suggested a sinister cause of bile-duct obstruction. The biopsy proved the cervical gland to be lymphadenomatous, and the laparotomy deemed necessary by the severe pruritus gave evidence of the rare nature of the obstruction to the main bile channel.

There are certain unusual features about this case. Death indirectly due to cholaemia from obstruction to the main extra-hepatic bile channel by a mass of lymphadenomatous glands is exceptional, although Rolleston and McNee do make reference to the possibility of compression of the chief bile channel by such a mechanism. These authors note that jaundice is infrequent in lymphadenoma, but allude to possible glandular compression of the common duct; they also mention two cases of periodic jaundice in Hodgkin's disease, the jaundice coinciding with fever and enlargement of superficial lymphatic glands. In Hodgkin's disease it is most exceptional for the clinical picture to be dominated by obstructive jaundice and its consequences; the rapidity with which these hastened the fatal ending of the case contrasts with the natural history of the malady: in 15 weeks from the first symptom the disease had proved fatal. The case presented other atypical features: the lymphatic glandular involvement was far less widespread than usual; one discrete enlarged lymphatic gland palpable on the right side of the neck, and the existence of a possible second in the posterior mediastinum demonstrated by radiograph, constituted the only evidence of the disease. The operation performed to relieve the pruritus enabled us to discover a glandular mass in the portal fissure which had produced the jaundice; further, the lymphatic involvement was more or less confined to those glands. It will be recalled that this patient was investigated after pleurisy some 18 months previously, and although no evidence of active tuberculous disease was found, the theory of the possibility of a coexistence of the two maladies or even of their causal relationship is revived.

Case IV. Calcified Mass embedded in Head of Pancreas compressing Lower End of Common Bile Duct: Removal: Recovery

A stoker aged 49 was admitted to a Naval hospital with 4 months' painless jaundice. An enlarged liver and a distended gall-bladder suggested a growth obstruction of the choledochus. A two-stage operation was done after taking pre-operative measures. At the preliminary cholecyst-gastrostomy a firm lump could be felt near the lower end of the common bile duct, and the pre-operative diagnosis of an "ampullary carcinoma" seemed to be confirmed. At the second operation the mass was found embedded in the head of the pancreas, and was removed with some adjacent pancreatic tissue by a retro-duodenal approach. The choledochus was seen to be compressed but not infiltrated, and was not injured during removal of the "tumour."

The pathological material proved to be a mass of agminated calcified tuberculous glands. Surgeon Rear-Admiral Gordon-Taylor, who operated on the case and recently reported it, remarks: "There was perhaps some justification for the mistake in diagnosis, but at least the patient is to be congratulated on the pathological nature of the compressing mechanism, which before this experience I might have seriously doubted."

Summary

Four cases of jaundice have been described in which a diagnosis based on careful clinical examination, reinforced by laboratory and other investigations, was proved by operation to be inaccurate. The experience and knowledge to be gained from them appear to act as a deterrent, and to justify restraint on the practitioner who feels confident in his capacity to assign correctly to a particular category any case of jaundice on clinical grounds alone. The descriptions given above demonstrate that although the cases had not a few features in common, nevertheless the exact pathological detail obtained as the result of operation proved that the morbid process varied greatly. Specific infectivity, toxicity, granulomatous disease, could all be considered in the course of diagnosis. It is also worthy of note that despite our surprise in being able to exclude malignant neoplasm on three occasions (Cases II, III, and IV), yet in two of these (Cases II and III) the disease ran a fatal course in a comparatively short period. Case IV claims special mention in being apparently illustrative of its author's hope that palliative treatment for neoplasms in the region of the pancreatic head may sometimes be replaced by radical surgery, offering a reasonable prospect of cure.

I wish to express my thanks to the medical officer in charge of this hospital for permission to publish this communication and for the facilities which he constantly offered me in the collection of case details. My acknowledgments are also due to Dr. W. W. Woods, Consulting Pathologist to the Navy, and to Dr. I. Doniach for the pathological reports.

DEFICIENCY DISEASE AND ACADEMIC EVIDENCES OF SUBNORMAL VITAMIN METABOLISM

BY

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The present war with its food restrictions and black-out conditions inevitably focused attention on vitamins throughout Great Britain. Interest in the essential food factors, which was extensive before the war, flared up in both academic and trade circles. Eventually, through the media of the medical and general press and official and unofficial propaganda by circular, screen, and air, the public and the profession became almost hysterically vitamin-minded.

In certain directions there was a complete loss of perspective, incompatible with an emergency which demands a realistic view of the practical issues at the fighting fronts over-seas, and conservation of academic energy at home for more essential problems. In fact, the cult of vitamin deficiency both here and in the U.S.A. has become in part a racket. This state of affairs is largely due to the premature booming of experimental observations, and the attempt to fit them into the jigsaw of human physiology, psychology, or pathology as the case may be. The clinician is not blameless. He lends support to the situation by the empirical use of proprietary vitamin products in all manner of affections and in acclaiming their value by *post hoc* argument. However important the study of vitamin deficiency, the application of academic findings to the maintenance of fighting efficiency should be discussed at a level compatible with total war. Such discussions can hardly be conducted in perspective by those who have no first-hand experience of the clinical aspects of the vitamin deficiency disease syndromes as they exist in man and of the conditions appertaining at the various fronts. Yet just now probably more attention is given to theoretical considerations in this connexion, both here and in the U.S.A., where the clinical picture of frank vitamin deficiency disease as it appears in man is familiar to few, than in parts of the world—such as China, Russia, India, Africa, and Japan—where the human manifestations constitute a familiar everyday problem, the practical economic importance of which is great but subordinate to more urgent issues.

General statements such as these demand at least some support. Let us take the case of night-blindness in vitamin A deficiency.

Vitamin A Deficiency and Night-blindness

Night-blindness, better referred to for psychological reasons as "hemeralopia," is a prominent symptom of A-deficiency disease. It is the only subjective symptom until the later stages of the disease syndrome. This syndrome constitutes an important ever-present economic health problem in large population groups in various parts of the world, such as in the above-mentioned countries.

Frank predominant vitamin A deficiency disease is common in the Madras Presidency, which has a population bigger than that of England and Wales. Its manifestations differ in children and adults or, as Frazier and Hu (1934) have suggested, in the pre- and post-puberty periods. I have for years urged that it is the greatest cause of preventable blindness in children in South India on account of the associated corneal metaplasia or keratomalacia (Wright, 1931, 1937). The latter term is commonly used for convenience throughout the Far East for the whole syndrome, which emphasizes the importance of this complication. The most common sign, and possibly the earliest clinical evidence, of this syndrome is smokiness of the conjunctiva. This is my own view, and might possibly be disputed by such experienced clinical observers as Frazier or Pillat. I formerly held that night-blindness was the earliest evidence of keratomalacia (Wright, 1934). This conjunctival sign is unrecognized or not considered worthy of mention by those who discuss the effects of vitamin A deficiency in this country, probably because few of them have ever seen the disease as it exists in man. Kirkpatrick (1936) mentions it. It is well recognized in China (Mu *et al.*, 1937). It is not referred to by Nicholls (1938) of Ceylon: this is hardly because he does

not recognize it, as it has been known to medical men in his part of the world for years, but because both he and Aykroyd—in South India—have found it more convenient to use “phrynoderma” (pilosebaceous hyperkeratosis) in their surveys. Among children of the poorer classes Aykroyd and Rajagopal report a frequency of phrynoderma of 14% for certain groups in South India. Smokiness of the conjunctiva would probably give a higher frequency and might well be a better index. There are in the museum of the London School of Tropical Medicine water-colour pictures of this condition which I had copied years ago from some of my pictures in the museum of the Government Ophthalmic Hospital, Madras: these give an idea of its appearance. Whether this sign or the symptom of night-blindness is the earliest or most common manifestation of A-deficiency is beside the point. We have no adequate frequency figures for either to guide us. Chou (1930) has reported normal dark-adaptation in 7 out of 20 patients with early ocular signs (pigmentation) of vitamin A deficiency. The important thing for purposes of this communication is that either may be absent in cases which are otherwise clinical examples of frank predominant A-deficiency. This fact as regards the symptom is sufficient in itself to show what a false emphasis has been placed on the connexion between vitamin A metabolism and variations in night-vision here since the war began.

In discussing experimental photometric methods employed to demonstrate a correlation between defects of dark-adaptation and the so-called subclinical A-deficiency, Frazier and Li (1938) quote Jung (1938) on the applicability of the fallacy of centripetal drift to the conclusions from such observations. They say: “It would seem, therefore, that a more critical evaluation of the results of photometric testing is required before final conclusions can be drawn on either the incidence of subclinical forms of vitamin A deficiency or the effect of therapeutic measures on the results of such tests. For the present, at least, evaluation of specific treatment in human cases should depend upon observations on definite clinical manifestations such as straightforward night-blindness, xerophthalmia, and follicular hyperkeratosis of the skin.” This criticism seems as pertinent to-day as in 1938, and the application of Jung’s ideas on poor dark-adaptation to recent work in this country would probably show that in “conditions influenced by so many uncontrolled variables the readings are completely determined by chance.”

Again, this night-blindness does not constitute a labour problem in South India, where A-deficiency is so prevalent. It does not interfere with night work to any extent. I have rejected more candidates for specialized night employment, which required a simple night-vision test, on account of tapeto-retinal degenerations, of which retinitis pigmentosa is chief, than for the hemeralopia of A-deficiency. In either case the figure is so small as to be insignificant. Night-blindness, too, does not prevent such jungle tribesmen as the Sholagas of South India moving rapidly and safely through dangerous country on the darkest nights. I have followed such men, some of whom showed evidences of A-deficiency, in the dark with difficulty.

If a case of A-deficiency disease with well-marked night-blindness in a Tamil received the average daily ration of the British soldier in England once a week, I should expect recovery. The authorities here at home would shudder at the thought of maintaining the British soldier on a diet which in hospitals of South India or parts of China or Japan would be considered adequate to keep the individual free from hemeralopia. As I have indicated elsewhere (Wright, 1935-6), I cannot imagine there being any such thing as a practical vitamin A deficiency disease problem in this country or America on diets short of famine diets.

With regard to the anti-infective role of vitamin A—which may yet have a revival in connexion with the home Forces—I agree entirely with Pillat (1929) that ordinarily the pathogens grow as saprophytes in the metaplastic tissues of vitamin A deficiency disease; and with Kirkpatrick (personal communication), who holds that colliquative necrosis is the primary process which produces corneal ulceration, not an invasion by pyogenic organisms. My experience coincides with that of Frazier and Hu (1936), that an increased susceptibility of the skin to “boils, sores, impetigo, napkin rash, or other evidence of skin sepsis”

is not a clinical feature in keratomalacic subjects. Skin rashes other than pityriasis pilaris (pilosebaceous hyperkeratosis) are not more common in the keratomalacic population of Madras than in the general hospital population (Nayndu, 1935).

Evidently the condition in man cannot be gauged from observations on animals so far as practical clinical issues are concerned. If they were even approximately parallel, an increased frequency of stone in the bladder might be assumed to exist in South India by those in this country interested in vitamins but without experience of the A-deficiency disease syndrome in man. To find an increased frequency of stone in India one must look in parts of the North, where vitamin A deficiency disease is hardly known.

Night-vision in the Army

Before assuming, on theoretical academic considerations or animal (and human) experiments, that minor degrees of A-deficiency affect in any practical way whatever the military value of our man-power in this country, it is essential to consider the effects of gross A-deficiency on the physical activities of members of those populations largely afflicted with vitamin A deficiency disease. Apparently night-blindness has not interfered with the rapid night movements of Japanese troops through the Malayan jungles, although *prima facie* one might expect it to be a more practical difficulty in their case. Undoubtedly we have a night-vision problem here now. Modern methods of war have enhanced the value of good night vision and thrown poor dark-adaptation into prominence.

For convenience we may consider poor dark-adaptation as of three types—psychogenic, pathogenic, and physiogenic.

Psychological disturbances are a frequent and serious cause of poor night-vision in the Army, as pointed out last year in these columns (Wittkower *et al.*). This form of psychoneurosis received a considerable impetus from the ill-advised publicity campaign in connexion with the beneficial effects of vitamin A on night-vision. The evil effects of this campaign are enormous; the term “night-blindness” has attained a suggestion-value analogous to that of “shell-shock” in the last war.

Bad night-vision associated with well-known recognizable pathological ocular conditions is infrequent and of lesser moment. In this *pathogenic* group the night-blindness of vitamin A deficiency would find a place if it existed here. In the *physiogenic* group poor night-vision may be regarded as a variation in dark-adaptation at one end of the physiological curve. That this function is influenced by many factors, individual and racial, is known. Its investigation is essential in connexion with certain activities of the fighting Forces, and is having the serious attention of the medical authorities. It is not a vitamin A problem, and will not be solved by “following the carrot.”

Vitamins B and C

Criticism in like manner is applicable to recent activities in connexion with B complex and vitamin C. To assess deficiency in B₂ (riboflavin) mainly by means of minor variations in the capillary loops at the corneal margin—which are, to say the least of it, common to a number of causes—is futile in wartime. Yet Sydenstricker *et al.* (1940) seriously advocate such capillary changes as the main prop in a list of clinical criteria.

Among ophthalmologists familiar with corneal bio-microscopy since its inception, who is to say what are the capillary variations at the limbus within normal limits? Does the capillary invasion which is suggested as a criterion exceed that which is determined by dust, wind, weather, and other irritants associated with military activities? When a vitamin deficiency can be assessed quantitatively by chemical means, and a biochemical (subclinical?) abnormality established, it may be justifiable in wartime to subject large numbers of hard-worked officers and men to detailed examinations—provided competent clinical, public health, and pathological opinion can show a probable case for impairment of military efficiency on metabolic grounds. Even here a practical rather than an academic level should be adopted.

The processes of biological oxidation (cell respiration) with which the vitamins are eventually concerned are interdependent and overlap, just as the clinical evidences of deficiency overlap. This fact necessarily leads to important abstruse fields of

chemical inquiry. Such investigations, and mass biochemical observations, especially on children, will no doubt afford information which may be of use in post-war reconstruction. This war has still to be won by, for the most part, adults to whom the application of metabolic hypotheses is hardly of military value, as they must fight now under dietetic conditions largely imposed by the enemy.

Finally, in this matter of vitamins as applied to the supply of man-power in a grave emergency here and in the U.S.A., it is out of perspective and unrealistic to spend time, money, and energy by labouring academic findings when at least the younger observers may get in touch with practical issues by looking further afield and seeing the real thing in greater mass as it exists in man under conditions of total war over-seas.

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Medical Memoranda

A Case of Haemorrhagic Measles

While it is generally agreed that haemorrhage occurring into a measles rash is not uncommon, true haemorrhagic measles is so rare that well-known writers on infectious diseases such as Goodall and Ker state that they have never seen a case. It is thought that the more frequent reference to it by the older writers was due to its confusion with haemorrhagic small-pox. For this reason I think that the following case, though not quite typical, is worthy of publication.

The patient, a male child of 12 months, was seen at home on June 9, 1942, by Dr. Myerhoff, who considered the appearance to be typical of measles in the eruptive stage. The rash had started on the previous day. On the 12th the child became very ill and was admitted to Clayponds Isolation Hospital as a case of measles complicated by bronchopneumonia.

On admission the child, who was of normal nutrition and development, was seen to be very collapsed and dyspnoeic. The rash had completely disappeared. Although dyspnoea and cyanosis were severe—respiration rate 70—the chest was free from abnormal physical signs. The patient's condition at this stage would seem to correspond with the suffocative type of measles described by Rolleston and Ronaldson. The child was given 0.5 g. of sulphapyridine 4-hourly, continuous nasal oxygen, and frequent glucose drinks. About 4 hours after admission extensive haemorrhages into and under the skin of the face and limbs suddenly began to develop. One large haemorrhagic area, involving the greater part of the nose and adjoining skin, had a raised bullous appearance. No bleeding occurred from the mucous membranes, and the skin haemorrhages had reached their maximum extent in the course of a few hours. Subsequently the general condition of the child began to improve, but he remained very ill, with an irregular remittent temperature, for a further nine days. Sulphapyridine was discontinued on June 16 and no further complications occurred. Subsequent convalescence was rapid, and the patient was discharged from hospital on July 1. The haemorrhagic appearance had by then completely disappeared except for the presence of a scab on the bridge of the nose, where a large haemorrhagic bulla had resulted in superficial ulceration.

This case appeared to correspond with the description of true haemorrhagic measles in that there was a rapid recession of the rash followed by haemorrhagic extravasation. It differed in the absence of haemorrhages from the mucous membranes and in its ultimate recovery.

I am grateful to Dr. Thomas Orr, medical officer of health for Ealing, for permission to publish this case.

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Reviews

PAIN AND ITS MECHANISM

Pain. By Sir Thomas Lewis, M.D., F.R.S. (Pp. 192; 27 figs. 12s. 6d.) New York and London: The Macmillan Company. 1942.

Bacon wrote of books, "Some are to be read only in parts; others to be read but not curiously, and some few to be read wholly and with diligence and attention." Sir Thomas Lewis's *Pain* belongs to the third category. As a clear, exhaustive, and critical exposition it is a worthy successor to *The Mechanism and Graphic Registration of the Heart Beat and Blood Vessels of the Human Skin and their Responses*; while its content will appeal to the wider audience of practitioners and students already familiar with *Diseases of the Heart and Vascular Disorders of the Limbs*. The scope of the book can be gathered from two extracts from the preface:

"The chief purpose of this book is to review modern ideas of the mechanism of human pain and to bring into perspective with other observations the work of my own laboratory during the last ten years. While attempting to make a book of reference, one that will bring contact with the more important views, I have desired to . . . keep it in a readable form that will stimulate interest and enquiry."

"Our knowledge of pain, of its sources, of the nerve paths conveying it, has been built up, and will continue to be built up, chiefly by observations upon man. It is built up by tests of the sentient surface in the normal subject, tests of skin deprived deliberately or accidentally of its nerves, the innumerable probings of disease itself, stimulation of deep-lying structures during surgical operations, and ingenious forms of exploration of deep structure from without; all these sources have contributed so abundantly that I shall but rarely need to refer to evidence derived from animals. There is manifest wisdom in seeking knowledge from the direct, rather than from the indirect, source, and here the direct source is prolific; there is, too, the deep satisfaction of knowing that any evidence won from man is indubitably applicable to the human problem."

After reviewing the sensitivity of various human tissues to pain and the nervous paths subserving it, the author proceeds to unfold, against the background of earlier knowledge, the newer developments resulting from his own work and that of his laboratory. This begins with the demonstration that in respect to quality there are but two distinct kinds of pain, that arising from skin and that arising from deeper structures. Dealing first with skin pain the author describes the condition "erythralgia," in which the skin some hours after being injured by a variety of stimuli becomes red and tender. An analysis of this condition leads to the conclusion that the hyperalgesic skin "is one which has been brought to this state by the action of certain tissue substances upon the pain nerve-endings, the latter being rendered hyper-excitabile." The next chapter analyses the diffuse hyperalgesia which follows a few minutes after a small localized severe injury to the skin and which may last for 8 to 12 hours or as long as two days. An experimental analysis shows that this hyperalgesia is due to an axon reflex arising from the point of injury and spreading to the limits of the area involved, where the effector endings release in the skin substances increasing the excitability of the pain nerves. Since this axon reflex implies unusually long axonic branchings, and since the effector release of substances lowering the pain threshold cannot be ascribed to any known system of nerves, the author has postulated that besides the known sensory and motor nerves to the skin there exists another system, for which he has proposed the name "nocifensor nerves." The evidence for the existence of such special nerves is strong; it still lacks anatomical demonstration.

From the point of view of medical practice, the most significant part of the book is probably that dealing with deep pain and the associated phenomena of muscular tenderness and rigidity. Lewis and his pupil Kellgren have shown that not only is pain from a deep somatic structure indistinguishable in quality from the pain of visceral disease, but it is likewise referred to a distance in a segmental fashion, and is also accompanied by muscular tenderness and rigidity. This demonstration provides the basis for a review of the pain and associated phenomena of visceral disease. The controversy as to whether the source of pain and the associated reflexes