which implies an exhaustive and accurate index of all the books and periodical papers under a given subject or author, as distinguished from the bibliophilic sense, in which a book, incunabula or manuscript is described, like an object in natural history, in such a complete and unmistakable manner that its identification is always possible from the description. The scattered scientific papers and the varied public activities of Professor Welch are here set forth, for the first time, in a strict chronological order, which will be most useful to future medical historians and biographers. No one, for instance, could gain any just conception of the versatile and genial scientific work of Virchow or Weir Mitchell who has not gone over the "Virchow-Bibliographie" of 1901 or the catalogue which Mitchell himself prepared in 1894. As much of the best scientific literature of medicine is buried in the endless files of medical periodicals, medical bibliography, as standardized by Billings and Fletcher, enjoys the status of firearms in the early days of the far West—"sadly missed when badly wanted." The Welch bibliography, as Dr. Hurd tells us in the preface, has required the investigation of years, and is now printed because the interruptions of the present war have prevented the publication of the collective writings. In the first half of Dr. Burket's list (1875–1900), we find the larger scientific contributions of Welch, the great laboratory physician, his early investigations of the pathology of pulmonary œdema (1875), glomerulonephritis (1886), the structure of white thrombi (1887), his Cartwright lectures on the pathology of fever (1888), his discoveries of the staphylococcus which infects the edges of wounds (1891), and (with Nuttall) of the bacillus aerogenes capsulatus (1892), now of immense moment in Europe as the cause of gas infection in gunshot wounds, his synthesis of the many nondescript diseases caused by this bacillus (1900), his experiments (with Flexner) on the effects of injection of diphtheritic toxins (1891–2) and his monographs on thrombosis and embolism (1899). In his later period, Welch has been content to see his pupils carry out investigations inspired by him, so that the latter half of the bibliography, while replete with contributions on purely medical themes, is characterized by those addresses on public occasions in which Welch always acquits himself with the grace and charm of some distingué French academician.

As one who has had latterly to devote much of his time to the public good, Welch, like Dr. Johnson's Mead, has "lived more in the broad sunshine of life than any man." Many of the papers listed in this bibliography are described as "unpublished," which perhaps accounts for the appearance of the bibliography before the actual collected writings. Among, these, it is to be hoped that the many charming extempore talks at the Johns Hopkins Historical Club will be included. On such occasions, Welch, when the humor strikes him, improvises delightfully upon a set theme, like some genial musician of the past. The well-known "Ether Day Address" on "The Influence of Anæsthesia upon Medical Science" (1896) was written out without preparation in a railroad car, as he traveled to Boston, a fair example of his habit of improvisation. The two addresses on the evolution of scientific laboratories (1896) and the interdependence of medicine and science (1907), the latter also written out *en route* for Chicago, are perhaps the most interesting of Welch's contributions to medical history. Here, as everywhere, he has furnished young and old with food for thought, and often with new ideas. Dr. Burket is to be congratulated on the excellence and accuracy of his work, which follows the bibliographic norms set by the Surgeon General's Library. It is a most timely contribution. In the present emergencies, no man has labored more zealously and faithfully for the welfare of his country than William H. Welch.

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## SPECIAL ARTICLES

### WHAT SUBSTANCE IS THE SOURCE OF THE LIGHT IN THE FIREFLY?

IN at least three groups of luminous animals (fireflies, ostracod crustacea and mollusks),

two distinct chemical substances, besides water and oxygen, are necessary for light production. One of these is not destroyed by heat and is easily dialyzable; it can be prepared by extracting luminous animals with hot water. This substance has been termed *luciferin* by Dubois[1] and *photophelein* by myself.[2] The second substance is destroyed by heat and does not dialyze; it can be prepared by allowing a water extract of the luminous organ to stand until the light disappears. This has been called *luciferase* by Dubois[1] and *photogenin* by myself.[2] Whenever solutions (non-luminous) of these two substances are mixed, light immediately appears and is brighter the greater the concentration of the solutions.

According to Dubois, the thermolabile substance, luciferase (photogenin) is an oxidizing enzyme (hence the termination *ase*), which oxidizes the thermostable substance, luciferin (photophelein), which is therefore the source of the light. My own work has led me to belive that the thermolabile substance is not an enzyme, but is itself the source of the light and I have indicated this by calling it photogenin (phos, light; gennao, produce). The thermostable substance is, according to my view, a material which assists in the production of light and I have indicated this by calling it photophelein (phos, light; opheleo, assist).

Which is the source of the light, photogenin (luciferase) or photophelein (luciferin)? Fortunately the question can be answered by a simple crucial experiment. The two common eastern genera of fireflies produce light of different colors. *Photinus* emits an orange light, while *Photuris* emits a greenish yellow light. The difference in color is especially noticeable when the luminous organs of the two species are ground up in separate mortars. As shown by Coblentz,[3] the difference in color is real; the spectrum of *Photinus* extending further into the red than that of *Photuris*. The two light-producing substances can be prepared from each of the two species, and the photogenin of *Photinus* mixed with its own photophelein gives an orange light, while the photogenin of *Photuris* mixed with its own photophelein gives a greenish-yellow light, the color characteristic of the species. The two genera may also be "intercrossed" with respect to the two light-producing substances, *i. e.*, the photogenin of *Photinus* gives light with the photophelein of *Photuris* and vice versa. If the source of light is photophelein (luciferin) as Dubois believes, the light produced by *Photinus* photophelein (luciferin) $\times$ *Photuris* photogenin (luciferase) should be orange, the color characteristic of *Photinus*. I have found, on the contrary, that the light from this "cross" is greenish yellow. Conversely, the light from a mixture of *Photinus* photogenin (luciferase) and *Photuris* photophelein (luciferin) is orange. The color of the light in these "crosses" is that characteristic of the animal supplying photogenin (luciferase). The photogenin (luciferase) must, therefore, be the oxidizable substance and the source of the light.

How does photophelein assist in the production of light? The process is best studied in the marine ostracod crustacean, *Cypridina hilgendorfii*. The photogenin and photophelein of this animal are secreted into the sea water together, and in time the photophelein is used up and a perfectly clear colorless non-luminous solution of photogenin remains. If we add to such a concentrated solution, photophelein or certain specific substances in extracts of non-luminous forms, or fat solvents such as ether, chloroform and higher alcohols, or thymol, saponins, soaps, bile salts, or crystals of inorganic salts, such as NaCl, light appears. Many of these substances are not oxidizable (another proof of the inadequacy of Dubois's theory), but all of them are cytolytic agents. The cytolytic action of these substances on cells is the result of a dissolving action on the cell surface involving an increased dispersion of the colloids which results

[1] Dubois, R., *C. R. Soc. Biol.*, 1885, XXXVII., 559, and *Ann. de la Soc. Linn. de Lyons*, 1913, LX., and 1914, LXI., 161.

[2] Harvey, E. N., Science, N. S., 1916, XLIV., 652, and *Amer. Jour. Physiol.*, XLII., 318, 1917.

[3] Coblentz, W. W., Carnegie Inst. Wash. Pub. No. 164, 1912.

in the complete solution and dissolution of the cell. Photogenin is a colloid and I would suggest that these substances have a similar action on the colloidal particles of photogenin. We are not dealing here with a cytolysis of cell fragments present in the secretion, since these cytolytic agents (salts, thymol, etc.) cause light production even in solutions of photogenin filtered through porcelain or siliceous filters which remove all granules and cell fragments. I would suggest, therefore, as a working hypothesis rather than a formal theory, that photophelein acts by changing the aggregation state of the colloidal particles of photogenin toward that of greater dispersion, thus increasing the surface of the particles. It is known that oxidation occurs at the surface of many colloidal particles, and light production might easily result from auto-oxidation accompanying the dispersion of the colloidal particles.

Photopheleins from different species of animals have different chemical properties and, like the cytolysins, they are also specific to a considerable degree. Firefly photophelein will produce light on mixing with photogenin of other insects (*Pyrophorus*), but none or very faint light on mixing with photogenin from *Cypridina*. A non-luminous species of *Cypridina* contains a photophelein with marked light-producing action on the photogenin of the luminous *Cypridina*, but none with firefly photogenin. Photophelein, therefore, is to be compared with the specific cytolytic substances of blood sera, with this exception, that it is the photophelein of the same species which has the greatest light producing action whereas the blood of the foreign species is the one possessing the greatest cytolytic (hemolytic) power.

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## INOCULATIONS ON RIBES WITH CRONARTIUM RIBICOLA FISCHER[1]

THE white pine blister rust is established in the native white pine growth of many parts of New England. Since, in most sections of New England, the pine far outvalues the cultivated currants and gooseberries, the latter, together with the wild *Ribes*, are being removed to hold the disease under control. A cultivated currant or gooseberry, not susceptible to the disease and possessing commercial qualities, would be of much practical importance for future planting within the diseased area. Even a wild species of *Ribes* immune to the disease might be of value for breeding new resistant commercial varieties to replace those now being removed. For the purpose of discovering such resistant varieties or species of *Ribes*, inoculations under controlled conditions have been made during the past three years on 82 varieties of cultivated red, black and white currants, 23 varieties of cultivated gooseberries, and 48 species and hybrids of *Ribes* from various parts of the world. Field tests are also being made with many of the above varieties and species.

The varieties of a cultivated species show considerable variation in the degree of their susceptibility to the disease. The cultivated species of *Ribes* also vary decidedly in susceptibility. Some varieties and some species, notably *Ribes nigrum*, are very congenial hosts for the rust, very abundant uredinia and telia being produced thereon. In other varieties and species the rust spreads rapidly over the leaf surface and produces abundant uredinia, but the leaf tissue often dies before many telia are formed. In other cases a few uredinia form, at which time irregular areas of the leaf tissue die quickly, with or without further spread of the fungus around the dead area. Sometimes, instead of a definite area being killed, small streaks or flecks are killed. These dead spots often enlarge slowly, producing occasionally a few uredinia or telia. All intergradations are found between *R. nigrum*, upon which the maximum number of fruiting bodies form, and *R. leptanthum*, on which small dead areas and flecks are formed, on less than 10 per cent. of which rust spores are produced. The vigor of the plant and the age of the leaves have an influence on the development of the disease. The

[1] Published by permission of the Secretary of Agriculture.