A MEDICAL FISH STORY*

[The claim by Mr. R. F. Shropshire to cure cataract with injections of fish-lens protein has drawn some attention in Great Britain, which has been fostered by misleading reports in the lay press. The following extracts reprinted from the Journal of the American Medical Association may interest our readers. Ed.]

EDITORIAL

A report of the Committee on Ophthalmology of the National Research Council, Division of Medical Sciences, on the fish-lens protein treatment for cataract appears elsewhere in this issue. As is mentioned in the report, an investigation was made because of widespread public interest in what appeared to be an escape from necessary surgery in the treatment of cataract. Such interest resulted from newspaper stories, which, unfortunately, aroused false hopes in many persons. These stories were based on a report which appeared in Science, a reputable scientific weekly, in September, 1952 (Shropshire, Ginsberg, and Jacobi, 1952). Since that time two or three physicians in the New York metropolitan area have treated many patients. The Journal of the American Medical Association has published an earlier warning (Posner, 1953) of possible untoward results of this injection therapy.

The principal author of the Science report is, according to most recent authentic information, in prison in Florida, awaiting a hearing on the matter of revocation of his parole for alleged violation of the terms thereof. Presumably, these alleged infractions did not involve the matter of participation in the treatment of persons with cataracts with what may well have been contaminated fish-lens protein material. Such activity would, however, appear to be the most serious aspect to be considered. His medical confreres should consider seriously these effects.

MR. R. R. SHROPSHIRE'S NONSURGICAL TREATMENT OF CATARACT

Report by the Committee on Ophthalmology of the Division of Medical Sciences of the National Research Council of the U.S.A.

On September 12, 1952, there appeared in Science an article reporting beneficial effects from the nonsurgical treatment of cataract with injections of fish-lens protein (Shropshire, Ginsberg, and Jacobi, 1952). Because of the widespread public interest that it aroused and because of the inadequacy of the evidence presented, the Council of the American Academy of Ophthalmology and Otalaryngology petitioned the National Research Council to investigate the authors' claims. An investigation was made by the National Research Council Committee on Ophthalmology, whose findings and recommendation form the basis for this report.

The hypothesis that lens antigens might be useful in the treatment of cataract is not new. Römer (1908) reported success in treating cortical cataract with tablets of mammalian lens protein. Davis (1923, 1925), in the U.S.A., attempted active immunization with bovine lens material. His favourable reports led to a number of other investigations (Beren and others, 1927; Ellis, 1928; Kirby

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and Giles, 1930; Biffis and Quaglio, 1933; Selinger, 1935). These, however, failed to confirm his findings, and the proposed therapy lapsed into obscurity.

The use of fish-lens protein was attempted by Lewis (1933), with whom its present proponent, Mr. R. F. Shropshire, was then associated. Again favourable results were claimed, but the ophthalmological details presented were unconvincing, and the report aroused little interest on the part of the profession.

Mr. Shropshire's interest, however, continued, and in 1937 he published two papers on the subject (Shropshire, 1937 a,b). In addition to reviewing Lewis's work, he cited Hektoen and Schulhof (1924) as evidence that the lens proteins of fish are immunologically different from those of mammals. In fact, these authors had specifically stated that fish lens contains antigens that interact with mammalian lens, in addition to others that are species specific. Shropshire also reported chemical differences between piscine and mammalian lenses; being able to account for only a part of the sulphur content of fish lenses, he postulated the existence of a previously undescribed sulphurbearing amino acid of therapeutic value. Unfortunately his analytical methods were not suitable for the detection of either cystine or methionine; the latter alone accounts for about half of the sulphur present, and cysteine and cystine almost completely account for the rest (Dische and Zil, 1951).

The chemical argument is extended in the recent paper of Shropshire and others (1952), which reports that differences were found between the electrophoretic and ultracentrifugal patterns of mammalian and piscine lens protein. According to the detailed report furnished to the Committee on Ophthalmology, these studies were performed by Dr. Kurt G. Stern with human and piscine lenses. Since the patterns of bovine and human lens proteins are also very different from one another, the observations of Stern do not support Shropshire's claim that fish lens has distinctive qualities of possible therapeutic value. In any case no deductions as to anti-genic behaviour can be made legitimately from physicochemical measurements of the type described.

The article in Science is chiefly notable for its reports of the successful treatment of cataract in rats and humans with injections of fish-lens protein. On investigation, it developed that cataracts had been induced in the rats by feeding them galactose. Since such cataracts appear superficially to clear when the administration of galactose is stopped regardless of treatment, these observations do not provide convincing evidence in favour of the fish-lens therapy.

The most impressive claim was that of improved visual acuity in the patients treated by Shropshire's co-authors, Drs. Ginsberg and Jacobi. The article referred to an initial group of fourteen patients, described in general terms, and an additional twelve whose acuities before and after treatment were given in a Table. In order to provide an independent evaluation of these claims, arrangements were made for a subcommittee of the Committee on Ophthalmology to examine a group of patients selected by the proponents of the therapy. Eleven patients were examined, all of whom were enthusiastic about the benefits that they had obtained. The findings were compared with those recorded when the treatment was begun. In six patients the visual acuity was less than before treatment, and the cataracts appeared to have progressed steadily in the usual fashion. Two others showed the little or no change. The remaining three showed slight or questionable improvement; of these two had vitreous opacities, and their subjective reports clearly supported the conclusion that the improvement had been due to shifting these opacities out of the
line of vision. In only one patient did the data appear to suggest an actual improvement; since, however, neither Shropshire nor his collaborators were ophthalmologists their original estimate in this case may have been in error.

The subjective improvement, in most cases, was in near vision; the obvious explanation of this is the development of functional myopia in a progressing cataract. Two patients, as mentioned, were pleased because their vitreous opacities seldom bothered them, and another because his sensitivity to light and multiple vision when looking at lights had disappeared. With the possible exception of one patient, therefore, there was no evidence that the normal course of the cataracts had been affected by the treatment.

A later report received by the Committee on Ophthalmology described the results of treatment administered independently by an ophthalmologist on the staff of a recognized medical school, using fish-lens protein supplied by Mr. Shropshire. The cases were unselected, and included fourteen eyes with cataracts in nine patients. No objective change in the cataracts could be discovered; in four cases vision as measured by the test chart was slightly improved, while in two it was worse. Seven patients reported subjective improvement which the physician considered to be psychological; one felt that she was worse.

Further evidence indicates that treatment with foreign lens proteins is not merely ineffective but also hazardous to the patient. Posner (1953) called attention to serious reactions, leading in one case to total blindness, in patients sensitized to their own lens protein by injections of both beef and fish-lens extracts; he warned ophthalmologists of the dangers that may arise when such patients come to operation. This was corroborated by a member of the Committee, who referred to the unfortunate post-operative histories of patients treated unsuccessfully with beef-lens protein. It should further be noted that of twelve sample bottles of the fish-lens preparation furnished to the Ocular Research Unit of the Walter Reed Army Hospital by the Cataract Institute, ten were contaminated with pathogenic organisms.

The Committee also inquired into the backgrounds and qualifications of the proponents, to determine how much credence might be given to their reports. No evidence was found that Mr. Shropshire had had any formal scientific training and claims that he was a graduate physician and had conducted research in ophthalmological chemistry at two universities were not substantiated by the institutions concerned. He has, however, tried his hand at a variety of scientific undertakings. As noted above, he was an assistant to the late Dr. F. Park Lewis, an ophthalmologist, about 1933, at which time he published a paper on the eye of the trout. Subsequent activities included two appointments as a laboratory technician in pathology, from which he was dismissed for lack of competence and for unreliability due to drug addiction, and brief experience in research in underwater sound. In 1944 he posed as a pathologist in Florida, and, after pleading guilty on three counts of forging prescriptions for narcotics, was sentenced to serve five years on the first count and five on the second, the sentences to run consecutively. About one year later he was paroled. This parole was revoked in 1948; excessive use of alcoholic drinks, suspected use of narcotic drugs, and issuing of bad cheques were given as the reasons. It was after a second parole in 1949 that he engaged, with private sponsorship, in his recent studies on experimental cataract in the rat.

In a chance meeting with Shropshire, a New York business man, Mr. Saul Gaynes
became interested in the financial possibilities of the fish-lens preparation. Clinical trials were begun by his brother, Dr. Ginsberg, a general practitioner, and Dr. Jacobi, an internist. Encouraged by the early reports, Gaynes and Shropshire incorporated the Kortright Industries to manufacture and sell the preparation. With three others they also established the Cataract Institute, as a nonprofit corporation to conduct research on the pathogenesis and therapy of cataract, and Shropshire was given a five year contract as consultant. A third physician later joined the group, Dr. Jacob Weynert, an orthopaedist. For a time patients were examined by opticians in the employ of a New York optical company.

In summary, the Committee found nothing in the theoretical background or in the experimental and clinical results of this therapy to recommend it. It did, however, find evidence that the treatment might seriously interfere with the subsequent surgical removal of the cataracts that it had failed to cure. In view of these facts, the Committee adopted the following statement of its conclusions:

Because of the total lack of evidence that the lens antigen treatment of cataract described by Mr. R. F. Shropshire (Science, September 12, 1952) has any efficacy, because adequate evidence is now available to the Committee that it is, in fact, without demonstrable efficacy, and because treatments of this type have been thoroughly investigated in the past and proved not only invalid but potentially dangerous to the patient, this Committee does not recommend further investigation of this treatment by any agency.

REFERENCES

Madrid.