Papers and Originals

Periodic Paralysis Complicating Thyrotoxicosis in Chinese

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In Europe and the United States of America periodic paralysis would appear to be a rare complication of thyrotoxicosis. In contrast, in Japan this complication has been reported to occur in some 2% of all thyrotoxic patients, consequently 90% of the case reports in the literature have come from Japan (Engel, 1961). Before the investigation which is the subject of this communication was made it was apparent to us that periodic paralysis also commonly complicated thyrotoxicosis in the Chinese, yet, strangely, this had not been reported in the literature. Indeed, up to the present there has been but one report of its occurrence in a Chinese in Taiwan (Chen, Hung, and Lin, 1965).

Material and Methods

In the six-year period 1960–5, inclusive, all new patients with thyrotoxicosis attending for the first time the thyroid disease clinic of the University Department of Medicine were questioned specifically on the occurrence of periodic attacks of paralysis. The 25 patients who gave a history of such attacks were admitted to hospital. All were southern Chinese. Throughout their stay in hospital they were encouraged to walk about. Urine was collected for the estimation of the daily excretion of potassium and sodium. From time to time the serum concentrations of potassium, sodium, and inorganic phosphorus were determined. Additionally the daily faecal excretion of potassium was estimated in one patient who had the most frequent and severe spontaneous attacks of paralysis.

Eight of the 25 developed one or more spontaneous attacks of paralysis while in hospital, and the serum electrolytes were determined in 13 of these attacks. Attempts were made to induce attacks in 23, including the eight who developed paralysis spontaneously. Since the initial report by Aitken, Allott, Castleden, and Walker (1937) of its effectiveness in precipitating attacks of paralysis a combination of insulin and a high carbohydrate intake has been widely employed for this purpose in both the familial and thyrotoxic forms of periodic paralysis. Soluble insulin, 30 units, was injected subcutaneously before the midday meal, which included 200 g. of carbohydrate in the form of rice. At 5 p.m. the injection of insulin was repeated, and it was followed by the evening meal, which again included 200 g. of carbohydrate. Between the two meals all patients were encouraged to take glucose drinks and to walk about the hospital. After the evening meal they went to bed, and thereafter were under continuous cardiac monitoring. On this regimen 18 of the 23 had an attack of paralysis. Serum electrolytes were estimated at the height of the paralysis in these 18 and at midnight in the case of the five failures. The five failures were given 9-α-fluorohydrocortisone, 0.6 mg. daily, for from three to five days before a further attempt at induction was made.

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To determine whether the administration of potassium or spironolactone would prevent the induction of paralysis eight of the 18 patients in whom paralysis had been successfully induced were given potassium chloride 12 g. daily for five days before a second attempt at induction was made. The attempt was successful in four, and these four, together with an additional two drawn from the above 18, were given spironolactone (Aldactone-A) 200 mg. daily for five days, when a further attempt at induction was made. It proved successful in three who were given the same doses of potassium chloride and spironolactone for five days, when a further attempt at induction was made.

Attempts were also made to induce paralysis in nine of the 25 patients with a history of periodic paralysis when they had become euthyroid after treatment, and in 13 male patients with moderate to severe thyrotoxicosis but without a history of periodic paralysis. All the patients who participated in the study were volunteers.

Results

During 1960–5 1,366 new patients (1,188 females and 178 males) with thyrotoxicosis were seen. Twenty-three (13%) males and two (0.17%) females gave a history of one or more attacks of paralysis. It will be seen from Fig. 1 that among males the incidence of periodic paralysis in the various decades, with the exception of the sixth, corresponded approximately with the incidence of thyrotoxicosis. The ages of the female patients were 39 and 44 respectively.

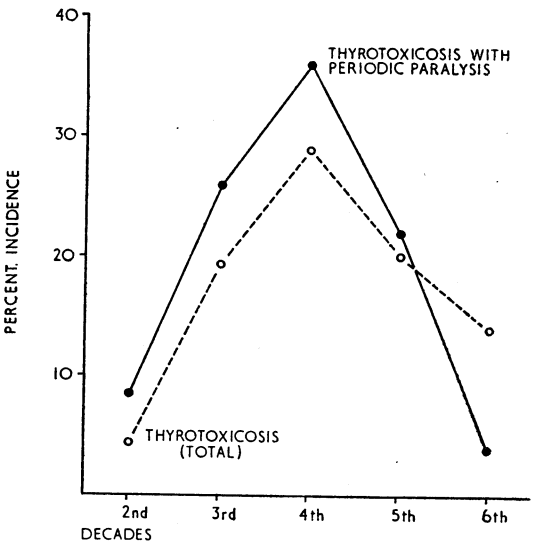

FIG. 1.—Age incidence among Chinese males of thyrotoxicosis complicated by periodic paralysis compared with that of thyrotoxicosis.

With one exception, to whom reference will be made later, the men's jobs or recreations involved considerable muscular exertion, and they had well-developed muscles. Both women were married and had children. One was employed as a seamstress working long hours, and the other was a labourer in a factory. The customary diet of all had a high caloric value, and consisted mainly of rice. With the onset of symptoms of thyrotoxicosis there had been a substantial increase in the quantity eaten.

From the history the onset of episodes of paralysis appeared to coincide with the onset of symptoms consistent with thyrotoxicosis in five instances. In the remaining 20 symptoms of thyrotoxicosis anticipated the first occurrence of the paralysis by from three months to nine years (mean=2.4 years). The diagnostic index (Crooks, Murray, and Wayne, 1959), basal metabolic rate, serum protein-bound iodine, radioactive iodine tracer test, and the resin or red cell uptake of triiodothyronine were consistent with moderate-to-severe thyrotoxicosis, but by none of these indices could patients with paralysis be distinguished from those without.

The attacks of paralysis had a well-marked seasonal incidence. They were most common from May to October, but excessively rare from December to March. They never occurred in the forenoon and never during exertion. Paralysis occurred only when the patient was at rest, and usually in bed at night. The rest commonly followed a period of unusually great physical activity and the consumption of a high carbohydrate meal.

A common and frequently early symptom ushering in an attack was a sensation arising in the affected muscles variously described as aching, stiffness, pain, or cramp. Intelligent patients, realizing that paralysis did not occur while they were active, rapidly learned to "work off" an impending attack on the appearance of these premonitory symptoms. The attacks of paralysis varied widely in severity, and ranged from weakness of the muscles of the pelvic girdle lasting several hours to a total paralysis of all muscles from the neck downwards lasting up to 48 hours. None knew respiratory distress, and speech and swallowing were not involved. Recession of the paralysis was in the reverse order to its appearance. Importantly, the paralysis on occasions was asymmetrical or atypical in distribution, and in these instances it was restricted to, or more severe in, those muscles which had been exercised most before the period of rest in which the episode occurred.

The common sequence of events and the seasonal incidence are shown in the following case.

A man aged 36 had had symptoms of thyrotoxicosis for 14 years. His job involved a great deal of walking. Seven years after the onset of thyrotoxicosis, after an unusually tiring day, he had a heavy meal later than was customary. He awoke during the night to find his legs paralysed. By morning recovery was sufficient to allow him to return to work. In the next four years he had similar attacks five or six times each year, but in the next three years the attacks became more frequent and severe, and involved also, in varying degrees, the trunk, shoulders, and arms. In each instance the provocations and sequence of events were the same as in the first attack, but only the first attack occurred in winter.

That the severity of the paralysis is proportional to the amount of antecedent exercise is illustrated in the following case.

A man aged 41 had had symptoms of thyrotoxicosis for two years when first seen. In this period he had had "several" attacks of paralysis involving the legs and shoulder muscles, which occurred at night. Recovery was complete before morning. These attacks occurred only at the week-end and only when he had spent the previous afternoon swimming. He was treated with carbimazole (Neo-mercazole), and was euthyroid for two years. During this time there were no attacks of paralysis, and he learned to water-ski. Carbimazole was withdrawn, and symptoms of thyrotoxicosis returned. Early in the relapse, which was classified as mild, he spent an afternoon swimming and water-skiing. At 5 p.m. he had a large carbohydrate meal and drank a quantity of sweet drinks. After the meal he rested. The early symptoms of aching and weakness were thought to be the natural outcome of his exertions, but around 6.30 p.m. he realized that he was paralysed from the waist downwards. Thereafter the paralysis rapidly spread to involve successively the shoulder girdle, the arms, and the muscles of the trunk. Next morning the paralysis started to recede slowly in the reverse order to its appearance, and muscle power was completely restored 48 hours after onset.

An atypical distribution is illustrated by the following case.

A messenger aged 32 had had episodes of paralysis in the summer months involving dominantly the pelvic girdle and legs since the onset of symptoms of thyrotoxicosis two years previously. In order to supplement his income he spent a day cutting out and assembling models, using as tools razor blades and a penknife. He started work at 6 a.m., and at 11 a.m. stopped for a meal. On returning to his task he noticed that his fingers were stiff and his hands and forearms painful. These symptoms rapidly disappeared, and he continued to work until 9 p.m., when he had an unusually large meal before going to bed. He awoke around midnight to find his upper limbs completely paralysed. He volunteered the information that prolonged immersion of his arms in cold water had provoked an attack, and this was subsequently confirmed.

An example of asymmetrical distribution is afforded by a bus driver who in some of his attacks had complete paralysis of the right leg but only weakness of the left leg and shoulders.

The exception, referred to earlier, was a male school-teacher aged 45 who had led a sedentary life. He was poorly developed, and had had symptoms of thyrotoxicosis for three months. One afternoon he attended an unusually long meeting in an air-conditioned room which he found chilly. He sat throughout the meeting, and at the end of some two hours found that he could not get up from his chair.

Observed Attacks of Paralysis

The spontaneous and induced attacks of paralysis observed in hospital varied greatly in severity, and ranged from demonstrable weakness of the muscles of the pelvic girdle and legs to complete paralysis of muscles from the neck downwards, including the intercostals. The muscles of the head were not involved, and speech and swallowing were not affected.

The tendon reflexes were increased in the paretic phase, and, surprisingly, this increase persisted in the early phase of complete paralysis, but in the later phase both tendon reflexes and subsequently the superficial abdominal reflexes were lost. Even in the presence of total paralysis and absence of the tendon reflexes the muscles were not flaccid but firm in consistence. Recovery was in the reverse order to the appearance of the paralysis, and its duration was proportional to the severity and extent of the paralysis. The muscles were commonly tender during and for a short time after recovery.

Induced Paralysis

The combination of insulin and a high carbohydrate intake was successful in inducing paralysis in 18 of the 23 patients investigated. Weakness developed three hours after the last meal, and reached its maximum between two and four hours later. In the five patients in whom the first attempt at induction failed a second attempt was successful when made after the administration of 9-α-fluorohydrocortisone.

Eight patients in whom the first attempt at induction was successful were given potassium chloride, 12 g. daily for five days, when a second attempt at induction was made. It failed in four and was successful in four. The latter four and two additional patients with a history of successful induction were given spironolactone, 200 mg. daily for five days. The attempt at induction after this period failed in three but was successful in three of the four in whom potassium chloride failed to prevent induction. These latter three subjects were then given both potassium chloride and spironolactone for five days, but in none was the induction of paralysis prevented.

Effect of Treatment of Thyrotoxicosis

Twelve of the 25 patients were treated with radioactive iodine, nine with carbimazole, and four by subtotal thyroidectomy. No spontaneous attacks of paralysis have occurred subsequent to the patients becoming and remaining euthyroid in periods of observation ranging from one to six years. An attempt was made to induce paralysis in each of nine patients who had had frequent and severe attacks before treatment, and in each it failed. Four of the nine were given 9-α-fluorohydrocortisone, 0.6 mg. daily for five days, but attempts at induction thereafter again failed. Two of the four were given 9-α-fluorohydrocortisone for a further five days coupled with triiodothyronine, 80 μg. daily, but again the attempts at induction failed.

After withdrawal of the carbimazole six of the nine patients so treated relapsed. Early in the course of the relapse, when symptoms were adjudged mild, spontaneous attacks of paralysis recurred.

Thyrotoxicosis without History of Paralysis

Attempts to induce paralysis failed in 13 males with moderate to severe thyrotoxicosis but without a history of paralysis. In nine instances a second attempt was made after the administration of 9-α-fluorohydrocortisone, 0.6 mg. daily for from five to seven days, and in two instances it was successful.

Changes in Electrolytes

The only consistent change in the serum electrolytes during spontaneous and induced attacks of paralysis was a fall in serum potassium, which varied widely in its extent. Fig. 2 shows that the fall was to below the normal range in 8 of the 13 spontaneous attacks, in 10 of the 18 attacks induced by insulin and a high carbohydrate diet, and in four of the five attacks induced after priming with 9-α-fluorohydrocortisone. Of the four patients in whom paralysis was induced despite prior treatment with potassium chloride only one had a normal serum potassium level. None of the three patients with induced paralysis given spironolactone before induction had subnormal potassium levels, and this was also true of the three given both spironolactone and potassium chloride. Nevertheless, the paralysis was more extensive and more severe in those with subnormal potassium levels. The serum potassium levels at midnight were invariably within normal limits in those patients in whom the attempts to induce paralysis failed.

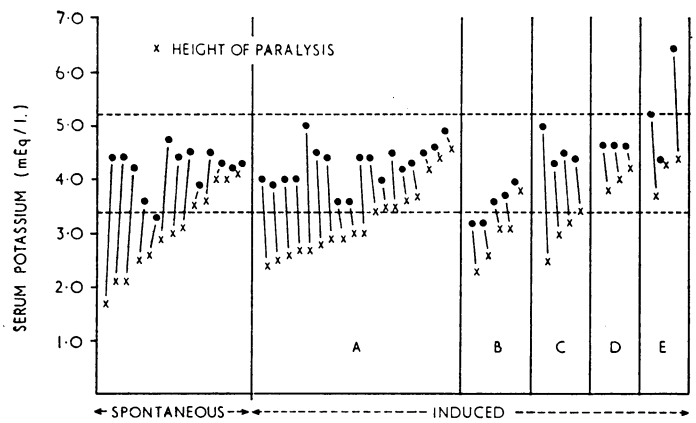

FIG. 2.—Changes in serum potassium concentrations during spontaneous and induced attacks of thyrotoxic periodic paralysis. The normal range lies between the horizontal lines. A=Induction alone. B=Induction after priming with 9-α-fluorohydrocortisone. C=Successful induction despite the prior administration of potassium chloride. D=Successful induction despite the prior administration of spironolactone. E=Successful induction despite the prior administration of both potassium chloride and spironolactone.

During attacks of spontaneous or induced paralysis the serum sodium concentration remained unchanged. Although in a majority there was a fall in inorganic phosphorus, this was not consistent.

Fig. 3 shows the serum potassium levels at midnight of the nine patients in whom attempts were made to induce paralysis when they had become euthyroid. In none was the attempt successful, despite potassium levels below the normal range in those given 9-α-fluorohydrocortisone.

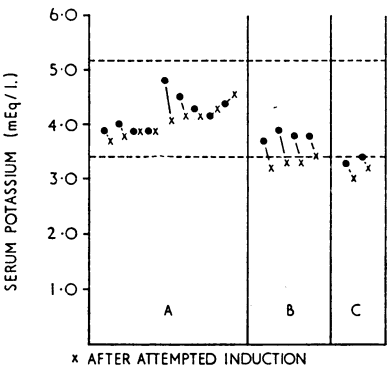

FIG. 3

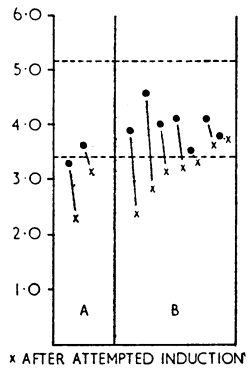

FIG. 4

FIG. 3.—Serum potassium levels at midnight after unsuccessful attempts to induce paralysis in nine patients when they were euthyroid. (All nine had had severe and frequent attacks when thyrotoxic). The normal range lies between the horizontal lines. A=Induction attempted alone. B=Induction attempted after priming with 9-α-fluorohydrocortisone. C=Induction attempted after priming with 9-α-fluorohydrocortisone and the administration of triiodothyronine. FIG. 4.—Changes in serum potassium concentrations in nine thyrotoxic patients without a history of paralysis during attempted induction after priming with 9-α-fluorohydrocortisone. The normal range lies between the horizontal lines. A=Successful induction. B=Attempted induction failed.

Fig. 4 shows the serum potassium levels after attempts to induce paralysis in 9 of the 13 patients with no history of paralytic incidents. In the two successful inductions after priming with 9-α-fluorohydrocortisone the serum potassium was below the normal range at the height of the paralysis, but this was also true of the findings at midnight in five of the seven patients similarly primed in whom the attempt at induction failed.

On the day of paralysis, either spontaneous or induced, there was a reduction in the excretion of water and sodium in the urine. There was also a consistent fall in the amount of potassium excreted, and this was proportional to the fall in serum potassium concentration. In no instance was the urinary loss of potassium excessive between attacks. In those patients to whom potassium chloride was given a proportional rise occurred in the potassium excreted in the urine, and there was no evidence of excessive retention. Spironolactone failed to reduce significantly the excretion of potassium, while 9-α-fluorohydrocortisone increased its excretion to the same extent in both paralytic and non-paralytic patients.

The potassium content of the faeces, determined in the patient with the most frequent and severe attacks of paralysis, was not increased.

In the nine patients investigated before and after they had become euthyroid the fall in serum potassium levels after the high carbohydrate intake and insulin ranged before treatment from 0.6 to 1.7 (mean=1.2, S.D. 0.4) mEq/l., whereas when euthyroid the corresponding findings were +0.1 to −0.7 (mean =0.14, S.D. 0.08) mEq/l.

Electrocardiographic Changes

In both spontaneous and induced attacks of paralysis in which the serum potassium concentration fell below the normal range the electrocardiographic changes consistent with hypokalaemia invariably developed, and, in the main, the greater the fall the more pronounced were these changes. However, the

changes were also encountered in four of the instances in which paralysis was associated with serum potassium levels within the normal range. Again, in both forms of paralysis a variety of arrhythmias were encountered, but all could be abolished readily by the administration of potassium intravenously. Atrial and ventricular extrasystoles were commonest. Auricular fibrillation and paroxysmal supraventricular tachycardia occurred, each in one instance. Reversible conduction defects also developed. Prolongation of the P–R interval, known to develop in hypokalaemia, occurred in 27% of the observed attacks, and three patients developed right bundle-branch block.

Discussion

The minimum frequency with which periodic paralysis complicates thyrotoxicosis in southern Chinese has been found to be approximately 2%, which is the frequency reported in Japanese (Okinaka *et al.*, 1957). The complication is not restricted to southern Chinese, for we have found it to occur in northern Chinese resident in Hong Kong. There have been two reports of single cases among Koreans (Lee, Kim, Lee, and Lee, 1964 ; Kim and Cha, 1965), but M. Lee (personal communication, 1966) thought that the incidence was higher than might be inferred from the paucity of reports in the literature.

As is also the case among the Japanese, the complication was more common in thyrotoxic males, among whom the incidence was 13%. However, since paralysis could be provoked in certain thyrotoxic males without a history of such, there was additionally a group of potential paralytics. Of the known factors which provoke the onset of paralysis it might be suggested that physical exertion would be greater in men. However, a large number of women in Hong Kong are employed in industry, a substantial number being engaged in heavy labour, and women so employed form a large proportion of the patients seen in our outpatient practice.

The frequency of attacks during summer and their infrequency or absence during winter were impressive. The summer months are hot, with temperatures above 30° C., the humidity is high, and there is little fall in either during the night. In winter the temperature falls to 20° C. and below, and the humidity also falls. Sweating, already excessive in the winter, is greatly increased during the summer, and the consequent loss of potassium may have a part to play. Further, in summer the resulting thirst is commonly quenched by cold drinks with a high sugar content, and, as was first shown by Shinosaki (1926), sugar precipitates attacks. The seasonal incidence is not commented upon by Japanese authors. An additional contributory factor may be the low potassium-carbohydrate ratio of the rice diet, which is common to both the Chinese and the Japanese.

The findings in the present series differed in one important particular from those reported from Japan. In all the reported series from Japan in which the levels of serum potassium are given the attacks of paralysis were associated with a precipitous fall to below the normal range. For example, Satoyoshi *et al.* (1963a) stated that attacks, either spontaneous or induced, were invariably associated with such falls. In the present series the fall in serum potassium was proportional to the extent and severity of the paralysis. In the more extensive and more severe paralysis there was invariably a fall to hypokalaemic levels, but when the paralysis was restricted in extent and in severity the serum potassium level was in some instances within normal limits at the height of the paralysis. We have also been unable to confirm in Chinese patients the claim of Satoyoshi, Suzuki, and Abe (1963b) that intramuscular thiamine lessened the number and severity of the attacks.

Although in the main the prominence of the electrocardiographic changes paralleled the degree of hypokalaemia, changes occurred in some instances when the potassium concentrations in the serum were within normal limits. In familial periodic paralysis, on the other hand, Grob, Johns, and Liljestrand (1957) found that these changes began when the arterial potassium concentration fell below 3.3 mEq/l. We have been unable to find any reference to the absolute incidence of prolongation of the P–R interval in other hypokalaemic states, but Friedberg (1966) held it to be an occasional occurrence. If this be so, there was an unusually high incidence (27%) of first-degree heart block, and also unusual was the development of right bundle-branch block. Presumably the occurrence of arrhythmias was due to an unmasking by the hypokalaemia of an effect of the thyrotoxicosis upon the myocardium, for it is known that the arrhythmias associated with the administration of digitalis occur more readily in the presence of hypokalaemia. Their occurrence has convinced us that induction of paralysis should be attempted only under continuous cardiac monitoring and with potassium readily available for intravenous injection, precautions which are not mentioned in the literature.

On comparison of the thyrotoxic patients with episodes of paralysis and those without such episodes it became clear that the occurrence of paralysis was not related to the duration and severity of the thyrotoxicosis. All socio-economic levels were represented in both groups. It also became clear that a high carbohydrate intake and exertion were but factors provoking the onset of individual attacks of paralysis, for there was no difference in the dietary habits and in exertion between the two groups.

Once the patients in the present series became euthyroid not only did spontaneous attacks of paralysis cease but all attempts to induce paralysis failed, even despite priming with 9-α-fluorohydrocortisone and the production of a short-lived hypermetabolic state by the administration of triiodothyronine. Nevertheless, relapse to the thyrotoxic state invariably was associated with the return of spontaneous attacks of paralysis. It appears that thyrotoxicosis unmasked a defect which in the euthyroid state was completely latent.

There is a widely held impression that familial periodic paralysis does not occur among the Chinese. This is erroneous, and arose from an absence of reports in the literature of its occurrence. However, Chen *et al.* (1965) reported 25 cases of "idiopathic" periodic paralysis in Chinese in Taiwan, and in two instances there was a well-documented family history. We have encountered two such families in Hong Kong, in addition to three cases without a family history. Periodic paralysis complicating thyrotoxicosis differs in certain important particulars from familial periodic paralysis. A family history was not elicited from any of the 25 patients reported. According to Engel (1961) a family history was obtained in only five of the 228 cases traced by him in the literature, and in three of these the affected relatives had thyrotoxicosis. The age at onset differs. In the thyrotoxic form it was found to be dominantly in the third, fourth, and fifth decades, a finding in agreement with the age incidence reported from Japan, whereas the onset in the majority with the familial form occurs in the first two decades, 60% presenting before the age of 16 (Talbott, 1941). Nevertheless, in both forms of paralysis there is a preponderance of males ; the factors which induce attacks are the same, and, if the manifestations of thyrotoxicosis are excluded the clinical pictures during the attack are identical.

The biochemical changes during attacks are similar: there is retention of sodium and water, and a fall in serum potassium which is associated with a proportional reduction in the potassium excreted in the urine. There is no evidence of excessive potassium loss in the stools. In both forms of paralysis all the evidence points to an influx of potassium into muscle during attacks. The claim that the level of serum potassium at which weakness occurs is lower in thyrotoxic periodic paralysis than in the familial form (McArdle, 1956) has not been substantiated. Weakness in the former was found to occur when the serum potassium was within the normal range, a finding also reported in the latter (McArdle, 1956 ; Shy, Wanko, Rowley, and Engel,

1961). The response to treatment is also similar in both groups. Salts of potassium were used empirically to treat familial periodic paralysis before the observations of Aitken *et al.* (1937) established that both spontaneous and induced attacks were commonly associated with a fall in the level of serum potassium. Aldosterone antagonists were proved effective in preventing attacks (Rowley and Kliman, 1960; Poskanzer and Kerr, 1961; de Graeff and Lameijer, 1965). Both agents were found effective in preventing the induction of paralysis in a proportion of patients with thyrotoxic periodic paralysis, an effect also reported from Japan (Okinaka *et al.*, 1957).

The similarities between the two forms of periodic paralysis led to the suggestion, first made by Shinosaki (1926), that thyrotoxicosis unmasks familial periodic paralysis, which, in the euthyroid state, is latent. However, there is no evidence that the administration of thyroid has an adverse effect upon familial periodic paralysis, as it is known to have in the thyrotoxic form (Shinosaki, 1926; Robertson, 1954). Wolf (1943) claimed that impending attacks of the former could be aborted regularly by the administration of 3 gr. (0.2 g.) of dried thyroid. One of his patients became overenthusiastic in his dosage, became toxic, and paralysis returned only when the thyroid was stopped. Engel (1961) found that triiodothyronine and thyrotropin had no immediately adverse effects, but exacerbations occurred after their withdrawal. These exacerbations were readily controlled by the readministration of thyrotropin. He concluded that either the basic metabolic abnormalities in the familial and the thyrotoxic forms of the syndrome were different or there was an additional reason for thyroid hormones affecting the familial cases differently.

The high incidence of periodic paralysis among thyrotoxic mongoloids suggests that the basic defect may be genetically determined. Unfortunately the possibility can be investigated only in families in which thyrotoxicosis affects more than one male member, since in the euthyroid state there is no method of determining the existence of the defect. If the basic defect is indeed genetically determined it is strange that the complication has not been reported among other mongoloids—for example, the Thais. It may well be that it has been overlooked as it has been in the Chinese.

As is the case in the familial form (McArdle, 1963), the periodic paralysis complicating thyrotoxicosis cannot be explained solely by a fall in serum potassium levels. Weakness developed in some instances when the serum potassium concentration was within the normal range. On the other hand, in thyrotoxic patients with no history of paralysis hypokalaemia was induced without the production of muscle weakness. Furthermore, in those patients rendered euthyroid when an attempt was made to induce paralysis after priming with 9-α-fluorohydrocortisone the serum potassium concentration fell to below the normal range without any impairment of muscle function, whereas when they were thyrotoxic these levels were associated with at least marked weakness. Nevertheless, the fall in serum potassium, and presumably the influx of potassium into muscle after high-carbohydrate feeding and insulin, was significantly greater when the patients were thyrotoxic than when they were euthyroid. McArdle (1963), in a review of the metabolic myopathies, wrote of periodic paralysis: "It is a measure of our ignorance that opinion is still divided on whether the primary abnormality lies in the muscle or elsewhere." The present observations contribute nothing to the solution of this problem.

Summary

Of 1,366 consecutive southern Chinese patients with thyrotoxicosis (1,188 females and 178 males) 25 (1.8%) gave a history of attacks of periodic paralysis, and of these 23 (13%) were males and 2 (0.17%) were females. Since it proved possible to induce attacks of paralysis in 2 of the 13 male patients without a history of such, there was additionally a group of potential paralytics. It is concluded that the incidence among the Chinese is approximately the same as that reported among the Japanese, yet, strangely, there is a lack of reports of its occurrence.

The clinical, biochemical, and electrocardiographic findings during spontaneous and induced attacks are described. In view of the frequency of occurrence of arrhythmias during both forms of attacks it is concluded that attempts to induce attacks should be made only under continuous cardiac monitoring.

There are similarities between thyrotoxic periodic paralysis and the familial form. In both there is a preponderance in males, the factors which induce attacks are the same, and if the manifestations of thyrotoxicosis are excluded the clinical pictures during attacks are identical. The biochemical changes are similar. There is retention of water and sodium without alteration in serum sodium concentration. There is invariably a fall in serum potassium concentration, associated with a proportional reduction in the potassium excreted in the urine. There is no evidence of excessive potassium loss in the stools. The response of attacks of paralysis to treatment is similar, and salts of potassium and aldosterone antagonists are effective in a proportion of patients in preventing the induction of attacks. However, neither of the two forms can be explained solely by a fall in serum potassium concentration.

On the other hand, thyrotoxic periodic paralysis differed from the familial form in certain important particulars. In none was there a family history. The age at onset was later and corresponded with the age incidence of thyrotoxicosis. The great majority of attacks occurred in the hot season. Furthermore, the attacks of paralysis occurred only during the period of thyrotoxicosis, and, in the euthyroid state, could no longer be induced even when hypokalaemia was produced by priming with 9-α-fluorohydrocortisone.

The occurrence of attacks of paralysis was not related to the duration or the severity of the thyrotoxicosis, and by no available evidence could distinction be made between those with and those without paralysis. This, together with the high incidence among mongoloids, suggests that the basic defect may be genetically determined. But the evidence presented indicates that the defect manifests itself only when challenged by thyrotoxicosis.

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