it follows no anatomical order—it may appear suddenly throughout the whole distribution of the affected nerve, and resembles nothing so much as the wearing off of the effects of local anaesthesia. In the few cases in which it is delayed it is still much more rapid than the fastest recovery from axonotmesis, and would demand a rate of growth of axons quite unknown in clinical or laboratory experience. Furthermore, the preservation of normal excitability of muscles is clear evidence against Wallerian degeneration of the nerve below the lesion, and we now have evidence on the motor side that the affected nerve is not only capable of conducting impulses but in fact does so, though no contraction of the muscle can be detected clinically. There is therefore a disturbance of conduction (which can be produced experimentally) that impedes the transmission of impulses but does not destroy the axon. Recovery is always perfect.

Neurapraxia is a non-committal but adequate description of this non-functioning of a nerve. Neurapraxia is produced by cocainization of a nerve, by mild degrees of refrigeration, and by slight injury.

Comment

It is obvious that by no means all nerve injuries can be classified under these simple headings; the accidents that produce them are not uniform in their effects unless the violence is great. An injury may affect the fibres of a nerve in varying degree, and the clinical picture will then be more complex. A lesion may be made up by a combination of any of the following: (a) neurotmesis; (b) axonotmesis; (c) neurapraxia; (d) normal fibres.

Indeed, neurapraxia is a lesion in which a certain number of normally functioning fibres are always present. Leaving this aside, there are no fewer than eleven possible combinations of these lesions, each with its own clinical characteristics! In complicated lesions of the brachial plexus, for example, the picture may be so mixed that precise diagnosis is impossible, though there is often plenty of scope for light-hearted speculation. We have seen almost every one of the possible combinations, and do claim that none of the phenomena of interruption of a nerve that we have so far encountered required other explanation. This is a very difficult field of clinical inquiry, and it is not proposed to discuss it here, seeing that the various combinations of lesions form the subject of a paper that will shortly be published by W. B. Highet, who has investigated all the cases of dissociated paralysis seen at the Oxford Centre since its inception in June, 1940.

CAROTINAEMIA

BY

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We have recently observed 5 cases showing pigmentation of the skin pronounced enough to warrant provisional diagnoses, by the attending practitioners, of "jaundice," "pernicious anaemia," "haemolytic anaemia," and "cholelithiasis." This pigmentation can only be properly described as "carroty," and while in the mild cases it is most obvious in the naso-labial folds and the palms of the hands, in the more advanced cases it is a generalized body tanning. The condition is due to the excessive consumption of carrots, though it has been recorded when other lipochrome foods are eaten in quantity.

The Literature of Carotinaemia

The term "carotinaemia" for the orange pigmentation of the skin observed after the excessive consumption of carrots and other vegetables was first applied by Hess and Myers

in 1919. The observation of this skin discoloration in diabetics whose diet consisted mainly of foods rich in yellow lipochrome—fruit, vegetables, butter, and eggs—was made by von Noorden (1907), who considered the condition to be a diabetic manifestation. Moro (1908) noted that normal infants developed a similar pigmentation when carrots were added to the diet. Van den Bergh and Snapper (1913) showed that there were lipochrome pigments circulating in the blood of diabetic patients with the orange pigmentation, and that these pigments were identical spectroscopically with those of carrots and other vegetables. Salomon (1919) referred to this pseudo-icterus in non-diabetic patients whose diet largely consisted of the foods mentioned, and the gradual disappearance of this pigmentation with abstinence from such foods. Stoeltzner (1919), commenting on Kaupé's observation (1919) that nurslings lost their yellow coloration when their high carrot diet was stopped, observed that the number of similar children had increased during the last war. He called it a "pseudo-icterus" and thought a high tomato diet might produce a similar pigmentation.

Greene and Blackford (1926) and Stoner (1928) discussed the condition under the heading of "carotinaemia." Boeck and Yater (1929) used the term "xanthaemia" for the circulation in the blood of lipochrome pigments (thereby excluding bile pigments) and "xanthosis" for the visible presence of these yellow pigments in the skin. They found xanthaemia in all their nephritics and in most diabetics, and even in most "normal" cases examined. However, xanthosis was present in only 10% of the renal and diabetic cases and in only 3% of other cases. All these patients with stained skin had eaten excessively of lipochromic foods.

Stannus (1929) called the discoloration "hyperlipochromia," and concluded that it resulted from the failure to oxidize the carotinoid pigments in the body. He first reported carotinaemia in myxoedema, and Wendt (1935) noted the condition in some cretins. Bomford (1938) confirmed the presence of carotinaemia in some cases of myxoedema on a normal diet. On thyroid medication the lipochrome index fell to normal. He remarks that as the colour of cream is due to lipochromes, the description of the myxoedematous facies as a "strawberry and cream" complexion is not without justification.

The Present Series of Cases

Our interest in carotinaemia was first aroused by the visit of a clerk's wife on account of "jaundice," though her sclera was contrastingly white. In the spring months further cases were referred as "pernicious anaemia" and "haemolytic anaemia"; the woman with "gall-stones" was visiting her husband, an in-patient with acute nephritis, when the ward sister drew our attention to her carroty complexion. None of these patients had symptoms of ill-health, though the curious discoloration was a source of anxiety.

Careful histories were extracted to find the actual pounds of carrots consumed per week (see Table). As kitchen standards

Table showing Amount of Carrots consumed Weekly

Occupation of Husband	Provisional Diagnosis (own Doctor)	Raw Carrots		Other Veg. and Eggs	Icteric Index	Serum Bilirubin (mg./100 c.cm.)	On Normal Diet Fading		Other Medical Conditions
		lb. per Week	Threshold Months				First Noticed (Weeks)	Complete (Weeks)	
Lorry-driver	Gall-stones	8	8	—	10	0.1	3	6	Cholecystectomy, 1932
Clerk ..	Jaundice	6	6	+++	8	0.3	2	4	Microcytic anaemia
Shop-keeper	Pernicious anaemia	5	7	+	12	0.6	2	4	Mitral stenosis
Corporal	Haemolytic anaemia	4	8	+	8	0.1	2	5	Microcytic anaemia
Baby ..		breast-fed	2	—	—	—	4	8	Healthy

of quantity are given vaguely in pinches, spoons, and cups, we sought and obtained the number and size of the carrots, from which a correct estimate was made. These weights apply only to the raw carrots, as the other vegetables and cooked carrots were always eaten in pre-war helpings. During the

winter carrots were cheap and easily obtainable, and "besides, they were so nice to munch." The lorry-driver's wife had been told "carrots were full of vitamins." The clerk grew so many carrots on his allotment that his wife felt she had to eat them. She liked the clean taste left in her mouth so much that she invariably carried one about in her pocket. Since June of last year the corporal's wife used to munch carrots, especially while preparing the family meals, in order to increase her vitamin intake during her period of gestation. A healthy baby was born at Christmas and thrived on the breast. It had no other treatment. In February the corporal noticed his wife and baby were carrotly and sought his doctor's advice. Jaundice was diagnosed and the breast dethroned by the bottle. On a light diet and milk feeds the pigmentation gradually faded.

The time taken for saturation before the carrotly skin was first noticed is tabulated as the threshold months. Each patient was thoroughly investigated for diseases which may have provided other factors; but they were quite healthy women, apart from one moderate case of mitral stenosis and the almost invariable hypochromic anaemia so prevalent in this area. These patriots of the "Kitchen Front" were congratulated on their heroic consumption both of carrots and of propaganda, and were asked to return to their basic helpings of vegetables, including carrots. On this moderation (it was not abstinence) the times in weeks of initial and then complete fading were noted.

Our threshold value corresponds approximately to that of a patient, quoted by Wood and Agnor (1941), who ate two carrots daily for a year. Kaupé's (1919) finding of carotinaemia in babies weaned on carrot soup, the lipochrome content of which must necessarily have been small, is in harmony with our baby's susceptibility in developing skin pigmentation after only two months on the breast milk of its carotinaemic mother. This is believed to be the first case reported of carotinaemia from the breast milk of an affected mother.

Laboratory Investigations

The routine estimations of icteric index and serum bilirubin were carried out in all cases. These revealed an obviously "jaundiced" serum of a high icteric index (on colour comparison with the potassium dichromate standard 1/10,000 dilution) but a serum bilirubin within normal limits. Obviously the orange colour was not due to bile pigment. However, the lipochromes are soluble in petroleum ether and the bile pigment in absolute alcohol, which will also precipitate the proteins in the serum.

This fact forms the basis of the test of Greene and Blackford, which we refer to as the three-layer test, to differentiate carotinaemia from jaundice. Equal quantities of serum, alcohol, and petroleum ether are shaken up in a tube. This may be left to settle, as the volatile petroleum ether, with its dissolved lipochromes, rises to the top as a distinct layer. If lipochromes are present in abnormal amount this top layer will show a definite yellow tinge which is pathognomonic of carotinaemia. The depth of colour may be compared with the potassium

a clear petroleum layer, then the sandwich is jaundiced and the bile index will equal the icteric index.

$$\begin{array}{lcl} \text{Icteric index} & = & \text{Bile index} + \text{Lipochrome index} \\ \text{(on whole serum)} & & \text{(on alcohol layer)} + \text{(on ether fraction)} \end{array}$$

In a hypothetical case of jaundice and carotinaemia both layers will be quite yellow, and the degree of each pigmentation can then be estimated separately.

Carotene is the yellow colouring matter—the lipochrome—of carrots, spinach, palm oil, and nettles. It is a highly unsaturated hydrocarbon, $C_{40}H_{56}$, which exists in three forms—alpha-, beta-, and gamma-carotenes. These can be separated by filtering a light petroleum solution through a Tswett column of calcium hydroxide. Each form adsorbs out of solution at a different layer in the column. All three forms are precursors of vitamin A, but owing to its internal pattern one molecule of beta-carotene yields two molecules of the vitamin, while the alpha and gamma forms produce only one molecule. Thus the beta form has twice the physiological activity of alpha- and gamma-carotenes. Natural products, however, contain much more beta- than alpha-carotene and little, if any, of the gamma form. The isomer of carotene is lycopene, which is the colouring matter of tomatoes, rose hips, and bittersweet berries, but is inactive physiologically in not forming vitamin A. Carotene is the principal though not the only lipochrome in human serum. It is always associated with its hydroxyl derivative, a xanthophyll. Lutein is the xanthophyll of alpha-carotene, and is the lipochrome in egg yolk and green leaves. Thus the term "xanthaemia," of Boeck and Yater (1929) is more accurate than the popular carotinaemia.

The absorption of the lipochromes from the bowel is stated by Wood and Agnor (1941) to depend on the presence of dietary fat and the bile acids with which it is absorbed as a water-soluble diffusible complex. Curtis and Ballmer (1939) have shown that liquid paraffin interfered with this transport of carotene across the epithelium of the intestine. In the plasma the carotene is probably adsorbed to the albumin molecule and carried in colloidal suspension. The plasma proteins can be precipitated down by absolute alcohol, which itself dissolves bile pigments, while the lipochromes are soluble in petroleum ether, which floats lightly as a separate layer above the alcohol. This provides the basis for the three-layer test of Greene and Blackford. The conversion of carotene into vitamin A probably takes place in the liver.

Ralli *et al.* (1936) showed that the liver of a carotinaemic diabetic contained an increased amount of carotene. Pariente *et al.* (1936) theorized that in diabetes the conversion of carotene to vitamin A was impeded and that this resulted in a damming up of carotene in the liver and a diminished absorption from the blood. They neglected the additional factor of the high lipochromic diet usual in diabetics.

According to Wood and Agnor (1941), any excess of carotene is either destroyed or excreted via the sweat. They state that when excretion is unusually heavy the carotene is re-absorbed by the horny layer of the skin. Palmer and Kempster (1919) found the lipochromes in fowls in the rete malpighii and cornified layers of the skin. Greene and Blackford (1926) observed the concentration of pigment in the naso-labial folds, where sebaceous glands abound, and in the palms and soles, where cornified skin is thickest. We find that the soles of Lancashire housewives are undistinguished, but that the palms of our hospital cooks, after scraping carrots for dinner, were stained like T.N.T. workers. However, this direct staining from handling carrots could be washed off almost completely—in contrast with that from excessive intake, which was undiminished by washing. In our cases, in addition to the naso-labial folds and palms, the rest of the skin was almost uniformly tanned, but the sclera was contrastingly white. This immunity of the sclera in carotinaemia is the chief clinical sign in differentiating it from jaundice. The colour of the skin and the details of food intake are additional factors in clinical diagnosis.

Several of our patients noticed a deep orange colour in the urine. Attempted extraction of the colour with petroleum ether was unsuccessful, and no typical absorption bands were found spectroscopically.

Boeck and Yater (1929) discuss the wide variation in the appearance of xanthosis and xanthaemia in individuals on

Diagram illustrating the three-layer test for the differentiation of carotinaemia from jaundice.

dichromate standard to give its lipochrome index. However, it is better to centrifuge the mixture in the tube. The precipitated proteins spin down to the bottom as a white curd, covered by the middle band of absolute alcohol with its dissolved bile pigments, on which the "true icteric index," or bile index, can be estimated against the dichromate standard. If this middle alcohol band is excessively yellow and is covered by

similar diets. To account for this, they believe that the rates of oxidation and excretion must vary widely. Bernheim (1926) fed large quantities of carrots to 3 patients, who quickly produced a high icteric index, which, however, fell to normal within 12 hours. In our cases the rate of metabolism seemed to be remarkably constant in the different individuals. The threshold quantity appeared to be a minimum of 4 lb. of excess carrots per week for a minimum period of seven months before skin pigmentation became visible. The rate of fading appeared to be equally constant once they returned to an average diet. Fading was first noticed in a minimum of two weeks and was complete within eight weeks. In view of Bernheim's findings of the rapid disappearance from the blood of excess lipochromes within 12 hours, it would seem that above the threshold quantity the body is unable to oxidize or excrete all the lipochrome, so that some pigment is slowly accumulating. The capacity of the body to eliminate lipochromes must be well above the normal requirements, as it takes a minimum of six months' accumulation before the high threshold is reached on such abnormal intake and before skin pigmentation is noticeable.

The findings of the remarkably constant threshold in the accumulation of pigment and of the steady rate of fading in normal individuals support the theories of diminished conversion of carotene to vitamin A in the liver of diabetics and poor urinary excretion in nephritics, as in both diseases carotinaemia occurs more frequently than in health.

Summary

Carotinaemia is a caroty pigmentation of the naso-labial folds and palms when mild and, when marked, a general body tanning except in the sclera, which distinguishes it clinically from jaundice. It is due to the excessive consumption of carrots and other lipochromic foods. The patients are healthy and do not require treatment apart from reduction to average consumption.

Four cases of carotinaemia are described in normal women after eating more than the threshold quantity of 4 lb. of raw carrots per week for a minimum period of seven months.

A baby fed only on the breast of its carotinaemic mother developed the condition within two months. This is believed to be the first case described.

The simple three-layer test of Greene and Blackford to differentiate between carotinaemia and jaundice is described.

We are indebted to Drs. S. Smithson and M. C. Welsh for allowing us to see and investigate their cases. We wish to thank especially Dr. M. L. Thomson for permission to investigate the case of the infant of the carotinaemic mother.

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W. E. Snell (*Tubercle*, 1942, **23**, 101) maintains that garden work is the main form of occupation for sanatorium patients for the following principal reasons: (1) it provides controlled exercise for patients under open-air conditions, and thus hardens them for return to a working life; (2) it relieves the boredom of institutional life and should provide the patient with a mental interest; and (3) the patient's labour theoretically provides some return to the institution. In any sanatorium of 300 beds about 50 patients will be available for garden work, consisting of the following groups of cases: (1) early or pleural cases for which no collapse therapy is indicated; (2) patients undergoing artificial pneumothorax and those convalescent from thoracoplasty; and (3) patients not suitable for artificial pneumothorax but whose general condition is good.

BEE-STINGS IN KENYA COLONY

BY

A. J. JEX-BLAKE, M.D., F.R.C.P.

East Africa is a good place for studying the effects of bee-stings, because people living there are stung more often than those in England. This is in part because the common native bee, *Apis mellifica adansonii*, is more savage and eager to attack than the honey-bee of Europe, *Apis mellifica*, its near relative—for example, an expert bee-keeper of my acquaintance would often get as many as 50 stings a day while looking after her few hives of native bees—and in part because the bee population is large, the native inhabitants being apt to put up barrels, hollow pieces of tree-trunks, boxes, and other contraptions in trees anywhere and everywhere for the wild bees to hive in, the honey being used for beer-making. Further, these bees swarm all the year round, so that there is never a day when flying or settled swarms may not be met with out of doors or indoors. Finally, many East African houses, especially those that have been unoccupied for a time, acquire nests of bees in roofs, hollow walls, or under the floors that are very hard to get rid of when the house is occupied again. When they do attack, nests, hives, or swarms of native bees are apt to do so on the heroic scale. This is illustrated by the following 3 cases occurring in European settlers:

Cases of Massive Stinging: Recovery

Case 1.—A small man aged 75 was attacked by a swarm of bees in his garden. Between 200 and 400 stings were removed from his face and neck, and he was given an intravenous injection of 2 pints of 2% sodium bicarbonate solution. He showed no reaction from either the stings or the treatment, and no severe signs or symptoms.

Case 2.—A man aged 64 was attacked by swarms of bees and heavily stung about the face, neck, and hands. In 2 or 3 minutes he was overcome by violent diarrhoea and vomiting, and soon after that became unconscious. He was presently rescued and came to himself quickly. His face was so beset with upstanding bee-stings that he said he looked as if he had not shaved for 3 or 4 days. Over 300 bee-stings were extracted, and ammonia solution was dabbed on. He slept well with a sedative, and next day, apart from a little thickening and itching of the skin of the face and hands, felt quite all right.

Case 3.—A young woman set upon by swarms of bees was badly stung; she had attacks of diarrhoea and vomiting, and was rescued in a fainting condition. The number of stings extracted from her scalp, face, neck, chest, back, arms, and legs was at least 500, probably more—an hour and a half's work, including extraction of a sting from the very back of the tongue. Fine curved entomological forceps were used, and care was taken not to squeeze the venom-sacs during extraction. Dilute ammonia was applied, and the patient required a sleeping-draught and morphine. She kept to her bed next day and then recovered rapidly.

The numbers of the stings removed in these instances are those estimated by the medical men who removed them or by other observers, and there is no reason to believe that they have been exaggerated. The amount of venom injected by a single bee-sting is said by Phisalix (1922) to be 0.33 mg.; its active constituent is a protein. Case 1 suffered no more than a severe but passing inconvenience from the stings and must have had an exceptionally high tolerance of or immunity to bee-stings; Cases 2 and 3 can probably be taken as having the normal degree (if there is such a thing) of sensitiveness thereto.

Two Fatal Cases

The following two cases illustrate the fact that a man who has suffered no more than the normal transient local pain and swelling after bee-stings all his life may suddenly become hypersensitive to bee venom and be very near to death or even die when stung again.

Case 4.—A healthy man aged 45, passed fit for insurance 6 weeks previously, was stung 4 or 5 times while driving a swarm of bees out of his veranda; these stings gave rise to the usual