

## PALINDROMIC RHEUMATISM\*

BY

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In 1941 and 1944 Hench and Rosenberg reported their observations on an hitherto undescribed recurrent, afebrile form of joint disease to which they applied the term "palindromic rheumatism". "Palindromic" means "recurrent" or "subsiding without coming to a head" and is descriptive of the many sudden and rapidly subsiding attacks which characterize the condition. The most remarkable feature of this rather rare disease is that the affected joints escape anatomical injury in spite of scores or even hundreds of attacks. These authors furnished the criteria by which this disease could be differentiated from other arthropathic disorders, and in particular from rheumatoid arthritis both in its well known and its "episodic" forms. A number of subsequent observers have reported additional cases which conform to the original descriptions. The aetiology remains obscure.

Because of the benign prognosis it is essential that such cases be recognized and so classified. It is hoped that a report of an additional case and a review of the literature will stimulate further observations and bring into relief factors which may help to explain the disease.

### Case Report

A white woman, 42 years of age, was admitted to hospital on June 20, 1947, with complaints of pain, redness, and swelling of the wrist, shoulders, and finger joints. She was a multigrapher and stenographer. The past history revealed only an "allergy to milk", manifested by "blotches on the hips and elsewhere", which disappeared while she was in military service but re-appeared following separation from the Service. Social, family, and menstrual histories and routine psychiatric survey were non-contributory. A review of the systems was negative other than for the presenting complaints. She had been in the Service from August 28, 1943, until April 30, 1946, and had not been overseas.

While in the Service the patient's duties, which involved

frequent lifting of heavy supplies, had to be modified because of pains in the back. She was assigned to a multigraphing machine, the operation of which required striking the ball of a lever-arm with the palm of the hand. Soon after this, in June, 1944, she experienced the first definite attack of pain, redness, and swelling of joints of the right middle and ring fingers. Shortly thereafter both shoulders became red, swollen, and painful. There then elapsed a period of almost three years during which time no attacks occurred.

Before entry to hospital she had been doing stenographic work after many months of no such occupation. In April, 1947, the left shoulder became stiff and painful without redness or swelling. This subsided in a few hours. In May, 1947, a metacarpophalangeal joint developed pain and swelling. This also subsided in about twelve hours. There then followed approximately five attacks of pain, redness, and swelling involving the hands, wrists, and shoulders over a period of one month. No two joints were involved simultaneously. Some relief was obtained from heat and the use of salicylates.

On June 14, 1947, the right shoulder became red, swollen, and painful. The patient consulted the school physician, who suspected an early rheumatoid arthritis and advised hospitalization for observation. She was hospitalized on June 20, 1947, by which time all signs of the attack had disappeared. Thus, there had been approximately eight attacks in two months, subsiding promptly and leaving no residuals. At no time had there been any loss in weight or other constitutional symptoms.

The patient was well developed, well nourished, and moderately obese. The conjunctivae were clear. The pupils were equal, regular, and reacted to light and accommodation. The ocular fundi were normal. The nose was normal. The teeth were in good repair. Small tonsillar tabs were present on both sides but were not infected. The ears were normal. The thyroid was not enlarged and there were no nodules. The trachea was in the midline. The breasts were normal. The lungs were normal. The heart was not enlarged and the rhythm was regular. The first sound at the apex and the second sound at the pulmonic area were split; P 2 was slightly louder than A 2 and there were no murmurs. The blood pressure was 110 systolic and 70 diastolic. The liver and spleen were not palpable. Pelvic and rectal examinations were negative. There were no

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hernias or adenopathy. Neurological examination was normal. The peripheral vascular system was normal. The skin was normal in colour and texture.

The erythrocyte count was 4,760,000 per c.mm. of blood and hemoglobin 94 per cent. The leucocyte count was 8,300 per c.mm., with 72 per cent. neutrophils and 28 per cent. lymphocytes. The bleeding time was 3 minutes and clotting time 7 minutes. The blood uric acid was 3.6 mg. per 100 c.cm. and blood cholesterol 243 mg. per 100 c.cm. with 191 mg. per 100 c.cm. esters (normal for cholesterol in this laboratory is 240 to 360 mg. per 100 c.cm.). Blood iodine level was 5.3 mg. per 100 c.cm. Urinalysis was normal and blood serology negative. Basal metabolic rates on two determinations were respectively plus 12 and minus 4. Agglutination test for *Brucella* was negative. The sedimentation rate was 23 mm. in 1 hour (Cutler—normal up to 10 mm. in 1 hour); subsequent determinations made between and during attacks were respectively 4 mm. and 22 mm. in 1 hour. The electrocardiogram showed a QRS time of 0.11 second in lead II and a left axis shift with a negative deflection in lead III which became positive on deep inspiration (Fig. 1).

Radiographs of the hands, wrists, shoulders, dorso-lumbosacral spine, and pelvis showed no evidence of arthritis or soft tissue changes (Fig. 2, 3, 4, and 5). A chest film showed no pulmonary or cardiac abnormality (Fig. 6). (For illustrations see pp. 156-8.)

Skin tests for food allergy were positive for lamb, clams, codfish, shrimp, rice, and wheat. The allergist attached no significance to these tests, and no relationship was observed between the ingestion of some of the foods and the attacks of arthritis.

The temperature and pulse remained normal. The highest recorded temperature was 99° F. on two occasions.

During hospitalization the patient had at least twelve episodes of pain and stiffness of the fingers, wrists, and shoulders, without redness or swelling. On approximately six occasions she had attacks of pain with redness and swelling which were observed by hospital personnel and other patients but which were not recorded. Attacks were specifically recorded on the following dates.

*June 23, 1947.*—There was pain, redness, and swelling of the proximal interphalangeal joint of the left middle finger. The swelling involved the articular, peri-articular and para-articular tissues with small, interspersed areas of normal colour in the para-articular area. The joint was tender and stiff. The attack subsided in twelve hours without residuals.

*June 24, 1947.*—The patient was awakened at 1.30 a.m. by pain in both shoulders. No redness or swelling was noted. Sedimentation rate was 23 mm. in 1 hour. The pain entirely subsided during the day.

*June 26, 1947.*—There was pain, redness, swelling, and stiffness of the proximal interphalangeal joint of the left index finger, but marked improvement three hours later and complete subsidence in twelve hours. The sedimentation rate taken the following day was 4 mm. in 1 hour.

*July 14, 1947.*—There was pain, redness, and swelling of the metacarpophalangeal joint of the right index

finger, with articular, peri-articular, but no para-articular involvement.

*July 16, 1947.*—There was swelling, pain, and tenderness without redness of the left wrist.

Pyribenzamine was prescribed in doses of 50 mg. four times daily to observe the effect on a possible allergic factor. However, at least three additional attacks were observed during the therapy.

The estimated number of attacks from April to July was thirty-four, of which nine were observed in a period of one month. They followed a consistent pattern and had no relationship to work or weather under our observation. The onset was very rapid and always occurred during the night. Both shoulders were painful on two occasions, and two fingers were red, swollen, and painful on one occasion, but the rest of the attacks were monoarticular. The height of the attack was reached in from one to two hours, at which time the pain was severe, aching in character, and intensified by slight motion. Improvement began as promptly as three hours after the onset, with the majority of attacks subsiding within twelve hours and none lasting longer than twenty-four. The condition always regressed completely and left no subjective or objective residuals. No subcutaneous nodules or involvement of finger pads were observed at any time.

In spite of the number and severity of attacks the patient remained in excellent health and frame of mind. A diagnosis of palindromic rheumatism was made. The patient was assured of an excellent prognosis, advised on the symptomatic relief of the attacks, and discharged from the hospital on July 24, 1947, after thirty-five days of hospitalization.

### Discussion

In their original description of palindromic rheumatism Hench and Rosenberg (1941, 1944) enumerated the following as the principal features of the disease: multiple attacks of pain, redness, and swelling of one or more joints, rapid to sudden in onset, of varying intensity, lasting hours to days, subsiding spontaneously, not attended by constitutional reactions, and showing articular exudation only in occasional instances; absence of abnormality in radiographic and laboratory examinations, and absence of functional and morphologic residues in spite of dozens or even hundreds of attacks over a period of years.

The only available pathological observations were made by Hench and Rosenberg. The changes which they observed consisted of acute inflammation of the synovial membrane and capsule of the joint with the presence of large numbers of polymorphonuclear leucocytes. In some instances the joint cavity contained a fibrino-purulent exudate, and tendon sheaths were sometimes involved in the inflammatory process. All tissues returned to normal after the attack, and cultures of the fluid from the joint and tendovaginal spaces remained

sterile. Hench and Rosenberg differentiated the disease from the angioneural arthroses of Solis-Cohen (1911) and the allergic rheumatism of Kahlmeter (1939).

Since the original report of thirty-four cases there have been only eighteen cases added to the literature. Four were reported in England (Parkes Weber, 1946; Wingfield, 1945; Neligan, 1946), one in France (Forestier, 1946), and thirteen in the U.S.A. (Thompson, 1942; Mazer, 1942; Ferry, 1943; Paul and Logan, 1944; Grego and Harkins, 1944; Cain, 1944; Paul and Carr, 1945; Salomon, 1946; Hopkins and Richmond, 1947). The present case brings the total to fifty-three.

The incidence of the disease as seen at the Mayo Clinic (Hench and Rosenberg, 1944) is approximately one-tenth of 1 per cent. of all cases of articular and muscular diseases. Bach (1947) gives the latest available figures for the incidence of rheumatism and arthritis in the U.S.A., based on the National Health Survey made by the United States Public Health Service in 1937. There were 6,850,000 cases of "rheumatism" yearly. Analysis of the survey disclosed that "arthritis" was the single largest group and attacked 3,000,000 persons, mostly adults, annually. Thus, using one-tenth of 1 per cent. as the estimated incidence, it is likely that there exist 3,000 cases of palindromic rheumatism yearly. It is highly probable that a number of cases are seen at various arthritic centres and additional reports may be anticipated in the future.

The sex ratio in the Mayo Clinic series was 15 males to 19 females. In the subsequent reports there were 12 males and 6 females. Thus, the total reported incidence is 27 males to 25 females. Inclusion of the authors' case brings the number for females to 26. As has been pointed out by Hench and Rosenberg and others the incidence in rheumatoid arthritis is predominantly female and in gouty arthritis predominantly male.

In the Mayo Clinic series the age of the patients varied from 21 to 73 years (average 42 years), the onset of the disease having occurred between the ages of 13 and 68 (average 34.9 years). In the subsequently reported cases the age varied from 4 to 53 years (average 33.1 years),\* the onset of the disease having occurred between the ages of 4 and 49 (average 23.5 years). The difference in average ages between the two groups is appreciable. This is in great part accounted for by Salomon's four patients who were 4, 6, 9, and 10 years old, respectively. The proper inclusion of these cases is doubtful inasmuch as all attacks subsided permanently within a few weeks. When these are omitted from

\* Wingfield failed to report the patient's age; and Weber recorded the current ages but not the ages at the onset of the disease.

the group of subsequently reported cases the average age becomes 41 years and the average age at onset of the disease becomes 29.2 years, and these figures differ very little from those of the Mayo Clinic.

The frequency and duration of the attacks, the number of joints involved, and the length of intervals between attacks in the cases reported differed in no way from the original observations by Hench. The reported frequency varied from two or three attacks a day to one in two months. Monarticular attacks involving a different joint at different times predominated over polyarticular attacks, and the joints most often involved were those of the wrists and hands. The arthritis developed rapidly to suddenly, varied in intensity from mild to severe, and lasted from one hour to two weeks.

Redness was reported in twenty-nine cases (88.5 per cent.) of the original series and in twelve (66.6 per cent.) of the later reports. Swelling occurred in all thirty-four (100 per cent.) of the Mayo cases and in seventeen (94.4 per cent.) of the subsequent cases. Subcutaneous nodules were reported in three of Hench's cases and in the only case in the subsequently reported series in which joint swelling was absent (Parkes Weber's Case 1). The authors' patient presented no nodules. More recently Hench (1948) reported occasional heat and swelling of the finger pads. Swelling in or about the joint is the most consistent objective finding.

Pain was present in all of Hench's patients and in sixteen of the subsequently reported eighteen cases. Grego and Harkins (1944) reported itching and white swelling in their case, which makes the diagnosis of palindromic rheumatism a little uncertain.

In Hench and Rosenberg's series all the patients were afebrile, but in later observations Hench noted that febrile attacks do occur, with elevations of temperature to 100° F. for a few hours to a day or two, but that such occurrences are rare (see Hopkins and Richmond, 1947; also Hench, personal communication). Fever was present in only one of the subsequently reported cases (Grego and Harkins, 1944), but Hench (1948) believes that this case may represent an early, atypical, episodic rheumatoid arthritis because of the marked anaemia, loss of weight, protracted symptoms, and frequency of polyarticular attacks.

In Hench's series there was no anaemia or leucocytosis; the differential count frequently showed a relative lymphocytosis but no eosinophilia. The sedimentation rate was generally found to be slightly elevated during but not between attacks. In reports by subsequent observers a reduction of haemoglobin was noted in three cases, a diminished erythrocyte count in four, leucocytosis in two, and

eosinophilia in none. Sedimentation rates were found to be normal or mildly accelerated. Hench found the blood uric acid, calcium, phosphorus, and phosphatase normal. Blood uric acid determinations performed by other observers in ten cases and blood cholesterol tests in two cases were all within normal limits. Hench reported a moderate elevation of fatty acids and total lipoids, but the significance of these findings has not as yet been determined. Brucella agglutination tests were done in three cases (Wingfield, 1945; Cain, 1944; Hopkins and Richmond, 1947) and were negative. A Brucella skin test performed in a single case (Paul and Logan, 1944) was also negative. Hench and Rosenberg as well as subsequent observers found radiographs of the joints to be consistently negative regardless of the number of attacks suffered by the patients.

No electrocardiographic studies were reported by Hench. Tracings were mentioned in only six of the subsequent cases (Wingfield, 1945; Paul and Logan, 1944; Grego and Harkins, 1944; Cain, 1944; Salomon, 1946; Hopkins and Richmond, 1947), and were reported as normal. In the authors' case the QRS interval was 0.11 second, but this finding is considered to be without significance. Allergy could not be proven as an aetiological factor at the Mayo Clinic. Skin tests in the author's case were positive for certain foods, but the results were not considered significant and attacks were not provoked by some of these foods ingested while the patient was under observation. Parkes Weber's (1946) Case 1 had episodes of Menière's syndrome and attacks of iritis in addition to the joint pains, but no two of these groups of symptoms developed concurrently. Parkes Weber believed that all three manifestations were allergic in origin and that the joint pains probably represented palindromic rheumatism in a mild form. In his second case he pointed out that there were subcutaneous nodules present but no pain or redness of the joints, and considered the condition to be midway between angioneurotic oedema and palindromic rheumatism. In a discussion of twenty-seven cases of recurrent allergic arthritis Vaughan (cited by Hench, 1948) stated that in ten there was a fairly close resemblance to palindromic rheumatism and that allergens might be a principal cause of the latter. Hench, commenting on Vaughan's conclusion, stated that the individual cases were not fully described and that data sufficient for an independent appraisal were lacking.

In none of the cases of the Mayo Clinic series, nor in subsequent reports of cases, were foci of infection believed to be related to the attacks.

Hench found only questionable relationship of trauma and work to the attacks. In only four of

his cases did slight trauma appear to provoke attacks, and in two cases the attacks were occasionally related to overwork. Trauma was discussed in relation to aetiology by Hopkins and Richmond (1947), Mazer (1942), and Paul and Logan (1944); and the authors' case presents a strong indictment of work and trauma except for the initiation of the attacks during the patient's stay in the hospital.

Psychogenic factors were apparently related to attacks in only one case in the Mayo series. In the subsequent reports six of eighteen patients appeared to have some psychogenic basis for their attacks. Mazer's patient became attack-free during one period and had diminished intensity and lessened frequency of attacks during another period after making spiritual and economic adjustments on both occasions. Ferry (1943) believed that there was a definite premenstrual timing in some of his patient's attacks and that the majority of attacks occurred under the stress of worry and emotional strain. This same patient was found to have a functional colitis and occasional tinnitus, vertigo, and nausea before the menses. She showed no reaction to skin tests with allergens.

Paul and Logan observed that their patient's attacks were associated with mild nausea and often followed episodes of anger and nervousness. Cain's patient had a definite tendency to worry, was irritable, and suffered from mild insomnia. Neligan reported that his patient's attacks began after months of great war strain and anxiety over a son who had disappeared in Malaya. Paul and Carr suggested that psychogenic factors may be involved. These observations are too few and too superficial to attach great significance to them. The progress in psychosomatic medicine in recent years has focused attention on the numerous physical manifestations of psychic disability, but much more detailed study will be necessary before a psychogenic basis can be accepted for the causation of palindromic rheumatism.

Hench (1947, 1948) stresses the importance of distinguishing palindromic rheumatism from episodic, atypical rheumatoid arthritis, in both of which there are evanescent attacks and appreciable intervals of freedom from symptoms. Ropes and Bauer (1945) believe that the former is actually a form of atypical rheumatoid arthritis, but Hench considers that the two conditions are unrelated and that they can readily be differentiated. He points out that in palindromic rheumatism the attacks are usually of very short duration, involve widely scattered joints, affect the finger pads at times, frequently include para-arthritis, and are not accompanied by constitutional reactions. On the other hand, episodic rheumatoid arthritis tends to recur in

"favoured" joints, shows higher sedimentation rates during seizures and often persistently elevated rates between seizures, and frequently attacks some particular joint which is thereafter never entirely free from involvement and which ultimately becomes the seat of chronic disease. Moreover, articular biopsies in the episodic cases may reveal changes which are characteristic of rheumatoid arthritis. Inasmuch as there is no evidence that the two conditions have a common aetiology, and inasmuch as Hench's extensive and careful observations have provided a valid basis for clinical differentiation, it is advisable to accept the concept of separate entities. It would indeed be difficult to regard a condition in which joints may survive hundreds of attacks without residual damage as identical with a disease in which a large number of attacks invariably leads to permanent and manifest injury.

#### Summary and Conclusions

A detailed report of a case of palindromic rheumatism is presented. The original cases of Hench and Rosenberg are reviewed and compared with those of subsequent observers. The clinical, laboratory, radiographic, and pathological-anatomical features are reviewed. The possible significance of work, trauma, and psychogenic influences in relation to aetiology are discussed, but definite conclusions must await future investigations. Utmost care should be taken to distinguish between palindromic rheumatism and the episodic form of rheumatoid arthritis, conditions which, under present knowledge, should be considered as separate entities.

#### REFERENCES

- Bach, T. F. (1947). "Arthritis and Related Conditions", F.A. Davis Company, Philadelphia, p. 9.  
 Cain, J. C. (1944). *J. Amer. med. Ass.*, **125**, 1037.  
 Ferry, J. L. (1943). *J. Indiana med. Ass.*, **36**, 348.  
 Forestier, J. (1946). *Rev. Rhum.*, **13**, 78.

- Grego, J. G., and Harkins, H. N. (1944). *J. Mich. med. Soc.*, **43**, 401.  
 Hench, P. S. Personal communication.  
 — (1947). *Arizona Med.*, **4**, 62.  
 — (1948). *Ann. intern. Med.*, **28**, 317.  
 —, and Rosenberg, E. F. (1941). *Proc. Mayo Clin.*, **16**, 808.  
 — (1944). *Arch. intern. Med.*, **73**, 293.  
 Hopkins, J. J., and Richmond, J. B. (1947). *Ann. intern. Med.*, **26**, 454.  
 Kahlmeter, G. (1939). *Acta med. scand.*, **102**, 434.  
 Mazer, M. (1942). *J. Amer. med. Ass.*, **120**, 364.  
 Neligan, A. R. (1946). *Brit. med. J.*, **1**, 205.  
 Paul, W. D., and Carr, T. L. (1945). *Arch. phys. Med.*, **26**, 687.  
 —, and Logan, W. P. (1944). *J. Iowa med. Soc.*, **34**, 101.  
 Ropes, M. W., and Bauer, W. (1945). *New Engl. J. Med.*, **233**, 592, 618.  
 Salomon, M. I. (1946). *N.Y. St. J. Med.*, **46**, 622.  
 Solis-Cohen, S. (1911). *Tr. Coll. Physicians, Philadelphia* **33**, 309.  
 Thompson, J. L. (1942). *Med. Ann. Distr. Columbia*, **11**, 189.  
 Weber, F. Parkes (1946). *Lancet*, **2**, 931.  
 Wingfield, A. (1945). *Brit. med. J.*, **2**, 157.

(See also abstracts, p. 191 of this issue.)

#### Rhumatisme Palindromique

##### RÉSUMÉ ET CONCLUSIONS

Les auteurs présentent une observation détaillée d'un cas de rhumatisme palindromique. Ils analysent les observations originales de Hench et Rosenberg et les comparent aux observations ultérieures. Ils passent en revue les caractères cliniques, biologiques, radiographiques, et anatomopathologiques. Ils discutent la signification étiologique possible de l'effort, du traumatisme, et des influences psychogènes, mais considèrent qu'il est indispensable de pousser plus avant les recherches avant de pouvoir formuler des conclusions définitives. Il est nécessaire d'établir une distinction très nette entre le rhumatisme palindromique et la forme épisodique de l'arthrite rhumatismale qui, dans l'état actuel des connaissances, doivent être considérées comme tout-à-fait distinctes.