The Journal of the American Medical Association

Published Under the Auspices of the Board of Trustees

VOL. 140, No. 9 — CHICAGO, ILLINOIS — JULY 2, 1949

ARTHRITIS

Comments on Differential Diagnosis and New Developments in Therapy

EDWARD F. ROSENBERG, M.D., Ph.D.
Chicago

Incidence of rheumatic diseases in this country is so high that only a small proportion of cases come to the attention of specialists. In most instances responsibility for diagnosis and treatment remains in the hands of family physicians. It is of utmost importance, therefore, for general practitioners to have an understanding of these diseases sufficient to aid in preventing the dreaded physical and mental crippling which often result in poorly handled or neglected cases.

In the past a cause of much confusion has been a complicated nomenclature and mysterious classifications employed for these diseases. Causes of the most important chronic rheumatic diseases still remain unknown, and consequently their designations and classification cannot be simplified. As a result of this confusion, roentgenologists report their observations in terms descriptive of altered appearances, but terms which they employ are often different from those which serve the practitioner in his daily work. Pathologists often report observations in terms which have a morphologic significance, describing alterations in gross and microscopic appearances of tissues, but these terms also frequently differ from those familiar to clinicians. European writers commonly discuss these diseases using designations which differ from those used in America.

To some extent, this confusion will probably continue until research has disclosed presently unknown causes for rheumatic diseases. Until that time, however, it would be very useful if uniform terms could be employed by all who deal with patients with rheumatic disease.

A committee on classification of the American Rheumatism Association has been laboring for a decade with this problem and, although still dissatisfied with results of its work, has recently prepared a classification recommended for inclusion in the "Standard Nomenclature of Disease" (outline). Only a small proportion of the hundred or more conditions which are included among "rheumatic" diseases are mentioned. However, as little can be gained by subclassification of many unknowns, subclassifications have been omitted. Many rare diseases are not mentioned. In its present form, the list provides usable terms for a majority of cases encountered during usual clinical work.

From the Department of Medicine, Michael Reese Hospital.
Read at the Interim Session of the American Medical Association, St. Louis, Nov. 30, 1948.

The following material reviews briefly some innovations in diagnostic and therapeutic aspects of several important rheumatic diseases.

SPECIFIC ARTHRITIS

From a numerical point of view, specific forms of arthritis constitute only a small proportion of "run of the mill" cases of arthritis. Most commonly encountered are gonorrheal arthritis, tuberculous arthritis and arthritis associated with streptococcic and staphylococcic infections. Arthritis of syphilis, pneumococcic infections, meningitis, brucellosis and typhoid are rare today. Articular disorders associated with coccidioidomycosis, although not often encountered, appear to be spreading in America.

Gonorrheal Arthritis.—Among the specific forms of arthritis, instances resulting from gonorrheal infection continue to hold an important place. The incidence of gonorrheal arthritis is decreasing significantly since discovery of sulfonamide drugs and penicillin but is still notable, and this must be kept in mind when one encounters acute arthritis in adults.

The laboratory may play only a supportive role in establishing this diagnosis in many instances. Prompt recognition more often depends on knowledge of the life history of gonorrheal arthritis than on laboratory reports. If this disease is not recognized promptly and if allowed to progress through its "normal" evolution, it ordinarily takes the form of acute polyarthritis. Less frequently arthralgias occur without actual synovial cartilaginous or osseous invasion. Affected patients are usually febrile at the onset, and the disease is often ushered in with a chill. The articular phenomena are generally migratory, as in rheumatic fever.

As a rule, a physician must be satisfied with a presumptive diagnosis of gonorrheal arthritis, a diagnosis based on analysis of behavior of the articular disease together with identification of Neisseria in genital secretions. Certification of the diagnosis in every instance by identification of Neisseria in articular exudates is impossible, since infection of intra-articular exudates occurs in only a fourth to a third of the cases. Neisseria are evidently excluded from synovial fluid in consequence of a barrier action of synovial lining membranes.

If a diagnosis of gonorrheal arthritis has been correctly made, the disease should be cured promptly by adequate doses of penicillin. Supposed failures of penicillin therapy in gonorrheal arthritis often reflect merely a lack of appreciation of the effectiveness of gonorrheal infection in stirring up latent rheumatoid arthritis or provoking its onset. "Penicillin-resistant gonorrheal arthritis" often proves to be rheumatoid arthritis provoked to activity by the gonorrhea. Not even millions of units of penicillin will significantly

hydrogen), accelerated in the magnetic field of the cyclotron, strike the target of the machine.

Until recently, on the basis of some experiments with mice, the assumption was granted that neutrons were no more than five times as effective as roentgen rays for biologic purposes. Recent work[4] and the sad experience of these young physicists point to the probability that a grave underestimate was made and that for certain organ systems, such as the lens and the gonads, neutrons may have four to eight times the effectiveness originally suspected.

Unfortunately for the physicists, protection procedures and exposure limits were based on the earlier assumption. Once again, as in the past with roentgen rays and radium, people have unwittingly been injured before an adequate understanding of a hazardous agent was had. Furthermore, even now dosimetric methods for neutrons are unsatisfactory.

An understanding of the mechanism of interaction of radiation with the components of biologic matter becomes important. In the case of roentgen rays the energy is first given to electrons, which move at high speed through the tissue. These electrons in turn dissipate their energy by collision with biologic matter, causing chemical alterations. However, the damage to any one cell by one electron is relatively small.

In the case of neutrons the energy is principally dissipated by collision with the hydrogenous component of tissue. The high speed protons thus set in motion liberate a large amount of energy per unit length of . Thus the passage of one high energy proton through a cell may produce sufficient destruction to injure it permanently.

There is evidence that roentgen rays are relatively effective only against dividing cells, while neutrons may injure the cell at any phase. Thus the biologic effects induced by neutrons may be both quantitatively and qualitatively different from the effects of the roentgen y. The urgency for research in this relatively unexplored field is evident.

In a broader sense, the experience of these young physicists points to the tremendous responsibility devolving on those—both the physicist-engineers and agencies supporting their work—who are concerned in exploring the new frontiers of the physical . It is not enough to dismiss the responsibility with the mere warning that a danger may exist or extrapolate, as was done with the neutron, from inadequate analogies. The biologic implications of the unknowns should be subjected to investigation parallel with their physical implications and with equal r.

4. ..., R. S.: Neutron Therapy and Specific Ionization, Am. J. . 59: 771-785 (June) 1948. Evans, T. C.: The Effects of ...ily Doses of Fast Neutrons on Mice, Radiology 50: 811-834 1948.

ASBESTOSIS AND CANCER OF THE LUNG

Until recently the coexistence of asbestosis and cancer of the lung was considered by many investigators a coincidence. Since 1935, 23 such cases were recorded by American, English and German physicians. Wedler[1] noted 14 cases of asbestosis cancer in a series of 92 necropsies on patients with asbestosis, or about 15 per cent of cancer of the lung in persons who died from this industrial disease. The exposure time ranged from 3 to 27 years (average 15 years). The ages in 17 cases were 35 to 75 years (average 50 years). Until now the question of a causal relation between asbestosis and cancer of the lung has been an open one. The recently published Annual Report of the Chief Inspector of Factories in England for 1947 provides additional data on the actual existence of such interrelations.[2] During 23 years, 1924 to 1946 inclusive, 235 deaths, either caused by asbestosis or in which asbestosis had been established at necropsy, were reported to the Chief Inspector. Cancer of the lungs or pleura was found in 31 of these cases (13.2 per cent). Of the 128 male deaths in this group 22 (17.2 per cent) were complicated by cancer of the lung, while of the 107 female deaths 9 (8.4 per cent) were similarly affected. The mean age at death from asbestosis complicated by cancer of the lung was 52.1 years. A causal relation between asbestosis and cancer of the lung is supported by the following observations: The incidence rate of cancer of the lung in this group is excessive, since the normal death rate from cancer of the lung among adults examined at necropsy at present is about 1 per cent of all necropsies. Moreover, there is a distinct shift in the sex distribution of cancer of the lung in the series of asbestosis cancers reported from England. The male-female sex ratio is 2.4:1, while it is 5:1 for cancers of the lung in general. This shift indicates that an environmental and evidently occupational carcinogen was active in the asbestosis group, tending to equalize the incidence rate of cancer of the lung for both sexes. Recent experimental observations support this interpretation of clinical evidence. Nordmann and Sorge[3] exposed mice to inhalation of asbestos dust and found that in 20 per cent of the surviving animals there developed squamous cell cancer originating from the bronchial mucosa, while other types of epithelial proliferation were present in 42 to 57 per cent of these animals, in addition to diffuse or nodular fibrosis of the lung. The histologic character of the cancers (squamous cell cancer instead of adenocarcinoma seen in the spontaneous cancer of the lung of mice) and the histogenetic derivation of the tumors (bronchial mucosa instead of alveolar epithelium of the spontaneous type) indicate that a specific factor of

1. Wedler, H. W.: Asbestose un Lungenkrebs, Deutsche med. Wchnschr. 69: 575, 1943.
2. Extract from Annual Report of the Chief Inspector of Factories for the Year 1947: Medical Section, London, His Majesty's Stationery Office, 1947, pp. 15-17.
3. Nordmann, M., and Sorge, A.: Lungenkrebs durch Asbeststaub im Tierversuch, Ztschr. f. Krebsforsch. 51: 168, 1941.

exogenous origin, represented by the inhaled asbestos dust, was responsible for the bronchial cancers observed.

Since some 20,000 workers are employed in the asbestos-producing industries of this country and Canada and many additional thousands in various asbestos-consuming industries, increased attention to this probable occupational hazard of cancer of the lung by the medical profession is desirable. Cytologic examinations of the bronchial secretion may well be included in the periodic examination of workers exposed to asbestos dust whenever clinical or roentgenologic evidence indicates the possible existence of a pulmonary cancer. As the available evidence shows that the occurrence of cancer of the lung is related to pulmonary asbestosis and is not merely a possible sequela of exposure to asbestos dust, in all fatal cases of asbestosis there should be postmortem examination with detailed histologic analysis. The anatomic lesions produced by asbestos dust in the lungs make difficult at times distinction by clinical and roentgenologic diagnostic methods between changes of pneumoconiotic nature and those that might indicate a cancerous growth.

Current Comment

NODULAR PANNICULITIS—WEBER-CHRISTIAN DISEASE

Weber-Christian's disease, or nonsuppurative nodular panniculitis, is characterized by recurring episodes of fever and the development of numerous painful and slightly tender subcutaneous nodules. In only 3 of 33 recorded cases was death apparently due to the disease. In the case reported by Kritzler,[1] in which necropsy was done, the nodular lesions were limited to the subcutaneous fat. However, fat emboli were found in the lungs and there was widespread acute necrosis of the liver and spleen. In the case examined at necropsy by Spain and Foley,[2] necrotic areas were found not only in the subcutaneous fat but in the mesenteric, omental and pretracheal fat. Fat emboli were not found in the lungs, nor were areas of necrosis observed in the liver or spleen. However, foci of fat necrosis were present in the region of the pancreas. A third case investigated at necropsy was that of Mostofi and Engleman,[3] in which nonsuppurative panniculitis involved the skin, the epicardium and the peripancreatic, periadrenal, perirenal and mesenteric tissues. The nodules in the fat are of variable appearance. The earliest lesions consist of small accumulations of fat-laden macrophages. Later, there are somewhat larger lesions that present small areas of central necrosis in the immediate vicinity of which are lymphocytes, polynuclear leukocytes and fat-laden macrophages. In still older nodules, the necrotic material is decreased or absent and the lesions are partially or completely replaced by fibrous tissue. In Spain and Foley's patient, who was an alcohol addict, there were changes indicating a late stage of chronic glomerulonephritis, and death occurred with the symptoms of uremia. Such changes in the kidney are perhaps best interpreted as accidental necropsy findings without direct relationship to the syndrome under discussion. A disease in rabbits apparently analogous to that of nonsuppurative panniculitis in man has been described by Duran-Reynals [4] and others. The cause of Weber-Christian's disease is unknown.

1. Kritzler, R.: A Case of Weber-Christian's Disease, Proc. New York Path. Soc., 1940-1941, p. 47.
2. Spain, D. M., and Foley, J. M.: Non-Suppurative Panniculitis, Am. J. Path. 20: 783, 1944.
3. Mostofi, F. K., and Engelman, E.: Fatal Relapsing Febrile Non-Suppurative Panniculitis, Arch. Path. 43: 417 (April) 1947.
4. Duran-Reynals, F.: A Necrotizing Disease in Rabbits Affecting Fatty and Muscular Tissues, Yale J. Biol. & Med. 15: 531, 1943.

CRISIS IN SCIENTIFIC RESEARCH

Further evidence that the medical profession must coordinate and intensify its protection of the right to carry on experimental studies on animals in laboratories is provided in a report on this type of legislation in the District of Columbia. Representatives from twenty-six national health and science groups, local hospitals, lay groups and governmental agencies have united behind Senate bill 1703, providing for laboratory use of the 7,000 to 10,000 unclaimed dogs now destroyed each year in the District pound. The usual frenzied distortion and political pressure by antivivisectionists have placed the bill in jeopardy, according to the National Society for Medical Research. The society quotes Dr. A. C. Ivy, its secretary-treasurer, to the effect that members of the special Senate committee to which the bill was referred are personally in favor of it but the bill probably will not be reported out. Dr. Ivy has issued an appeal that interested persons write letters of endorsement to Senator J. Howard McGrath, of Rhode Island, who introduced the measure, and Senator Margaret Chase Smith, of Maine, chairman of the subcommittee. Some such concerted action is necessary at state as well as national levels to beat back efforts of a small, misguided group to obstruct the advancement of science.

FIRST TELEVISION NETWORK HEALTH SHOW

The first health education program ever presented on a television network was viewed and heard from the NBC-TV studios in Radio City, New York, June 16. Transmitted as far west as Chicago, the program, titled "Your Good Health and the Mighty Atom," was arranged through the Bureau of Health Education of the American Medical Association and produced under the supervision of Mrs. Harriet Hester, radio coordinator for the Bureau. The program dealt with the use of radioisotopes in medicine, particularly radioactive iodine. Dr. Paul C. Aebersold, Chief, Radio-isotopes Division, United States Atomic Energy Commission, Oak Ridge, Tenn., was interviewed by an NBC announcer on the principles of radioactivity. With a Geiger counter specially amplified, Dr. Aebersold demonstrated first how radioactivity can be traced and atoms identified. Later, with a patient furnished by Dr. Sidney C. Werner, Columbia College of Physicians and Surgeons and Presbyterian Hospital, he demonstrated concentration of radioactive iodine in the thyroid.