THE ELECTROCARDIOGRAM IN PELLAGRA

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Deficiency in thiamin, a factor of the vitamin B complex, may cause severe circulatory insufficiency. It is, therefore, of interest to study the circulation in another type of B-avitaminosis—pellagra.

The circulatory disturbances encountered in pellagra are of no great clinical significance. Frequently low arterial pressure and tachycardia are present. Ædema, if there is any, can scarcely be attributed to circulatory insufficiency, even if exclusively present at the lower extremities. As shown by the example of beri-beri and the famine ædema, this accumulation of fluid is especially connected with changes of the tissue itself and the composition of the plasma.

For these reasons it is particularly the electrocardiogram that is dealt with in this paper. As far as we know only Porter (1934) and Feil (1936) have studied this question. The former found nothing more than sinus tachycardia; the latter, who investigated 38 pellagra patients, found in 14 of them electrocardiographic changes that could not be attributed to other circulatory disturbances. There was sinus tachycardia, low voltage of the ventricular complex, a high T, a Pardee-type of T, an abnormal shape of the S–T portion, as well as a negative T wave. In the chest lead also some abnormalities were found, e.g. low voltage, M-shape of the ventricular complex, a monophasic S–T, or an upright T. The changes in the electrocardiogram gradually disappeared, in part, when the pellagra itself was cured, thus revealing their relationship with the disease.

PRESENT INVESTIGATION

We have 45 electrocardiographic records of 23 pellagra patients (15 men and 8 women); 21 suffered from the chronic type of the disease and 2 from a first attack of the acute type (Cases 21 and 22). Eight of the men and one woman were over 50 years of age. This is of some significance since, with advancing age, the possibility of cardiographic changes due to coronary sclerosis increases, even without clinical symptoms. We therefore separated our material into two groups, below and above this age. Patients who had circulatory symptoms clinically were excluded from these investigations. The blood pressure of the patients varied from 85/55 to 190/95 mm. In one only
was not certain, findings were also classical leads, and among the figures. Alteration of the S-T interval, which tachycardia, showed a negative. The standard gauge of amplitude was 10 mm. = 1mV.

RESULTS

The results of these investigations are shown in the following tables and figures. Among the abnormalities observed, the most frequent was sinus tachycardia, which occurred in about one third. In one patient (Case 18) it was not certain, on account of his high temperature, whether there was an actual connection between this cardiac phenomenon and the pellagra. Similar findings were also obtained in some older persons, where they were particularly striking in view of the senile bradycardia.

Table I shows that in nearly half of the cases the electrocardiogram was normal, and also that the abnormalities observed were of various types. Alteration of the S-T interval and of the T wave were present in all the pathological records (13 out of 23). Moreover, there was frequently deformation of the ventricular complex (low voltage or notching) in a total of six cases. Pathological manifestations of this kind in lead IV were presented by practically half the patients (see Table I).

TABLE I

**ELECTROCARDIOGRAPHIC ABNORMALITIES IN PELLAGRA**

<table>
<thead>
<tr>
<th>Electrocardiographic Findings</th>
<th>Number of Cases</th>
<th>Number over 50 Years of Age</th>
<th>Percentage with this Abnormality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal records</td>
<td>10</td>
<td>2</td>
<td>—</td>
</tr>
<tr>
<td>Abnormal records</td>
<td>13</td>
<td>7</td>
<td>57</td>
</tr>
<tr>
<td>Sinus tachycardia (90 or over)</td>
<td>9</td>
<td>7</td>
<td>39</td>
</tr>
<tr>
<td>Auricular fibrillation (1 case) or Ventricular extrasystoles (3 cases)</td>
<td>4</td>
<td>1</td>
<td>17</td>
</tr>
<tr>
<td>Low voltage of QRS (below 5 mm.)</td>
<td>2</td>
<td>2</td>
<td>9</td>
</tr>
<tr>
<td>Notching of the QRS (4) or Large Q3 (1)</td>
<td>5</td>
<td>3</td>
<td>21</td>
</tr>
<tr>
<td>S-T interval above or below zero level</td>
<td>3</td>
<td>1</td>
<td>13</td>
</tr>
<tr>
<td>Negative T1 (1) or negative T2 and T3 (1)</td>
<td>2</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>Abnormalities of lead IV (18 cases only)</td>
<td>11</td>
<td>4</td>
<td>61</td>
</tr>
<tr>
<td>Low voltage</td>
<td>3</td>
<td>1</td>
<td>16</td>
</tr>
<tr>
<td>Notching of R (3) or M form of QRS (2)</td>
<td>5</td>
<td>3</td>
<td>27</td>
</tr>
<tr>
<td>Upright T (4) or Absent T (3)</td>
<td>7</td>
<td>2</td>
<td>39</td>
</tr>
</tbody>
</table>

* It will be seen that the lead IV records were taken before the publication of the recommendations of the Cardiac Society and the American Heart Association and do not conform to these recommendations.
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The findings in these records show no features characteristic of pellagra. Two clinical arguments, however, favour the assumption that the disturbances have some causal relationship with pellagra.

The first argument is the high incidence (57 per cent.) of a pathological electrocardiogram in pellagrins with an otherwise normal circulation. This holds true even remembering that in older persons such findings may result from coronary sclerosis without clinical symptoms and that half our patients with a pathological electrocardiogram were over 50 years of age. On the other hand, there was a very abnormal electrocardiogram in one female pellagrin of 23, who subsequently succumbed to the disease.

The second and decisive argument concerns the parallelism between the course of the disease and the development of the electrocardiogram, in cases either with improvement or even cure and in those with deterioration or death. Decisive proof, however, is furnished by the fact that the pathological electrocardiogram returned to normal, parallel to the proceeding improvement of the process; while such an occurrence could scarcely be expected if the changes were due to coronary sclerosis (apart from the occurrence of acute infarction). Other irreversible heart affections that might have induced the electrocardiographic symptoms could be ruled out by the clinical findings.

### TABLE II

**Cases of Pellagra with Abnormal Electrocardiograms**

<table>
<thead>
<tr>
<th>Case Number</th>
<th>Age</th>
<th>Sex</th>
<th>Blood Pressure</th>
<th>Rate</th>
<th>Abnormalities</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>50</td>
<td>M</td>
<td>95/55</td>
<td>70</td>
<td>Extrasystoles, S-T above zero level (II, III).</td>
</tr>
<tr>
<td>4</td>
<td>50</td>
<td>M</td>
<td>110/70</td>
<td>78</td>
<td>Flat T₁, Upright T₄</td>
</tr>
<tr>
<td>6</td>
<td>46</td>
<td>M</td>
<td>110/55</td>
<td>80</td>
<td>Flat T₁, Low voltage lead IV</td>
</tr>
<tr>
<td>9</td>
<td>70</td>
<td>M</td>
<td>135/70</td>
<td>115</td>
<td>S-T₂ below zero level</td>
</tr>
<tr>
<td>10</td>
<td>60</td>
<td>M</td>
<td>110/65</td>
<td>92</td>
<td>Low voltage, Absent T₂</td>
</tr>
<tr>
<td>11</td>
<td>54</td>
<td>M</td>
<td>145/80</td>
<td>79</td>
<td>Notching of QRS₃, M complex of QRS₄, Absent T₄</td>
</tr>
<tr>
<td>12</td>
<td>66</td>
<td>M</td>
<td>130/80</td>
<td>72</td>
<td>Notching of QRS₄ and S, Flat T₁, Negative T₂ and T₄</td>
</tr>
<tr>
<td>13</td>
<td>55</td>
<td>M</td>
<td>90/70</td>
<td>88</td>
<td>Flat T₁, M complex of QRS₄</td>
</tr>
<tr>
<td>14</td>
<td>58</td>
<td>M</td>
<td>120/70</td>
<td>85</td>
<td>Low voltage, Notching of QRS₃, M complex of QRS₄</td>
</tr>
<tr>
<td>17</td>
<td>36</td>
<td>F</td>
<td>95/60</td>
<td>120</td>
<td>Flat T₁</td>
</tr>
<tr>
<td>18</td>
<td>23</td>
<td>F</td>
<td>95/55</td>
<td>120</td>
<td>Absence of T₁, T₂, and T₄, Low voltage lead IV</td>
</tr>
<tr>
<td>22</td>
<td>46</td>
<td>F</td>
<td>120/80</td>
<td>85</td>
<td>Large Q₂, S-T depressed (I, II), Negative T₁, Flat T₂</td>
</tr>
<tr>
<td>23</td>
<td>80</td>
<td>F</td>
<td>110/80</td>
<td>110</td>
<td>Aur. fib., Notching of QRS₂ and S, Absent T₄</td>
</tr>
</tbody>
</table>

* From several records of the same patient, we have chosen, in this Table, the most characteristic one.

Table II is supplementary to Table I and gives a brief description of the clinical data and pathological records observed in the 13 pellagra patients, who had such abnormal records. There were a total of 11 cases in which we had the opportunity of following up the development of the electrocardiogram.
Details of these 11 cases follow and they could be divided into three groups—those with no electrocardiographic change after recovery (3 cases), those with electrocardiographic improvement after treatment (3 cases), and those with the electrocardiogram becoming worse as the disease progressed (5 cases).

**Group I.**—**Cases with No Electrocardiographic Change after Recovery**

In three cases no change of the cardiogram was observed after recovery following nicotinic acid treatment.

The first (Case 21) had acute pellagra (first attack) and the cardiogram was normal from the beginning.

In the second (Case 7) conditions were similar. A woman, aged 46, suffered from a mild type of pellagra, the duration of which could not be determined from the history. At the climax of the disease the cardiogram showed no pathological features, and during recovery there were no changes except a moderate increase of T, which had been normal from the beginning in all three leads.

The third was a woman of 80 (Case 23). Although the pellagra symptoms rapidly improved (diarrhoea, psychic manifestations, and dermatitis) the pathological cardiogram—possibly arteriosclerotic in nature—persisted unchanged throughout the 18 days' of observation.

**Group II.**—**Cases with Electrocardiographic Improvement after Treatment**

In the second group (three patients, all treated with nicotinic acid) decrease or disappearance of the pathological character of the cardiogram was observed, parallel to the clinical improvement of the pellagra.

It must be admitted that the first two did not show such peculiarities of the cardiogram, even at the climax of the process, that the record could be called pathological (and they are, therefore, not recorded in Table II). The records taken during convalescence, however, differed greatly from the earlier ones, so that it appears that these had been pathological.

**Case 15.**—A man, aged 65, was under observation for two months in 1939. Since 1934 there had occasionally been diarrhoea. He showed moderate glossitis and the typical pellagra dermatitis of the backs of both hands, which was suggestive of a long-standing process. Nicotinic acid rapidly caused the disappearance of these symptoms, the old pellagra skin coming off in pieces.

The first cardiogram showed no pathological change. Another, taken no more than 5 days later, showed slowing of the rate from 100 to 83 and an increase of the ventricular complex in all leads, as well as a more distinctly formed S4, this having been but rudimentary in the first record.

**Case 5.**—A boy, aged 5, had been under clinical treatment for alimentary anaemia accompanied by cutaneous haemorrhages in 1938. Then he was again in hospital for pellagra for three months to March 1939. There was frequent diarrhoea, glossitis, hyperkeratosis of the arms, pigmentation of the face, and a hypochromic anemia. With an adequate diet and vitamins A, D, and C, as well as nicotinic acid, iron, and liver extract, the symptoms subsided.
The first cardiogram could not be called pathological. It presented a large $T_1$, a large $T_2$ and a slightly negative $T_3$ with a pulse rate of 95. In the record taken towards the end of the treatment $T$ was more distinctly separated from $S-T$ in leads I and II. $Q_3$, which had been present previously, had disappeared and $T_3$ had become positive.

Case 22.—A woman, aged 46, who had been under clinical treatment from February to May, presented pellagra dermatitis of the backs of both feet of five months duration. There were psychic changes in addition, but no particular digestive troubles. Nicotinic acid treatment improved the psychic condition within a few days and later the skin symptoms.

The first cardiogram (Fig. 1) was pathological. $S-T_1$ was below the isoelectric level, and there was only a suggestion of $T_1$; $S-T_2$ and $T_2$ had melted into a straight line slightly upwards, $S-T_4$ was above the zero level, and $T_4$ was positive. In the record taken 18 days later $S-T_1$ and $S-T_2$ were on the zero level. $T_1$ and $T_2$ were positive, well developed, and distinctly separated from the $S-T_1$ interval. $S-T_4$ was now on the isoelectric level and $T_4$ was absent.

Group III:—Cases with the Electrocardiogram becoming Worse as the Disease Progressed

The third group included 5 patients all of whom belonged to the period before nicotinic acid treatment was introduced into the therapy of pellagra. In all of them the cardiogram became more pathological in the course of the process.
This occurred in two patients during their stay in hospital. One responded insufficiently to the treatment (yeast and liver extract) and another did not respond at all. In the three others the pathological development of the cardiogram appeared during relapses at home, after the first attack had readily responded to the treatment. The relapses had been caused by a return to their usual diet. As in the second group, these patients could be separated into those in whom the curves were at first normal or practically normal (although the pellagra process was already present) and the development of pathological signs occurred later, and those in whom the cardiogram was abnormal from the beginning and became more so during the course of the disease. Most of the cases of this group were of the type in which, at the beginning, the cardiogram showed insignificant changes that by no means ranked as abnormal, but took on a pathological character during the development of the disease.

Case 13.—A man, aged 55, had been admitted to the hospital in spring 1937 for chronic pellagra with diarrhoea, dermatitis, and psychic disturbances. After two months' treatment with yeast and liver extract he was discharged without symptoms. In November he was re-admitted with a relapse, which had begun 20 days earlier with diarrhoea. The same treatment that had been given during his first admission was not so satisfactory and the intestinal troubles persisted.

We have at our disposal four records of this patient, three taken during his first stay in hospital and one in the relapse. The first showed nothing pathological. The two following (taken at intervals of one month) were characterized by a diminishing voltage of T₁, although the clinical improvement progressed. Eight months later (during the relapse) this decrease of voltage had reached such a degree that T₁ was now scarcely to be seen. R–S₃ showed notching in this last record. In lead IV S–T and T had assumed a pathological shape, but the corresponding lead of the previous records was not at our disposal. The excursion of the ventricular complex, however, did not change.

Case 6.—A man, aged 50, was admitted to the hospital on account of pellagra in February 1938. There were typical changes of the skin on the face, neck, and hands. He had been suffering from diarrhoea for six weeks. Two months' treatment with yeast and liver extract caused the disappearance of his symptoms. Four months later (August), he was re-admitted with a relapse. No notes of his further course are available.

The cardiogram taken at the climax of the disease was not pathological. That, however, taken during the relapse (August) showed marked decrease of the voltage of the ventricular complex in all leads. There was only a suggestion of T₁, and T₃ had become smaller. S–T₂ and T₃ had melted into a slightly inclining convex line, and so had S–T₄ and T₄, except that in the latter the line declined slightly. The cardiogram had, therefore, become pathological.

Case 14.—A man, aged 58, was under clinical treatment for pellagra from May to August 1937. The skin of his hands had been affected two years earlier. For six months he had been suffering from diarrhoea. After ten weeks' treatment with yeast and liver extract the pellagra dermatitis disappeared, while the diarrhoea improved but had not subsided altogether when he was discharged.

The first record showed notching at R–S₂ at its base. The S–T₃ interval and T₃ had melted into a slightly convex curve. In the record taken one month later the ventricular complex as well as T had decreased in voltage in all three classical leads. At the top of R₃ notching has appeared and in lead III the ventricular complex has assumed an M shape (Fig. 2).
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Case 17.—A woman, aged 36, was under treatment from November 1936 to January 1937. Her pellagra had set in three months before her first admission. In the early stages there had been a painful glossitis and a dermatitis of the hands, and later pronounced psychic disturbances. The abnormal excitability of this patient (it was during the pre-nicotinic era) rendered every attempt at suitable treatment impossible. Three times she left hospital during an attack of depressive agitation and remained at home for several days. In view of these conditions, the disease proceeded, and in January 1937 she died.

The first cardiogram was normal. In a later one the voltage of the ventricular complex had decreased and T₁ was scarcely recognizable. T₂ and T₃ had also become smaller and showed a growing tendency to fuse with the preceding S–T interval (Fig. 3).
Case 18.—A woman, aged 23, had been under treatment for severe pellagra from May until her death in August 1937. The disease had started with diarrhea in March and it was a febrile pellagra of the severest type, with dermatitis of the hands and feet, psychic disturbances, and anemia. Large doses of yeast and liver extract improved the anemia, but she succumbed to the disease.

The first cardiogram was of normal voltage, but T₂ was practically absent and in lead III the ventricular complex was M shaped and T₃ was negative. In the subsequent records, taken at intervals of 3–5 weeks, the voltage was gradually reduced, and in the last record, T₁, T₃, and Q₄ had disappeared. This group of cardiograms shows instructively the progressive increase of the pathological character (Fig. 4).

![Cardiogram deteriorating in a fatal case of pellagra (Case 18).](image)

(A) May 11. Flat T in lead II; (B), (C), and (D) June 23, July 19 and August 4. Showing voltage becoming lower and T waves flatter.

The P–R interval was on the whole normal, between 0.12 and 0.20 seconds. In three instances it was below 0.12 seconds. One child of five, where P–R was 0.11 sec. cannot be called abnormal (Case 22). The two other findings of this type, however where P–R was 0.10 sec. (Case 10) and 0.11 sec. (Case 13), were certainly pathological.

The duration of the electric systole as measured by the Q–T interval was not characteristically changed. This was plotted out in a diagram, comparing it with the pulse rate, but with one exception the points all fell within normal limits, showing that this is not influenced by pellagra (see Fig. 5). Further, a careful comparison suggested no correspondence between the Q–T interval and the clinical course of the pellagra process.

As regards the rate of the heart, sinus tachycardia was often encountered,
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as may be seen from Tables I and II. During the period of convalescence we found remarkable bradycardia four times (Cases 7, 19, 20, and 22).

Fig. 5.—Comparison of the electric systole of the heart (Q-T interval) with the heart rate (R-R interval).

COMMENT AND DISCUSSION

In contrast to the clinical picture, in which disturbances of the cardiac function play no important rôle, the electrocardiogram is often changed in pellagra. Abnormalities were encountered in about two thirds of our pellagrins whose cardiac condition was clinically normal.

That there is a close association between these findings and the pellagra process is shown by the marked parallelism between the clinical development of the disease and that of the electrocardiogram. It is shown by the fact that the cardiogram sometimes returns to normal when the clinical condition
is cured. Like Feil (1936) and Smith et al. (1937) we are in a position to furnish an example. Also two cardiograms that were borderline between the normal and the abnormal became normal as the cure of the pellagra advanced. The reverse, too, i.e. the appearance or accentuation of the pathological character of the cardiogram when the pellagra process deteriorates, is frequently observed.

The changes that were most frequently observed, which in view of the above arguments may be attributed to pellagra, are:

1. Low voltage (without edema),
2. Notching of the ventricular complex,
3. Deformation of the S–T interval and negativity of the T wave,
4. Shortening of the P–R interval in some cases.

We also observed sinus tachycardia at the climax of the disease and sinus bradycardia during the period of convalescence.

Other disturbances observed by Feil, namely, the Pardee-type of T and changes of the duration of the Q–T interval, were not detected in our material.

It is interesting to compare these changes in pellagra with the cardiographic findings in beri-beri. Since in beri-beri circulatory phenomena are mostly present, more thought has been given to the cardiogram in this disease than in pellagra and a number of reports have been published on the subject (Scott and Hermann, 1925; Aalsmer and Wenckebach, 1929; Keefer, 1936; as well as Weiss and Wilkins, 1936). As with pellagra, the cardiographic changes are by no means present in every patient with beri-beri, even when the heart is clinically affected; nor are the abnormalities characteristic of the disease. In beri-beri too, as a rule, tachycardia is encountered and the bradycardia, which has been observed by us during the period of convalescence of pellagra, has been found with the convalescence of beri-beri also (Keefer, 1936). The morphological findings described in beri-beri are the following: decrease and notching of the ventricular complex, deformation of the S–T interval and inversion of the T wave, lengthening of the electric systole (the Q–T interval): the same findings are, therefore, encountered in varied conditions resulting from a disturbed function of the heart muscle. That there is, however, actually a relationship between the symptoms described and beri-beri is shown by their disappearance when the clinical symptoms subside. The shortened conduction, time P–R, may be called a rather characteristic feature, since it does not often occur in connection with a disturbed muscular function. Aalsmer and Wenckebach (1929), who found the electrocardiogram of the beri-beri heart to be normal in the other respects (apart from that of the final stage), particularly stressed this peculiar disturbance. Keefer (1936) found it three times among his observations.

In our material we twice encountered a shortening of the P–R interval to below 0.12 sec. Feil (1936) also observed two cases of this type, in which the conduction time increased again with convalescence. This sign seems to us to be of particular significance.

During the last three years investigations have made it clear that the disturbances of the skin, digestive tract, and central nervous system that are found...
in pellagra are brought about by a deficiency in nicotinic acid. It would be rather rash to explain all symptoms of pellagra as due to this factor. The simultaneous occurrence of the various components of the vitamin B complex in nature brings it about that an insufficient supply of vitamin B involves, in man, a variety of factors, although in any one case clinical deficiency of one or the other is the most striking feature. Quite a number of findings support this assumption. Spies and Aring (1938) found that peripheral neuritis in pellagra could not be cured by nicotinic acid, but was cured by thiamin. Spiess et al. (1938), moreover, observed that in some cases of pellagra nicotinic acid treatment becomes less effective if continued, and must then be supported by lactoflavin treatment. Lehmann and Nielson (1939) recently reported a case, in which during the patient's stay in hospital with an adequate diet pellagra developed immediately after beri-beri had been cured with thiamin.

The occurrence of the above cardiographic abnormalities rather frequently in pellagra is not sufficient to conclude that they are caused by deficiency of nicotinic acid. However, the rapid disappearance of these abnormalities subsequent to nicotinic acid treatment gives strong support of this assumption. The occurrence of a phenomenon, rather characteristic of beri-beri (shortening of the conduction time), in the cardiogram of some pellagrins justifies the assumption that, similarly to the peripheral neuritis in pellagra, this symptom is brought about by the deficiency in vitamin B₁.

**Summary and Conclusions**

Forty-five electrocardiographic records of 23 pellagrins with normal circulatory condition have been studied.

In about three fifths the cardiogram was abnormal. That these abnormalities have a causal relationship to pellagra is demonstrated by the fact that their development is parallel to the clinical course of the disease, and particularly by the rapid disappearance of these changes in some cases subsequent to nicotinic acid treatment.

Tachycardia is mostly encountered at the climax of the disease and bradycardia during the period of convalescence.

The most frequent changes in the electrocardiogram are:

1. low voltage of the ventricular complex,
2. notching of the ventricular complex,
3. deformation of the S–T interval and inversion of the T wave, and less commonly
4. shortening of the P–R interval.

These changes are, however, not in themselves characteristic of pellagra. Since Aalsmer and Wenckebach (1929) consider this last characteristic of beri-beri, it must be assumed that in pellagra also it may be brought about by a deficiency of vitamin B₁, accompanying the deficiency of the pellagra-preventive-factor.
REFERENCES