of men of science which made that era so memorable in the history of science. Never before or since, perhaps, has there been gathered together in one city so many of the world's greatest contributors to the advancement of knowledge as there were in Paris at the beginning of the nineteenth century, and it was but natural that the Collège de France, with its unfettered regime and its public lectureships, should become one of the homes of those who spoke with authority. One eminent man who held office during the Revolution was Daubenton (1716–1800), the collaborator of Buffon. When he died, his chair passed to none other than Cuvier (1769–1832), the founder of palæontology and comparative anatomy, whose last lecture was given in the Collège only a few days before he died. Contemporary with Daubenton and Cuvier were the chemist Vauquelin (1763–1829), the discoverer of chromium; Thenard (1777–1857), in whose favour Vauquelin resigned in 1804; and Biot (1774–1862), who in 1800, at the age of twenty-six, was appointed professor of natural philosophy.

No less distinguished were the successors of these famous men. In the realm of physiology there are few names better known than those of Magendie and Bernard. Magendie (1783–1855), who described himself as a "rag-picker of facts", and on his death-bed remarked to a friend, "You see me here completing my experiments", became a professor in 1831, the year he visited Sunderland to study cholera. To him in 1847 as an assistant came Claude Bernard (1813–1878) who succeeded to Magendie's chair in 1855. Bernard's life as a Master of Medicine was written by Sir Michael Foster. To the chair of experimental physics at the college in 1824 was appointed Ampère (1775–1836), the centenary of whose publication of the fundamental laws of electro-magnetism was celebrated at the Sorbonne ten years ago; and at his death, Savart (1791–1841), who for eight years had been curator of the physical cabinet, succeeded him. Savart in turn was followed by Regnault (1810–1878), who, like Faraday, after having obtained a reputation as a chemist, turned physicist. Regnault in 1854 was made director of the Porcelain Factory at Sèvres, and it was there, and not at the Collège de France, that his apparatus for the investigation of the expansion of gases was destroyed during the German occupation of 1870. Two years after this Regnault resigned his position at the Collège de France, and his chair passed to his deputy Mascart (1837–1908), afterwards destined to be director of the Central Bureau of Meteorology and president of the Paris Academy of Sciences. What Biot and Ampère and their successors did for physics was paralleled by the work of the eminent chemists who followed in the chairs of Darcet and Vauquelin. Pelouze (1807–1867), the successor of Dumas at the École Polytechnique, lectured for many years at the Collège de France, and in 1850 was succeeded by Balard (1802–1876), who had achieved fame at the age of twenty-four by his discovery of the element bromine. Balard was closely associated with many notable men of science. He owed much to Gay Lussac; it was in Balard's laboratory, at the École Normale, Pasteur in 1848 made his remarkable discovery with tartaric acid; to him in 1837 as an assistant came Berthelot; while his assistant in later years, Schützenberger (1829–1897), in 1876 became his successor. Almost the whole career of Berthelot was bound up with the Collège de France, where in 1865 a chair of organic chemistry was created for him. When he died forty-two years later it was said that France had lost her most eminent man of science. No one ever associated with the historic Collège was more convinced of the moral and practical value of scientific inquiry, and he once wrote "La Science domine tout".

Induced Malaria.

IT is well known that, for some time past, malaria has been purposely induced as a remedial measure in persons suffering from general paralysis of the insane. The therapeutic value of this proceeding has been placed beyond doubt. Up to 1928, of 2499 patients in institutions in England and Wales so treated, 1188, or 47·5 per cent, were benefited sufficiently to be recorded as 'recovered', 'much improved', or 'improved'. Of 656 cases in 1929, 47·7 per cent came under the same heading. The 'discharged recovered' numbered nearly 12 per cent, and the 'discharged relieved' six or seven per cent. Thus nearly one-fifth of the cases treated by artificial infection with malaria benefit sufficiently to be discharged from hospital.

From a medical and a moral point of view, therefore, there is abundant justification for subjecting sufferers from one malady, grave and intractable, to the risks attendant upon infection with another which is controllable by drugs. At the same time, it has become apparent that the procedure affords a unique opportunity for the clinical study of malaria itself, a disease incomparably more important than general paralysis of the insane as a world problem, and one which is still beset by questions scarcely answerable in the uncontrolled conditions of the field.

Arrangements were therefore made at the suggestion of Col. S. P. James, adviser on tropical diseases to the Ministry of Health, whereby the Ministry, in consultation with the Board of Control, the London County Council, and Col. J. R. Lord of Horton Mental Hospital, Epsom, organised what is virtually a first essay in clinical investigation under strictly experimental conditions. Colonel James communicated a report on the first results to the Malaria Commission of the League of Nations in 1926, and communicates a record of the material which has since accumulated to the *Transactions* of the Royal Society of Tropical Medicine and Hygiene (**24**, 5, 477-538; March 1931.)

It is very difficult to find malaria patients who can infect *Anopheles maculipennis*. Of 305 mosquitoes dissected when sporozoites should have

been present in the salivary glands, ten only were found with zygotes in the stomach and none with sporozoites in the glands. They were among eight batches fed, some of them as many as five times, upon the blood of patients with a high gametocyte count. Dr. P. A. Buxton suggests that a gelatinous sleeve, such as Schaudinn has described (perhaps present only at a certain phase in the process of digestion), arises from the chitogenous cells of the fore-gut and intervenes between the blood and the epithelium of the mid-gut of the insect, thus accounting anatomically for the heavy infection of some *maculipennis* and not of others. While the problem of insect infection needs further study, it has been ascertained that the condition of the gametocytes of *P. vivax* in the blood of patients who are 'good infectors of *Anopheles*' is such that the male forms of the parasite in thin blood films kept moist at 25° C. 'exflagellate' within fifteen minutes. With *P. falciparum* and *P. malariae*, even this indication of infectability for *Anopheles maculipennis* is uncertain. There are good and bad receptors of infection as well as good and bad infectors. But there is no positive evidence that a particular species of *Anopheles* is a better 'malaria carrier' than another.

If susceptible patients are bitten by mosquitoes which have sporozoites in their salivary glands, infection does not always result. This may be accounted for by non-injection of sporozoites. Excluding such cases and also cases in which there was doubt whether or not the patient had suffered from malaria previously, 18 per cent of the number of patients who certainly received sporozoites failed to develop malaria within the usual incubation period. These are held not to be attributable to the presence of 'immune bodies' in the patients' blood. Some are examples of 'latent infection'; others may be due to an anaemic or otherwise abnormal physiological condition of the blood.

Failure may also result from the fact of a previous attack, and some of Col. James's most suggestive results concern the course of malaria in cases treated by quinine. In cases of so-called 'spontaneous recovery' from benign tertian malaria the infection 'smoulders', and the blood picture and parasite findings assume features akin to those of the blood of native children in hyperendemic areas. Usually, between the eighth and tenth months after primary infection, there is a definite recurrence of fever and a reappearance of parasites in the blood, followed in a few days by recovery. A few small doses of quinine then secure freedom from further attacks and from parasites. Before the recurrence, the patient can be reinfected with the same parasite, but after 'spontaneous recovery' such patients are proof against reinfection. This condition of immunity is inhibited by quinine therapy. On the other hand, immunity to reinfection by *P. vivax* confers no protection against *P. falciparum* or *P. malariae*, and complete immunity to reinfection by one strain of *P. vivax* confers at best only a partial protection against another strain. As immunity has hitherto been studied only as a mass problem among natives races, Col. James suggests that the development of these findings should be carried out by field workers.

Cases are recorded in which the expected malarial attack was six months or more late. Since infection is desired early in malaria therapy, such cases are rare in induced malaria; but it has been possible to study twelve in which from 28 to 45 weeks intervened between infection and attack. In one of these the patient had been infected with quartan fever when, nine months after infection with tertian, the benign type developed unaffected by a long attack of quartan followed by a curative course of quinine.

If a distinction is made between the return of fever within eight weeks of recovery from a primary attack (recrudescence) the return between 8 and 24 weeks (relapse) and the return later than 24 weeks (recurrence), about half the patients infected by mosquito bite have one or other of these manifestations, the other half none. Recurrence was found to occur within 27 to 39 weeks of primary infection, and all of the cases which 'recurred' in the twenty-seventh week became ill on the 190th to 194th day after their blood became free from parasites after their primary attack. This relationship led the investigators to construct a graph representing the history of 107 cases referred to the same starting-point. The resemblance between this graph and representations of the seasonal clinical incidence of benign tertian malaria in northern Europe suggests that the 'spring rise', about which so much has been written, is due not to any climatic circumstance but to recurrences in persons who had their primary attack in September, with primary attacks in persons whose infection in September remained latent throughout the winter.

Observations on prophylaxis by quinine support those made by Yorke and Macfie. Quinine taken prophylactically will not prevent infection, but this is different from saying that it will not prevent clinical attacks. Whether persons who have to live in a malarious place would be better advised not to take a daily dose of quinine but to wait until they get a true malarial attack which would be adequately treated by quinine, or whether they would be better advised to take a daily dose suppressing the outward clinical manifestations of the disease in order to 'carry on' during periods of moderate fever and indisposition, are questions to be answered differently in different cases. The daily dose taker gains little or no immunity, and a period of exceptionally hard work is likely to determine a more severe attack than he usually suffers. Large doses (30 gr.) of quinine given at any time during the incubation period have no effect; a single dose of 5 gr. after five or six paroxysms stops the fever but permits a recrudescence within a fortnight; a small dose (5 gr.) given later and repeated daily for a few days cures 50 per cent of cases. Existing practice would be revolutionised by adopting the indications afforded by these facts, but it would be unjustifiable to withhold quinine in a case of malignant tertian malaria later than the first discovery of parasites in the blood.