and carbon dioxide is eliminated. Oxygen intake, and carbon dioxide removal are carried on during the lifetime of the cell as respiratory activity.

In the form of a chemical equation the process of photosynthesis is usually written

[1]From the presidential address delivered at the Annual Meeting of The Ohio Academy of Science at Wittenberg College, Springfield, Ohio, on April 20, 1956.

$$\underset{\text{carbon dioxide}+}{x\ CO_2} + \underset{\text{water}+\text{light}}{x\ H_2O + \text{light}} \longrightarrow \underset{\text{carbohydrate}+}{(CH_2O)_x} + \underset{\text{oxygen}}{x\ O_2}$$

while metabolic combustion is symbolized by

$$\underset{\text{carbohydrate}+}{(CH_2O)_x} + \underset{\text{oxygen}}{x\ O_2} \longrightarrow \underset{\text{carbon dioxide}+}{x\ CO_2} + \underset{\text{water}+\text{energy}}{x\ H_2O + \text{energy}}$$

When a hexose sugar is used for the purpose of illustration, the two reactions may be represented as follows:

$$6\ CO_2 + 6\ H_2O + 672\ \text{kcal.} \underset{\text{Respiration}}{\overset{\text{Photosynthesis}}{\rightleftharpoons}} C_6H_{12}O_6 + 6\ O_2$$

During illumination of a plant the photosynthesis process is superimposed upon plant respiration, and the energy-storing activity exceeds the energy-consuming one manyfold. Both are responsible for the carbon dioxide cycle in nature, which involves the continuous regeneration of carbon dioxide, the most depreciated form of carbon, in form of energy-rich organic compounds and of oxygen. The latter will then be available to plants and animals for the vital activity of cell respiration.

In order to present a picture of the magnitude of the energy storing process, it may be mentioned that our present civilization derives more than ⅞ of its mechanical and heat energy from photosynthesis, either from food materials and from wood produced now, or from fossils like coal, oil, or natural gas, which are only the still available end products of the same process, when it took place in geological ages. Chlorophyll derivatives have been identified in small amounts in shale oils, petroleums, asphalt, and other bituminous deposits as well as in certain coals; these findings have confirmed the geological and paleobotanical views that these fossils are of plant and not of animalic origin. Incidentally, these discoveries also demonstrate that the plants growing in the Silurian period of the Paleozoic era—about 350 to 400 million years ago—contained the same chlorophyll which our plants produce.

The numerous chemical reactions involved in photosynthesis and in respiration are catalytically controlled: the green coloring matter of the plants governs the uptake of radiant energy, and a red pigment directs the oxygenation of blood in the lungs of animals. These pigments have been the objects of long and intensive studies. Pelletier and Caventou extracted the green matter from plants in 1818, and named it chlorophyll, but only in 1906 did M. Tswett definitely establish by chromatography that many plants contained actually two green pigments. He also isolated a number of yellow and orange-red pigments, which accompanied the green ones. At the beginning of this century Willstätter demonstrated the chemical identity of the chlorophylls irrespective of the plant from which they were isolated. Further work established that the ratio of the blue-green chlorophyll *a*, $C_{55}H_{72}N_4O_5Mg$, to the yellow-green chlorophyll *b*, $C_{55}H_{70}N_4O_6Mg$, was usually about 2.5 or 3 to 1, but that in some plants the *b*-component was entirely lacking. Improved experimental techniques also ascertained the ratio of the yellow pigments carotene to xanthophyll in green leaves as 1:2, and demonstrated the presence of several other pigments in plant tissue. So far no plant containing chlorophyll *b* only has been found.

If one pours defibrinated beef blood into hot glacial acetic acid, which has been saturated with sodium chloride, one obtains, upon cooling, beautiful dark red brown crystals. They represent the coloring matter from blood, and were called "hemin". The method described yields a chlorine-containing product, while the hemoglobin of the blood, from which the hemin was formed, is chlorine-free. Thus hemin is an artificial product. Its formula is $C_{34}H_{32}N_4O_4FeCl$. Hemoglobin

of the red blood corpuscles of human blood consists to 96 percent of the histone globin, and to 4 percent of pigment. In the animal kingdom hemoglobin is the most common respiratory pigment. Its all important property is its ability to react reversibly with oxygen, taking it up in the lungs at a certain pressure, and releasing it later in the tissues under diminished pressure. In this "oxygenation" the valency of the iron atom remains +2. Oxyhemoglobin has a characteristic two-banded absorption spectrum, while the oxygen-free hemoglobin exhibits a spectrum with only one rather diffuse absorption band.

The globin portion in the hemoglobin of different animals is typical for a particular species. The hemoglobins show differences in crystal form, solubility, molecular weight, and sometimes in the absorption spectra. The percentage of the component amino acids and consequently the electrochemical behavior, as well as immunological reactions vary also. But the pigment component, the so-called prosthetic group, is in all cases the same. Thus hemin prepared from human blood is identical with hemin obtained from the blood of cattle.

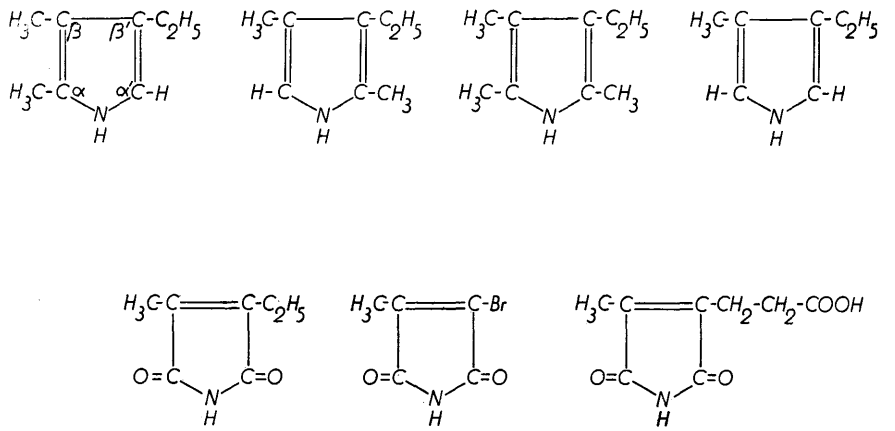

FIGURE 1. Cleavage Products. Reductive cleavage products* (Top row) from left to right, hemopyrrole, cryptopyrrole, phyllopyrrole, and opsopyrrole; oxidative cleavage products (Bottom row) from left to right, methyl ethyl maleic imide, bromo citraconic imide, and hematinic acid.

*In the corresponding carboxylic acids the ethyl group,—C_2H_5, is replaced by the propionic acid group,—CH_2—CH_2—COOH.

In the human organism the red blood corpuscles as living cells are continuously produced, they grow to maturity, and die after a certain life span. The pigment component is then also decomposed, and eliminated in form of bile pigment, while the iron is retained to be available for the synthesis of red pigment of young blood cells. Indeed the output of bile pigment has been used to gain information about the rate of decomposition of red blood corpuscles in the human body at the time, before radioactive tracer elements were available for such investigations.

An interesting similarity of hemin and chlorophyll lies in the fact that these important bio-catalysts contain a metal atom complexly linked to the pigment molecule, and that they occur in nature as chromo-proteides: to the pigment + protein combination hemoglobin corresponds in the plant the chlorophyll + protein union, for which most commonly the term chloroplastin is used.

Hans Fischer concentrated his studies upon the pigment components of these pigment + protein compounds. He was able to elucidate the chemical relationship of hemin and chlorophyll by degradation and synthetic investigations, which

extended over about 30 years. Drastic reductive cleavage of derivatives of hemin and of chlorophyll with hydriodic acid in glacial acetic acid yielded substituted pyrroles: bases, which carried in their β-positions one methyl and one ethyl group each, and the corresponding carboxylic acids with methyl and propionic acid residues in these positions. Total oxidation with CrO_3 or with PbO_2 resulted in products, for which the same principle of substitution was valid, again from either of the two pigments.

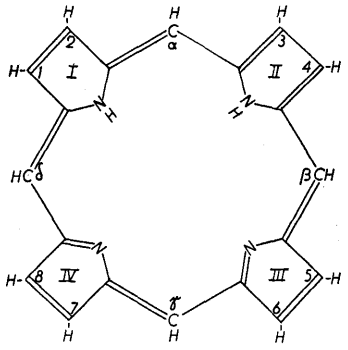

FIGURE 2. Porphin and nomenclature.

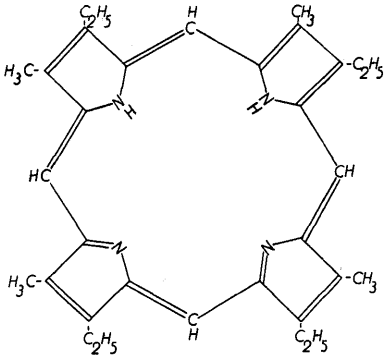

FIGURE 3. Etioporphyrin III.

Four of such nitrogen-bearing five-membered rings were present, linked in their α-positions by $-\overset{H}{\underset{C}{}}=$bridges. For the unsubstituted ring system Fischer suggested the name "porphin". Its structural formula and the conventional nomenclature for it are given in figure 2.

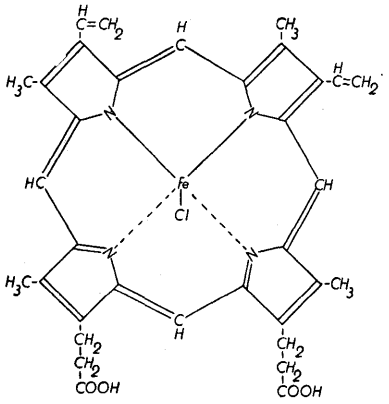

FIGURE 4. Hemin.

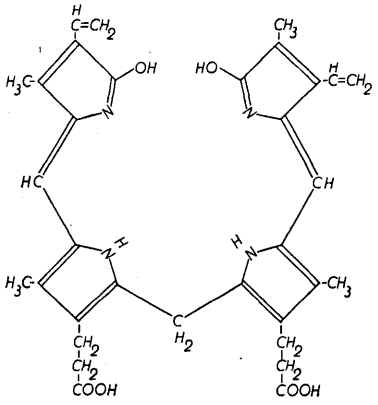

FIGURE 5. Bilirubin.

All identifying marks are counted in clockwise direction. Starting with the ring in the left upper corner the rings are given Roman numerals I to IV, and beginning on the same ring, the hydrogen atoms in the β-positions are designated by Arabic numbers 1 to 8. Hydrogen atoms on the bridge carbon atoms receive lower case Greek letters α to δ, starting between rings I and II.

Porphin, the fundamental ring system in hemin as well as in chlorophyll can be synthesized from pyrrole and formaldehyde, or from pyrrole-α-aldehyde. Controlled degradation reactions on hemin and on chlorophyll resulted in the isolation of numerous substituted porphins. Many of them exhibit in neutral ether solution a beautiful porphyry-red color. On account of this property all substituted porphins, and porphin itself, have been given the collective designation "porphyrins".

The decomposition of hemin may be performed to yield a porphyrin of the following structure,

If one stays within the limitation for the substituents presented above, viz. one methyl and one ethyl group only on each pyrrole ring, then there are only four isomers possible. They were given the name etioporphyrins, and their structural arrangement of substituents may be tabulated as follows:

Isomer	Location of Substituents	
	CH_3	C_2H_5
I	1.3.5.7	2.4.6.8
II	1.4.5.8	2.3.6.7
III	1.3.5.8	2.4.6.7
IV	1.4.6.7	2.3.5.8

It should be noted that the Roman numbers for these etioporphyrins were arbitrarily assigned during Hans Fischer's investigations of these compounds. It was found that the etioporphyrin from hemin, the "natural etioporphyrin" followed the arrangement assigned as structure for the isomer III. For an arrangement of four like substituents, and two pairs of different ones, 15 isomers are found. Thus, when one eliminates the > Fe-Cl grouping in hemin and replaces it by two hydrogen atoms, one obtains the so-called protoporphyrin IX, which has its four methyl groups in 1.3.5.8-positions, and belongs therefore to the isomer type III. This porphyrin carries two vinyl groups $-\overset{H}{\underset{C}{}}=CH_2$ in positions 2, and 4, and two propionic acid residues, $-CH_2-CH_2-COOH$ in positions 6, and 7.

The structure of hemin, as established by Hans Fischer's synthesis, is

In the bile pigment bilirubin, $C_{33}H_{36}N_4O_6$, the common structure with hemin is still recognizable, when it is written as in figure 5, although the main ring has been opened.

As already mentioned this break of the ring is performed continuously in the animal organism, apparently with great ease. In vitro the cleavage of the porphin ring system to obtain compounds of the type of bile pigment can be performed, but is experimentally far from simple. Yet in the living organism it may be also brought about mechanically: a short blow of proper intensity in the right location will promptly initiate the reaction, the beautiful color scheme of the "black and blue mark" demonstrates its progress in the decomposition of blood pigment to bile pigments. With a faint yellow the ultimate absorption of the pigments is in due time terminating.

The chlorophylls are also patterned according to the arrangement of substituents in the isomer type III, as the following formula for chlorophyll *a* indicates: Chlorophyll *b* carries in position 3 an aldehyde group (=formyl group) $-\overset{H}{\underset{C}{}}=O$, where n the *a* component a methyl group is located. The total synthesis of the chlorophylls has not been performed as yet, although all the fundamental work to accomplish this task seems to be available. Figure 6 represents the most

likely picture of the structure according to our present knowledge of the molecule. The fundamental differences between hemin and chlorophyll—other than the fact that one is an iron, the other a magnesium complex salt—may be summarized as follows: in chlorphyll *a* an ethyl group replaces one vinyl group in position 4, the double bond between carbon atoms 7 and 8 in hemin is hydrogenated in chlorophyll; chlorophyll is complicated by the 6, γ-ethanone ring, which carries a methyl ester group, its propionic acid group in position 7 is esterified by the unsaturated aliphatic alcohol phytol, $C_{20}H_{39}OH$. It is interesting to note that this alcohol is also a constituent of the natural vitamin K. Hemin is a dicarboxylic acid, chlorophyll an ester of an acid of high molecular weight with an alcohol of high molecular weight, which accounts for its character as a waxy material, which is difficult to obtain in crystallized form. Hemin and chlorophyll are porphin pigments, but the bile pigment with its opened porphin ring and the linear arrangement of the four pyrrole rings no longer belongs to this class of pigments.

A very close relationship exists between hemin and chlorophyll on one hand, and bacteriochlorophyll *a* from certain microorganisms on the other:

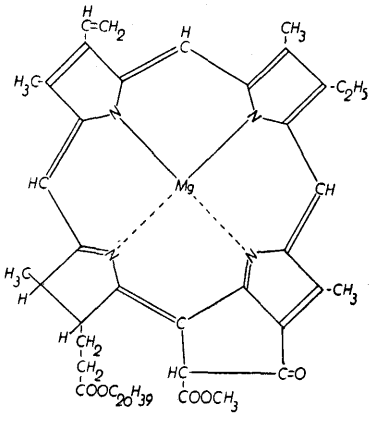

FIGURE 6. Chlorophyll *a*.

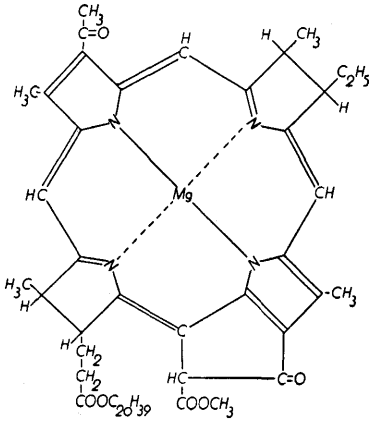

FIGURE 7. Bacteriochlorophyll *a*.

The comparison of its structure with that of chlorophyll *a*, Fig. 6, shows that two pyrrole rings are partially hydrogenated, and the vinyl group in position 2 has been replaced by an acetyl group $-\overset{\displaystyle O}{\overset{\|}{C}}-CH_3$.

Another porphin pigment, closely related to hemin and to chlorophyll, occurs in plants in extremely small quantities, namely the oxygen-transfering respiratory cell "ferment", the "cytohem" of Warburg. It is of hemin type, a porphyrin-iron complex, linked to protein in the cells, and of paramount importance in cell respiration. Cytohem is at present the subject of intensive studies on four continents. It has been demonstrated that Vitamin B_{12} is also related to hemin and chlorophyll structurally. For comparison the formula of the hexacarboxylic acid from this vitamin is given in figure 8.

The differences are already more pronounced: the $-\overset{\displaystyle H}{\overset{|}{C}}=$ bridge between rings I and IV is replaced by a single bond, hydrogenations have modified the ring system greatly; in addition to methylations and carboxylations the complexing metal

in the molecule is cobalt, linked to chlorine, and to the nitrile group, in addition to its linkage to one of the nitrogen atoms of one of the four five-membered rings.

A few more experimental facts concerning the pigments hemin and chlorophyll may be inserted here to illustrate their chemical behavior. Treatment of hemin with certain acids removes iron and chlorine under porphyrin formation. The various porphyrins so obtained can be recognized by their characteristic absorption spectra. Introduction of the > Fe-Cl group into protoporphyrin IX yields the natural hemin. When the same reaction is used on other porphyrins, the corresponding iron chlorides are formed. They have received the class designation "hemins" to indicate their structural analogy to hemin from blood.

If either of the two natural chlorophylls is exposed to even very dilute acids, the magnesium atom in the molecule is replaced by two hydrogen atoms. Suitable reagents allow to introduce magnesium again into the magnesium-free pigments, and the original chlorophylls are restored. Controlled chemical decomposition of

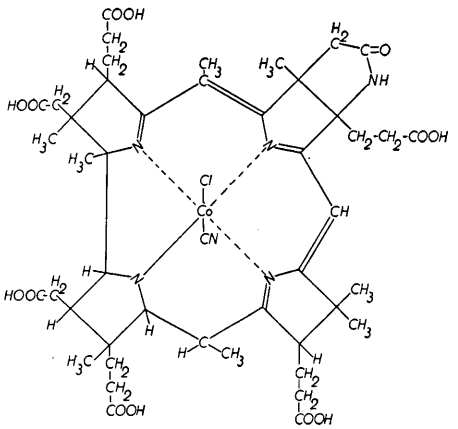

FIGURE 8. Hexacarboxylic acid from Vitamin B_{12}.

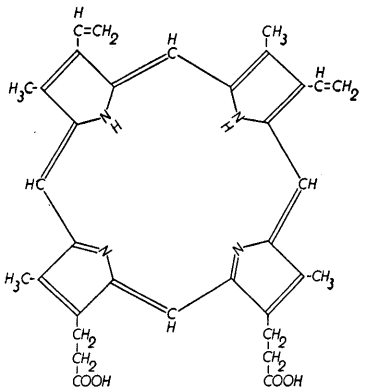

FIGURE 9. Protoporphyrin IX.

the chlorophylls yields numerous magnesium-free compounds of porphyrin type, and even those, which are structurally intermediates between the chlorophylls and the porphyrins. Into their molecules magnesium may also be built again. It is even possible to degrade the chlorophylls to the porphyrin stage without eliminating the magnesium in the process. The name "phyllins" is applied to all such magnesium complex salts which are still structurally closely related to the chlorophylls.

The synthetic efforts of the modern chemist have by far outdone Nature in the number and types of porphyrin compounds, which have been synthesized. Much of this work was, and is still at present, undertaken in order to elucidate the steps by which the organisms perform syntheses of pigments of porphin type.

Obviously the last steps in these syntheses in nature are the introduction of the metal, iron or magnesium respectively, and the attachment of the prosthetic group to the protein molecule, but the methods of the physiological syntheses of such complicated pigments have not been learned so far. Studies of the subject are rendered more difficult yet because in the tissues of animals and plants the normal concentration of porphyrins is very low. The isolation of possible precursors of hemin or chlorophyll can take advantage of the availability of several reliable tests for porphyrins and their complex salts. The solutions of these compounds fluoresce characteristically pink or red under ultraviolet radiation.

Differences in basicity toward hydrochloric acid permit separation and identification of many pigments by fractionating them with selected concentrations of this acid. Other suitable techniques for separation are chromatography and electrophoresis. The isolated pigments have often characteristic melting points. The latter determinations may be improved for porphin carboxylic acids by also determining the melting points of their esters. Of great aid in this field are the optical properties of the entire class of compounds: solutions exhibit absorption or fluorescence bands, whose wavelength ranges and intensities allow often the positive identification of several pigments in a mixture. Many substances also have typical powder spectra. Some of the naturally occurring materials, like the chlorophylls, have asymmetric carbon atoms in their molecules, and rotate the plain of polarized light.

In order to stress the need of reliable determination of these compounds the topic of porphyrins in health and disease may be briefly surveyed. Such a discussion will underscore the importance of hemin and chlorophyll for life on earth. The pigments derived from them are commanding ever increasing attention, especially since failure of the animal organism to synthesize hemin properly leads to a number of startling, dangerous, and oftentimes fatal conditions.

Porphyrins and their metal complex salts occur in nature normally in small quantities only. The green leaves and other green parts of plants contain them; they are found in many foods, in bread, fish, and milk, also in beer. Relatively high is their content in potatoes, rutabagas, and in spinach. In the animal the young cells of the erythrocyte series, and the bone marrow possess porphyrins. The spotted egg shells, and the feathers of certain species of birds owe their color to free porphyrins, or to their metal complex salts. Naturally occurring porphyrins and porphyrin derivatives are of the types I, or III, as outlined in the table on page 197. Due to the complicated structure of these compounds it cannot be assumed that the two different types arise from one common prototype, or that one type alone is synthesized and changed by chemical means into the other in the body. Independent synthesis of the two types from simple pyrroles must take place by mechanisms still unknown. This concept was first pronounced by Hans Fischer as the "dualism of porphyrins in nature". In human hemoglobin the ratio of type III to type I is greatly in favor of type III, about 10,000:1, and this almost exclusive synthesis of the isomer pattern III is normally very strictly maintained, as far as the blood pigment is concerned. The "natural" protoporphyrin IX (type III), into which iron is introduced in the synthesis of the prosthetic group of hemoglobin, is present in human blood (8 to 15 micrograms per 100 ml.). The formulae of two closely related porphyrins, coproporphyrin (fig. 10) and uroporphyrin (fig. 11) are given due to their importance in nature. In both figures the types III have been represented to show the relationship to protoporphyrin IX (fig. 9). Uroporphyrins are tetraacetic acid-tetrapropionic acid porphins, coproporphyrins are easily obtained from them by decarboxylation and are tetrametyl-tetrapropionic acid porphins. A human adult excretes in urine during a 24 hr. period normally 12 to 100 micrograms coproporphyrin, and usually it is stated that about 80 percent of this quantity belong to type I, and 20 percent to type III. Some authors claim, however, absence of type III; in one case a large quantity of pooled urine (10,000 liters) was analyzed and the coproporphyrins I and III were found in a ratio of 1 : 1. It has been suggested that this result may have been caused by the inadvertent admixture of pathological urines of undiagnosed cases with higher coproporphyrin III content in the material examined.

Human bile and human feces contain normally coproporphyrin I. The total urinary and fecal excretion of coproporphyrin for human adults is between 150 and 350 micrograms per day. Infants and children eliminate smaller amounts. Uroporphyrins are absent from normal urine; the role of uroporphyrin in the synthesis of the pigment component of hemoglobin has recently been discovered,

and it seems that all of the uroporphyrin is used up so promptly that no excretion takes place.

Under pathological conditions the amounts of porphyrins excreted are increased, and the ratios of the isomers are altered also. Thus, in certain hepatic diseases coproporphyrin I is found in the urine almost exclusively, and in greatly increased amounts, while in alcoholic cirrhosis coproporphyrin III causes the larger content of urinary porphyrin. Coproporphyrin III is present in the urine in most cases of acute poliomyelitis, and of poisoning by certain elements, or drugs. Out of the long list of such materials only a few may be given here: arsenic, phosphorus, lead and selenium, acetanilide, aspirin, barbiturates, ethyl ether, morphine, phenacetine, salvarsan, and the sulfa drugs. Coproporphyrin I elimination exceeds that of coproporphyrin III in many febrile conditions, and in certain blood diseases.

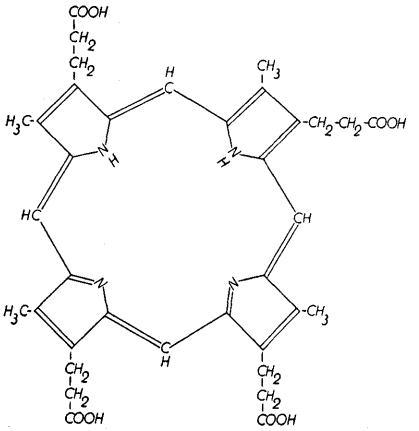

FIGURE 10. Coproporphyrin III.

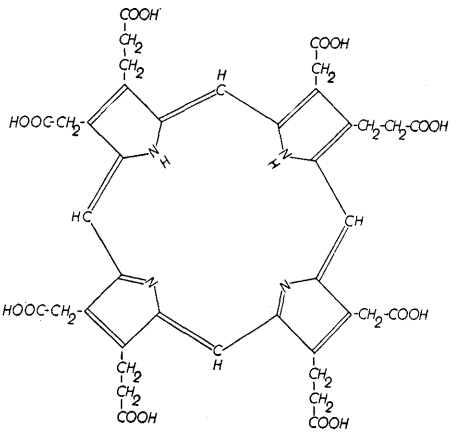

FIGURE 11. Uroporphyrin III.

In addition to these causes for increased temporary porphyrin excretion in urine (porphyrurias), the conditions of congenital defective porphin pigment metabolism, the porphyrias, must be mentioned. Patients with congenital porphyria excrete large amounts of type I porphrins, so much in some cases, that the urine is of deep Burgundy-red color, and they are very sensitive to light. This rare recessive metabolic error is found more frequently in men than in women (ratio about 2 : 1). The sensitivity of the skin to light causes itching, erythema, blister formation on the exposed areas (usually face and hands), and skin eruptions, which leave pigmented scars. Necrosis of the tissues involved leads to severe and disfiguring destructions, especially of the thinner parts of the body, where light could penetrate from different directions, like ears, nose, and fingers. Often blindness is observed due to scar formation. The bones and teeth become discolored due to impregnation with porphyrin. Neither cause nor cure for the disease are known. The disease is also well known in animals (ochronosis of cattle, pigs, and squirrels).

The so-called "acute porphyria" is also a disorder of the porphin pigment metabolism, inherited as Mendelian dominant in the ratio of ♀ : ♂ about 4 : 1. It is more common than the congenital form, usually in the ages between 30 and 50 years, and is rare in children. There is neither sensitivity to light, nor discoloration of skin, or bones, or teeth, but many other intermittent acute symptoms, like abdominal pain, constipation, vomiting, elevated blood pressure, and, very

characteristically, nervous and mental manifestations are observed. Progressive paralysis, and sometimes polyneuritis, effect a mortality of about 50 percent among individuals with nervous symptoms. Still more important is the fact that the mental picture in acute porphyria may resemble almost any type of psychic disorder. During an attack the urine is colored red or deep yellow, and contains a porphyrin of type III with only 7 carboxyl groups as compared with the 8 groups of this kind in uroporphyrin. Uroporphyrin I and coproporphyrin I are also found. Often the porphyrin is present as the zinc complex salt. During the intervening periods of time the urine carries so little of these pigments that its color is normal. But their presence reveals that the disease, though called "acute", is actually a chronic one. In latent cases of "acute porphyria" the therapeutic application of certain drugs, like the ones mentioned above, may cause all the manifestations of the disease, including the mental symptoms. It has been pointed out in the medical literature that the neuropsychiatric aspects of this form of porphyria have often been overlooked, and that many patients have been considered psychoneurotic for many months, and even years, before the diagnosis of porphyria was made. Furthermore, some of the drugs commonly used as sedatives may actually trigger off a porphyria of the "acute" type with all its nervous symptoms. Hayman has in this connection suggested "That the psychiatrists might run a few more urine analyses before embarking on extensive psychotherapy seems eminently sound." No effective treatment is known for the form of abnormal pigment metabolism called "acute porphyria".

Porphyrin solutions fluoresce, that is the incident radiation of a given wavelength is transformed in part into radiant energy of another, usually longer, wavelength, and re-emitted in that form. This transformer effect is common to all fluorescent materials, though to different degrees, and causes the phenomenon of rendering organisms sensitive to light. For example, Paramecium in weak eosin solution will be killed, when the suspension is exposed to visible light. The intensity of the photosensitizing effect of different porphyrins varies; in man it decreases for the same quantity of porphyrin per kg. body weight as follows: uroporphyrin I > coproporphyrin I > coproporphyrin III. In injection experiments with different species of animals the entire range of effects from slight skin irritation to lethal "light shock" has been produced. It should be mentioned that only white, or light colored animals with clean skin or fur show sensitivity to light from fluorescent pigments. Animals with dark fur, or those with white fur not freshly washed, will not react to exposure to light. In our civilization there are many possibilities for the individual to come in contact with water-soluble fluorescent dyes, *e. g.*, red pigment from lipstick, or dyes from other cosmetic preparation, dyes of many different colors from garments may enter the body through smallest abrasions or through cuts in the skin in minute quantities. The ensuing symptoms may be pronounced "allergic", until the response to the radiation of the sun is noticed. In such cases the search for the offending dye, and its removal, will alleviate the symptoms, and as the pigment is eliminated from the body, the sensitivity to light will disappear completely, and with it the allergic manifestations.

The purpose of this brief presentation was to show the importance of the pigments hemin and chlorophyll to our lives. Today we recognize them primarily for their role in respiration and in photosynthesis. But if and when these two vital processes become completely understood, the field of porphin pigments will not have lost either importance, or attractiveness for further research. On the contrary, the relationship of these pigments to other fields of organic and biochemistry, and their metabolism in health and disease, will continue to pose a multitude of new questions and problems for further study.