Correlation of Mittelschmerz with Fluctuations in the Waking Oral Temperature

Since fluctuations in the body temperature are now widely used to indicate the time of ovulation a record of the daily waking oral temperature has been kept for the last 13 cycles. The results are plotted in Fig. 2, the mittelschmerz being indicated by arrows.

The temperature recordings conform in general to the usually accepted pattern, though they are not so clear-cut as some that have been published. In the middle of the cycle, however, there is usually a slight fall in temperature, followed by a steep rise to a plateau, which is maintained until near the onset of the subsequent period. Occasionally this rise is indistinct.

An independent observer was asked to estimate the most likely time of ovulation from temperature charts alone. In eight of the 14 cycles ovulation, as judged in this way, agreed with the day of onset of the mittelschmerz. In three cycles the estimate was one day early, and in three it was one day late.

A change in the temperature curve, particularly when the whole chart is available and when attention is directed to the mid-cycle, is at best only indirect evidence of ovulation, but the close relation between the temperature change and the mittelschmerz is of interest.

Discussion

Early workers who described the mittelschmerz were in difficulties in ascribing a cause to the pain. This was due primarily to the fact that ovulation was thought to be closely related temporally to the onset of menstruation. It is now known from both direct and indirect evidence that ovulation occurs at some moment in the middle of the cycle. Intermenstrual pain, like changes in hormone excretion in the urine, physical changes in the cervical mucus, electrical potential changes, and so on, is obviously an indication of some alteration in the reproductive tract, and may be accepted as further evidence that ovulation occurs in the middle of the cycle.

The cause of the pain is still obscure. It is abolished by ovariectomy, but is not affected by operations that interfere with nervous pathways from the uterus. Painful tubal contractions may, however, be a possible explanation.

If, as the evidence suggests, the pain is connected with ovarian changes, the immediate cause may be either the pressure of a distending follicle just before ovulation or the actual rupture of the follicle.

It seems probable that the pain gives a closer indication of the time of ovulation in those women who are aware of it than any other method. In view of the experience of McSweeney and Wood (1940) that 21 out of 134 women could identify some discomfort in the mid-cycle, careful questioning about the mittelschmerz of patients who attend fertility clinics would seem to be worth while. Cases have certainly been reported (Wharton and Henriksen, 1936) in which the pain had been severe enough to prevent intercourse and in which advice to disregard the pain was immediately followed by conception.

Summary

The cyclical occurrence of intermenstrual pain (mittelschmerz) has been followed for 4½ years in a married woman aged 28.

The onset of the pain is closely correlated with changes in the waking oral temperature, and is taken to be a reliable index of ovulation.

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SYNDROME OF DIAPHRAGMATIC HERNIA AND ANAEMIA

BY

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No medical or surgical disease presents a clinical symptomatology so varied and unstable as that of congenital or acquired diaphragmatic hernia. Harrington (1945) studied 320 cases of oesophageal hiatus hernia and found that an average of three previous erroneous diagnoses had been made before the correct diagnosis was established. In order of frequency the most common erroneous diagnoses were: cholecystitis, cholelithiasis, gastric ulcer, secondary anaemia, duodenal ulcer, hyperacidity, cardiac disease, carcinoma of the cardia, stricture of the oesophagus, appendicitis, and intestinal obstruction. Chevallier and Danel (1944) reported that diaphragmatic hernia was commonly associated with anaemia.

Katsigras (1946) reviewed the published reports of 955 cases of oesophageal hiatus hernia and observed that anaemia was associated with the hernia in 80 cases, a proportion of 8.3%.

In my view (Codounis, 1946) diaphragmatic hernia can provoke the appearance of microcytic or hypochromic anaemia, or of macrocytic or hyperchromic anaemia. The personal case here described appears to be unique in medical literature. A severe anaemia persisted for 24 years, as did the diaphragmatic hernia. At first there was a microcytic anaemia and later macrocytic anaemia.

Case Record

J. A., a man of 60, had previously suffered from malaria and jaundice. He had three children in good health, two born after the beginning of the anaemia. His present illness started in April, 1922. After an emotional disturbance he had been feeling increasingly weak, tired, and anxious. His skin was pale and his eyes yellowish. These symptoms, with anorexia and loss of weight, became more serious, and he consulted Professor Schlesinger in Vienna, who diagnosed hypochromic anaemia and prescribed iron and a change of climate.

Phase of Microcytic Anaemia.—After three months' rest at Semmering J. A. returned feeling better. In December, 1922, pallor and progressive weakness reappeared, with vomiting, nausea, and epigastric swelling after meals. In February, 1923, he went to Vienna to consult Dr. Eppinger, who diagnosed Banti's disease and advised splenectomy. X-ray examination of the gastro-intestinal tract revealed no abnormality—probably due to a technical defect.

J. A. later went to France, where the diagnosis of hypochromic anaemia was confirmed. After four months' rest in the country he came home in good health and noticed no symptoms during the year 1923.

In 1924, after the same clinical and haematological symptoms and some loss of weight (100 kg. to 82 kg.), he returned again to France and consulted Dr. P. E. Weill, who confirmed the diagnosis of hypochromic anaemia. The patient was given iron and liver extracts, which improved his condition. His red cell count fell to 3,000,000 per c.mm. in 1925, and Dr. Weill gave him a blood transfusion, after which the improvement was nearly complete. Between 1926 and 1938, during which twelve years he had iron therapy and a change of air each summer, the patient was free from symptoms and lost no more weight. His usual weight was 100 kg., which was considered normal in relation to his height.

After an attack of influenza in November, 1938, J. A. felt very weak and dizzy. There was marked pallor of the skin

and mucous membranes, and a generalized oedema. Iron and liver extracts were prescribed and he was given three blood transfusions; the second provoked a severe anaphylactic shock, which was nearly fatal. Five days later the red cell count was only 900,000 per c.mm. Slowly the anaemia improved again; large doses of iron, 10 to 12 g. daily, were prescribed, but the patient could take only 4 to 5 g. daily.

He felt no pain between 1939 and 1941, but because of war-time food shortages he lost 25 to 30 kg. in weight.

In July, 1941, apart from weakness and pallor, J. A. complained of pains in the left upper abdomen and palpitations. Dr. Maroulis, a colleague who saw him during this period, noted besides the anaemia hyperresonance in the left chest. The same iron therapy was continued and the patient improved again over the next five years (October, 1945).

Altogether the evolution of the first phase of microcytic and hypochromic anaemia included three long periods in which the condition was absolutely quiescent; after the appearance or reappearance of symptoms improvement was brought about by treatment with iron, and the patient could live a normal life.

Phase of Macrocytic Anaemia.—Marked pallor and oedema reappeared in November, 1945, together with pain in the left upper abdomen radiating to the scapular and lumbar regions. A blood count showed: r.b.c., 4,120,000; w.b.c., 6,400; Hb, 70%; colour index, 0.85. His symptoms grew rapidly worse, however, and on Dec. 26, 1945, J. A. came under my care.

At that time his temperature was 38.4° C. (101.2° F.), pulse rate 80, and he had slight tachypnoea. His face was like that of a case of nephritis, oedematous and very pale. His lips were bloodless, he was very weak and, besides the puffiness of the face, there was marked oedema of legs and meteorism. He had a slight thoracic kyphosis. His chest was of the emphysematous type; the percussion note was tympanitic; rales were heard at both bases.

Blood pressure: 170/90 mm. Hg. X-ray examination of the chest and heart indicated no abnormality. Radiographs of the spine revealed changes in the third and fourth dorsal vertebrae, probably due to a healed spondylitis. Examination of the urine showed some white cells and some calcium oxalate crystals.

Final Diagnosis

With this history and the findings here tabulated it was easy to assume a relapse of the anaemia which had affected the patient for 24 years. But we were surprised to see that instead of a microcytic and hypochromic anaemia there was a macrocytic and hyperchromic anaemia. Then, on Jan. 5, 1946, an x-ray examination by Dr. Xanthakis,

TABLE I.—Haematological Findings

Date	R.B.C. End of Microcytic Phase	Hb %	Colour Index	W.B.C.	Differential Count %			
					Poly- morphs	Lympho.	Eosino.	Mono.
7.11.45	4,120,000	60	0.85	6,400	60	32	4	4
Macrocytic Phase								
27.12.45(A)	1,880,000	37	1.02	8,600	50	46	—	4
5.1.46	2,440,000	50	1.04	—	—	—	—	—
7.1.46	2,770,000	50	0.92	—	—	—	—	—
11.1.46	3,080,000	43	0.70	8,400	78	22	—	—
14.1.46(B)	2,540,000	46	0.72	6,000	66	28	4	2
15.1.46	3,000,000	45	0.75	—	—	—	—	—
21.1.46(C)	3,430,000	52	0.76	7,000	62	34	2	2
30.1.46(D)	3,040,000	55	0.91	5,200	56	38	2	4
2.3.46	3,660,000	65	0.90	4,600	66	22	8	4
6.3.46(E)	4,480,000	75	0.85	5,000	66	28	4	2
Phase of Relapse								
29.3.46	4,000,000	70	0.87	—	69	25	3	3
1.4.46	3,800,000	72	0.94	—	78	16	2	4
4.4.46(E)	3,120,000	—	—	—	—	—	—	—
5.4.46	1,850,000	35	0.94	12,000	—	—	—	—
8.4.46	1,030,000	17	0.82	18,400	—	—	—	—

A. Evidence of polychromasia, anisocytosis, poikilocytosis, and predominance of macrocytes—among them are oval and well-coloured macrocytes (Naegeli's megalocytes). No granular erythrocytes. Some white cells with globular nuclei.

B. Average anisocytosis and poikilocytosis and hypochromia. Predominance of macrocytes and among them some Naegeli's megalocytes. Some giant platelets.

C. Average hypochromia and anisocytosis and poikilocytosis. One acidophilic normoblast per 100 white cells.

D. Some polychromasia, slight anisocytosis and poikilocytosis.

E. Bleeding time, 3 minutes; coagulation time, 9 minutes; blood urea, 0.45%; 380,000 platelets.

TABLE II.—Bone-Marrow Picture

Reticulo-endothelial Series	I	II	III
Reticulocytes	% 4	% 2	% 13
Endothelial cells	2	2	3
Fatty cells	—	—	—
Erythroblasts:			
Proerythroblasts	5	2	2
Basophilic erythroblasts	12	6	1
Polychromatophilic erythroblasts	8	34	85
Normoblasts	10	37	12
Megaloblasts	8	—	—
White cells:			
Myeloblasts	2	2	2
Promyelocytes	5	4	6
Myelocytes	7	12	25
Metamyelocytes	10	20	15
Rod cells	15	17	16
Polynuclear cells	50	31	18
Eosinophilic myelocytes	1	—	1
Eosinophilic polynuclears	1	—	1
Basophils	1	—	—
Monocytes	1	—	—
Lymphocytes	1	7	—
Ferrata cells	—	1	—
Platelets:			
Megakaryocytes	—	2	—

I.—Dec. 27, 1945. Mitosis chiefly among the basophilic erythroblasts and anisocytosis with predominance of Naegeli's macrocytes. Vacuoles in the protoplasm and in the cellular nuclei.

II.—Jan. 17, 1946. Normoblasts present with relatively few mature nuclei in comparison with the protoplasm. Mitosis. Rods of giant cells and a good number of cells with lobulated nuclei.

III.—Immediately after death on April 10, 1946. Majority of reticulocytes are of Ferrata type. Majority of nuclei of polychromatophilic erythroblasts are in mitosis. Macroblasts rarely found. Asynchronism in maturation. Immature megakaryocytes noted with basophilic protoplasm and without lobulation of the nucleus.

undertaken to exclude the possibility of gastric ulcer or cancer, explained clearly the anaemia and the digestive symptoms and thoracic pains.

Immediately after the patient had taken the barium meal a displacement to the right of the lower end of the oesophagus was observed. A large pocket of air in the herniated and distended stomach extended seven finger-breadths above the diaphragm. The stomach was elongated, and immediately below the diaphragm, on the lesser curvature, a diverticulum was noted. Another small diverticulum was observed in the descending part of the duodenum. Here then was a case of diaphragmatic hernia in a man who had been treated for anaemia for over twenty-four years. This is the fortieth case of this syndrome to be described in the literature and the first case to be observed in Greece up to April 16, 1945, when a preliminary communication was made to the Medical Society of Athens. Reviewing the long history of this case, it may be seen to fall into six successive stages.

Stage 1.—Apparently perfectly healthy until the age of 36.

Stage 2.—Onset of hypochromic anaemia, from 36 to 39 years of age. It is at this stage that J. A. complained of the first dyspeptic disturbances—post-prandial discomfort, epigastric fullness, and occasional vomiting. Over these four years improvement in the anaemia would be followed by recrudescence, followed again by rapid improvement.

Stage 3.—The twelve years from the age of 39 to 51 are characterized by almost normal good health.

Stage 4.—From the age of 52 to 54 there was a new and intense recrudescence of anaemia, following a severe attack of influenza in 1938. He lost 25 to 30 kg. in weight and his red cell count fell to 900,000 per c.mm. Later, on consulting the patient's wife, we were told that at this period she heard some gurgling in his stomach, even at some distance away from him. At the same time he complained of acute pains in the left hypochondrium, disappearing a few minutes after protracted belching. Physical examination at that time showed a pronounced hyperresonance of the left hemithorax.

Stage 5.—Quite well again from 55 to 60 years of age.

Stage 6.—The final stage lasted six months, and coincided with a hyperchromic and macrocytic anaemia.

In our opinion this hernia was congenital, favoured by the patient's kyphosis, and it progressively dilated through

the diaphragmatic hiatus over a period of 24 years and was responsible for provoking the alternating anaemic syndrome. Diagnosis in these cases is extremely difficult. Often a secondary anaemia due to cancer is suspected, but an x-ray examination reveals the diaphragmatic hernia instead of cancer. This was true with our case as with the cases of Welti and Mahoudeau (1948). The discovery of a diaphragmatic hernia must often lead to surgical intervention. In fact, according to Welti and Mahoudeau, the only effective cure is surgical. In addition, the results of operation prove that the diaphragmatic hernia is the cause of the anaemia, since the latter disappears after operation.

Cause of the Anaemia

To explain the mechanism of this anaemia, Anglo-Saxon authors have invoked repeated haemorrhages. But in our case, and in many others, analysis of the stools has not revealed the least evidence of melaena. Chevallier (1944) suggested that the anaemia might be due to atrophy of the gastric mucosa and gastric achylia. Chevallier could not determine this point in his case, and the same applied to J. A. We tried several times to withdraw gastric juice, but failed to do so because of the extreme nervousness of the patient. Nevertheless, it was possible to withdraw gastric juice from another patient of approximately the same age and with a diaphragmatic hernia. This showed a complete achylia, even after the caffeine test. This patient, in spite of his pronounced emaciation and severe illness, paradoxically does not show any anaemia. His red cell count was 4,200,000 per c.mm., with haemoglobin 100%.

It is the fact that a proportion of cases of diaphragmatic hernia show some degree of anaemia. In most cases this is a microcytic hypochromic anaemia responding as rapidly to iron therapy as to surgical treatment of hernia. Hyperchromic macrocytic anaemia is very rare in these cases. Only one case was mentioned by Cain and his collaborators (1939), with a colour index of 1.50 and a severe hyperchromic and aplastic anaemia. This hyperchromic macrocytic anaemia has nothing in common with Biermer's anaemia. The anisocytosis is not accompanied by megalocytosis but by normoblastosis and macrocytosis, although to-day, according to some authors, megalocytosis and macrocytosis are almost synonymous. This anaemia also presents a distinct resemblance to that of avitaminosis B₁ and B₂ and to certain other primitive or secondary anaemias. In the case described by Cain liver therapy proved ineffective, whereas cure was effected by gastric extracts.

In the macrocytic stage in our patient liver extracts and small direct transfusions of fresh blood over 27 days raised the red cell count from 1,800,000 to 3,430,000 per c.mm. and notably improved the myelogram (see Table II). The improvement was remarkable, both clinically and haematologically.

In the 44 days following admission our patient received 350 ml. of fresh blood (by direct transfusions), 48 g. of iron, and 78 ml. of liver extract (by intramuscular injection). Clearly our patient needed not only anti-anaemic factor but also iron, owing to the presence of alternating microcytic and macrocytic anaemia.

Crisis and Death

After his discharge on March 6, 1946, with 4,180,000 red cells per c.mm., the patient remained well only until March 15.

He then began to feel slight pains in the left hemithorax and in the abdomen, which from time to time was distended. These pains were intermittent, and were relieved by belching. On March 30 the patient complained of

severe pains in the right and left chest. At the same time he presented pallor, anorexia, insomnia, and extreme asthenia.

On March 31 he was much worse and was readmitted. The radiologist's examination showed that the intrathoracic gastric pouch seemed more voluminous. There was also a gross distension of the ascending and transverse colon, displacing the liver to the left. We were obliged to assume that a sudden dilatation of the intrathoracic hernial pouch due to fermentative gases had provoked diaphragmatic spasms at the level of the oesophageal hiatus, which, by exciting the vago-sympathetic system, affected in turn the abdominal segment of the stomach as also the small and large intestines.

These spasms, being repeated, disturbed the function of the digestive tract and respectively, by compression, the circulatory and respiratory functions. It is possible that this spasm contributes (by a mechanism which we have still not explained) to the production of putrefaction and fermentation (given the existence of an obstinate constipation), and so to the dysfunction of the haematopoietic system. In a case of this nature it may be that haemolytic factors discharged by the digestive tract into the circulatory system contribute to the production of this kind of anaemia. In any case, this last stage of severe anaemia was provoked from the second day by an intense hernial crisis simulating a strangulation. Once and only once we noted a positive Meyer's reaction in the faeces after an enema. There had been such obstinate constipation that we were obliged to extract the faeces digitally, and this probably caused small anal erosions which would explain this positive reaction.

We claim that this stage of the disease in our patient furnished indisputable proof that a diaphragmatic hernia can provoke an anaemia so severe that it may lead, with or without strangulation, to a fatal issue. On the eleventh day of this intense crisis J. A. died. We regret to say we could not proceed to necropsy owing to the objections of the relatives.

Conclusion

During the evolution of any form of diaphragmatic hernia different anaemic syndromes can occur. These ordinarily take the form of a microcytic or hypochromic anaemia—rarely the hyperchromic or macrocytic anaemia; and sometimes these syndromes alternate, as in our case.

In any case of anaemia in which the aetiology is not known a complete x-ray examination should not be omitted. This may reveal a diaphragmatic hernia. Conversely, whenever a diaphragmatic hernia is found we should not neglect a complete study of the patient's blood and bone marrow.

Summary

A case of diaphragmatic hernia is described in which a long-standing microcytic anaemia was succeeded by a severe and ultimately fatal macrocytic anaemia.

I am indebted to the Director of the laboratory of the Red Cross Hospital, Dr. S. Papageorgiou, for his help in the detailed study of the blood and the bone marrow.

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The Ministry of Health has issued a circular drawing the attention of hospital management committees and boards of governors to the importance of close liaison with the resettlement services of the Ministry of Labour. During the war the Ministry of Labour set up a staff of disablement resettlement officers to give advice and assistance on the employment of disabled people who have difficulty in getting or keeping a job. In many cases the disability was mental or complicated by mental factors. This service will now be extended as widely as the mental health resources of the National Health Service permit. The Ministry hopes that psychiatrists and D.R.O.s will get into personal touch with each other and co-operate in working the scheme.