

Over the last twenty years most physiologists have favoured some form of the trichromatic theory. Hecht and Roaf, for instance, elaborated theories which, while differing profoundly from one another and from the "classical" theory associated with the name of Helmholtz, were alike in being trichromatic. Three books published in English within the last twelve months give it general support. Wright's<sup>3</sup> contains a wealth of valuable and accurate data on the luminosity of spectral colours, on the facts of colour mixture, and on the discrimination of colours. It is argued that these are all consistent with, and most simply explained in terms of, three primary colour sensations. Willmer's<sup>4</sup> is more speculative and less firmly rooted in personal researches, but is stimulating and provocative. Granit's<sup>5</sup> brings together under one cover his important researches on the eye by electro-physiological methods. He shows, among other things, that individual fibres of the optic nerve are connected with receptors of several different types as judged by their responses to monochromatic light falling on the retina. Many receptors are sensitive only to a narrow range of spectral colour. Yet, although there is strong evidence for seven such "modulators," they fall into three distinct groups, corresponding with blue, green, and red light.

Prof. Hartridge, elsewhere in this issue (p. 913) and in his earlier articles,<sup>6,7</sup> has sought to extend Granit's outstanding work to the human eye by studying the sensations aroused in himself when very small images of monochromatic light were formed on his own retina. He claims to be able to confine the stimulus to single cones or to small clusters of functionally identical cones. From these and other experiments, he concludes that there are not less than seven types of retinal receptor. The difficulties of explaining some of the facts of hue discrimination, colour mixture, and colour-blindness in terms of the trichromatic theory also lead him, as they have in the past led others, to postulate more than three primary colour sensations. If his arguments should, after careful scrutiny, be generally accepted, it will mean that the trichromatic theory has served its purpose as a useful working hypothesis and must now be declared, in the words of its originator, "inconsistent with the phenomena."

### TREATING THE SYMPTOMS OF DEPRESSION

We have all experienced disturbances of affect, but with good fortune they are so short-lived and so mild that when the cause has passed our normal tranquillity returns without the help of treatment. As Stockings points out elsewhere in this issue (p. 918) the more severe disorders of mood make up a large part of general practice. The depressed and anxious patient, who may or may not have organic symptoms or signs, is so well known that he needs no description here. Whatever the exact pattern of the disturbance of feeling-tone that the patient has, there always exists the problem of how much of the disturbance is the result of difficulties the sufferer has encountered in his daily living and how much is the result of physical and perhaps constitutional changes within him. There was a

tendency once to refer to exogenous and endogenous depressions, but these terms lost favour when it was believed that in many instances the illness was compounded of endogenous and exogenous causes. The term "reactive depression" is still used, and some maintain that in any persistent disorder of affect—whether a depression or an anxiety state—the causes have inevitably arisen in the circumstances of the subject's life: there may be precipitating environmental causes, but the predisposing causes are environmental too. Others recognize a precipitating cause or set of causes in such a case but maintain that the predisposition to the disorder was mainly inborn, and refer to evidence in the patient's family history and in his reactions to previous life situations to support this view. The recent dramatic results which have followed electric convulsion therapy in depressive illnesses, and particularly in involutional depressions, suggest that in these cases at any rate the illness has persisted as a result of a physical disorder.

In recent weeks, and again in this issue (p. 942), our correspondence columns have shown among our readers some lack of unanimity on this theme. Stockings, however, has no hesitation in referring to all these affective disorders as "the syndrome of thalamic dysfunction," and he assumes that the illness is in fact the result of a disorder in the behaviour of neurones in the thalamo-cortical network, but whether as a result of psychological or physical causes he does not say. Although there are many who would not follow him all the way in such a direction, most would agree with his statement that in many cases of anxiety and depression psychotherapy may be prolonged and, though prolonged, ineffective. Because of this, whatever the causes of the illness and the concomitant distress may be, any treatment which will alleviate that distress is most welcome to the patient and the discouraged practitioner. He reports favourably on a new substance called variously synhexyl, pyrahexyl, or parahexyl. This substance, which was reported upon by Adams in 1940, is allied to cannabis indica, which is taken because of the pleasant dream states which it induces. Synhexyl produces rather similar roseate states in normal people, and in larger doses it removes the distress of the subjects of anxiety and depression. Stockings found that in a group of 50 patients, some with neurotic and some with psychotic depression, there was considerable amelioration of the disturbances of feelings (dysphoria) without similar improvement in the other symptoms. The neurotic patients were helped more than the psychotic. There were no immediate complications of oral administration and no sequelae. Unfortunately the effects are temporary, but since results with other substances, such as benzedrine, are usually disappointing synhexyl may be worth further study. If it should become widely used it is to be hoped that we shall not forget that it treats only symptoms and not causes. We usually withhold opium until we know the cause of the pain.

### TRIPLE CARDIAC RHYTHM

The third heart sound was first clearly described by Gibson<sup>1</sup> in 1907. It is soft and low-pitched, may be felt as well as heard, and varies in intensity with respiration. It is appreciated best at the apex beat, and is accentuated when the subject lies on the left side, especially if the venous pressure is raised by compressing the abdomen. As early as 1913 Ohm<sup>2</sup> proved that the third heart sound coincided with the lower part of the descending limb of the V wave of the jugular phlebogram—that is, with the end of the phase of rapid ventricular filling. He suggested in 1921

<sup>3</sup> *Researches on Normal and Defective Colour Vision*. London. 1946. 383 pp.

<sup>4</sup> *Retinal Structure and Colour Vision*. Cambridge. 1946. 231 pp.

<sup>5</sup> *Sensory Mechanisms of the Retina*. London. 1947. 412 pp.

<sup>6</sup> *British Medical Journal*, 1946, 1, 637.

<sup>7</sup> *Philosoph. Trans. roy. Soc. London, Series B*, 1947, 232, 519.

<sup>1</sup> *Lancet*, 1907, 2, 1380.

<sup>2</sup> *Dtsch. med. Wschr.*, 1913, 39, 1493.

that the sound was caused by the vibration of the ventricular walls set up by their sudden distension at this time.<sup>3</sup> This explanation is now generally accepted. According to Orias and Braun-Menendez<sup>4</sup> the third heart sound begins 0.11 to 0.14 seconds after the commencement of the second heart sound. Margolies and Wolferth<sup>5</sup> pointed out that this is distinctly later than the opening of the mitral valve, which coincides with the top of the V wave of the phlebogram.

Nothing is gained by calling a third heart sound "triple heart rhythm, type I a." Evans<sup>6</sup> and other authors agree that the sound is very common in childhood, but not in infants, and becomes more and more infrequent with advancing age. O'Meara describes in an article published in this issue (p. 922) how he heard the third heart sound in 54 to 71% of 745 young men aged 17-20, and 35-49% of 255 men aged 21-30. His ability to detect the sound improved with experience. Its presence in the older groups is interesting (15.5% in 103 men aged 41-50; 5.7% in 70 men aged 51-60), particularly since Evans stated that a third heart sound is not heard in normal subjects over 40. Thayer<sup>7</sup> reported a similar relationship to age. His figures for the second, third, fourth, and fifth decades were 84%, 60%, 42%, and 14% respectively.

The normal third heart sound may be confused with protodiastolic gallop, with the short diastolic murmur of active rheumatic carditis, with summation gallop, and with the opening snap of mitral stenosis. Protodiastolic gallop occurs when the third sound develops or reappears as a result of left ventricular failure. The murmur of active carditis should be distinguished with ordinary care. Summation gallop disappears when the heart is slowed. The opening snap of mitral stenosis is heard earlier and is more easily confused with a widely split second sound. The diastolic murmur of mitral stenosis is determined by the rapid ventricular filling phase, and may directly follow the opening snap or may be heard a little later.

### SEVERE ERYTHEMA MULTIFORME

In 1860 Hebra<sup>8</sup> separated from the collection of ill-defined erythematous eruptions described by Willan and others a group which he regarded as a clinical entity of obscure aetiology and called erythema exudativum multiforme. The eruption commonly affects the extremities and is characterized by erythema with which may be associated congestion, oedema, and purpura, and sometimes vesication or bullous formation. The lesions are nummular, often target-like, and though Hebra did not mention the fact mucous membranes may be involved, especially in the vesico-bullous type of eruption. The incidence of such lesions is not less than 25% and is put by some authors as high as 60%; occasionally the lesions of mucous membrane are profuse and severe. Recurrence at variable intervals over the course of years is another common feature of the disease, and rarely the recurrences may be so frequent as to make the affliction a continuous one. The first attack of erythema exudativum multiforme is often associated with a fever, suggesting, perhaps, an upper respiratory tract infection, but subsequent attacks may be without such an onset. Toxic eruptions resembling the classical picture occur with other specific infective diseases and sometimes as an expression of sensitization to drugs.

Osler<sup>9</sup> was impressed by the severity of visceral lesions sometimes accompanying the exudative erythema, especially the gastro-intestinal, renal, and mucosal haemorrhages, and in reviewing a series of sixty-one cases from the literature, including six of his own, he found that thirteen patients had died from the disease. Under various names cases resembling the severe mucosal form of erythema exudativum multiforme have been reported whose notable features were severe eye complications from a purulent conjunctivitis, pneumonia of a non-bacterial type, and sometimes death. In all these cases there was a sudden onset, with serious constitutional symptoms, grave sequelae, and seemingly little tendency to recur. Rendu,<sup>10</sup> using the term "ectodermose érosive pluriorificielle," regarded the group as a separate entity, while Stevens and Johnson<sup>11</sup> described the condition as a new disease hazardous to life and vision. Low and Davies<sup>12</sup> used Baader's<sup>13</sup> term "dermato-stomatitis," and Dowling<sup>14</sup> reported a series under the title of "a pemphigus-like eruption."

Stanyon and Warner,<sup>15</sup> in a paper on the "mucosal respiratory syndrome," reported a non-bacterial pneumonia in fourteen out of seventeen cases of erythema multiforme, with two deaths. They emphasized the mononuclear character of the infiltration; animal investigations in a search for viruses were negative. The association of pneumonia with this disease was noted in a Report<sup>16</sup> by the Commission on Acute Respiratory Diseases (Western Reserve University), where, in six cases of severe erythema multiforme three showed a non-bacterial pneumonia. Elsewhere in this issue Sneddon (p. 925) reviews some of these reports and describes a series of six cases. He draws attention to some features which this disease has in common with glandular fever. Keil<sup>17</sup> reviewed the subject and maintained the unity of the benign and severe forms of the disease. Because of its mode of onset cases of severe erythema multiforme are commonly admitted to fever hospitals. Costello<sup>18</sup> in a series of 75,000 admissions to the Willard Parker Hospital for Contagious Diseases found thirty-three cases of erythema multiforme of which seventeen were severe; three of these patients died. In his opinion penicillin was of value in preventing grave sequelae and death in some cases.

To sum up, severe erythema multiforme particularly affects children and young adults, has a sudden febrile onset, and severely affects the buccal mucosa, with frequent spread to the bronchial tree and sometimes to the gastro-intestinal tract. Conjunctivae and genitals are commonly affected, and the lesions in these sites may lead to ulceration and scarring. Death has occasionally been reported. Whether this syndrome is a separate entity cannot be determined in the absence of a recognized causative agent, but the weight of evidence suggests that both benign and severe forms of erythema exudativum multiforme constitute a single and distinct disease entity.

The Humphry Davy Rolleston Lectures will be delivered before the Royal College of Physicians of London (Pall Mall East, S.W.) on Tuesday and Thursday, July 15 and 17, at 5 p.m., by Dr. P. C. P. Cloake, F.R.C.P. His subject is "The Treatment of Disseminated Sclerosis by Artificial Pyrexia and Prolonged Administration of Arsenic."

<sup>9</sup> *Amer. J. med. Sci.*, 1895, **110**, 629.

<sup>10</sup> *Rev. Gen. de Clin. et de Thérap.*, Paris, 1916, **30**, 351.

<sup>11</sup> *Amer. J. Dis. Child.*, 1922, **24**, 526.

<sup>12</sup> *Brit. J. Derm. Syph.*, 1938, **50**, 141.

<sup>13</sup> *Arch. f. Dermat. u. Syph.*, 1925, **149**, 261.

<sup>14</sup> *Lancet*, 1940, **2**, 759.

<sup>15</sup> *Canad. med. Ass. J.*, 1945, **53**, 427.

<sup>16</sup> Report of the Commission on Acute Respiratory Diseases (Western Reserve University). *Arch. Intern. Med.*, 1946, **78**, 687.

<sup>17</sup> *Ann. Intern. Med.*, 1940, **14**, 449.

<sup>18</sup> *J. invest. Derm.*, 1947, **8**, 127.

<sup>3</sup> *Berl. klin. Wschr.*, 1921, **58**, 600.

<sup>4</sup> *The Heart Sounds in Normal and Pathological Conditions*, 1939, London, Oxford University Press.

<sup>5</sup> *Amer. Heart J.*, 1932, **7**, 443.

<sup>6</sup> *Brit. Heart J.*, 1943, **5**, 205.

<sup>7</sup> *Arch. Mal. Cœur*, 1910, **3**, 145.

<sup>8</sup> *Diseases of the Skin*, Vol. 1. New Sydenham Society, London. 1866.