COMMENT

In reviewing the malacic diseases of bone from the standpoint of the roentgenologist, one cannot help but be impressed with the variety of roentgenographic changes that are presented when such a fundamental metabolic change as demineralization is provoked by various causes. Histologic studies offer a reasonable explanation for these variations and, in my opinion, a carefully correlated study of the microscopic changes and roentgenograms in the conditions noted in this paper will do much to further our knowledge of malacic diseases of bone, and of osteoporosis in general.

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REFERENCES

1. Mandl, F.: Therapeutischen Versuch bei einem Falles von Osteitis fibrosa generalisata mittels Extirpation eines Epithelkörperchentumors, Zentralbl. f. Chir., 53:260-264, 1926.

2. Knaggs, R. L.: The Inflammatory and Toxic Diseases of Bone, Bristol, England. John Wright & Sons, 1926, 416 pp.

3. Loöser, E.: Ueber Spätrachitis und osteomalacie klinische roentgenologische und pathologisch-anatomische Untersuchungen, Deutsche Ztschr. f. Chir., 152: 210-357 (Feb.), 1920.

4. Parsons, L. G.: The Bone Changes Occurring in Renal Coeliac Infantilism, and Their Relationship to Rickets. I. Renal Rickets, Arch. Dis. Child., 2:1-25, 1927; II. Coeliac Rickets, Arch. Dis. Child., 2:198-211, 1927.

5. Teall, C. G.: A Radiological Study of Bone Changes in Renal Infantilism, Brit. J. Radiol., 1:49-58 (Jan.), 1928.

6. Kummer, R. H.: Quoted by Hunter, Donald: Critical Review—The Metabolism of Calcium and Phosphorus and the Parathyroids in Health and Disease. Quart. J. Med., 24:394-446 (April), 1931.

7. Plummer, W. A., and Dunlap, H. F.: Cases Showing Osteoporosis Due to Decalcification in Exophthalmic Goiter, Proc. Staff Meet., Mayo Clin., 3:119-121 (April), 1928.

8. Hunter, Donald: The Significance to Clinical Medicine of Studies in Calcium and Phosphorus Metabolism, Lancet, 1:897-904 (April 26); 947-957 (May 3); 999-1008 (May 10), 1930.

9. Morrison, L. B., and Bogan, I. K.: Bone Development in Diabetic Children—A Roentgen Study, Am. J. M. Sc., 174:313-319 (Sept.), 1927.

10. Golden, Ross, and Abbott, Hodson: The Relation of the Thyroid, the Adrenals and the Islands of Langerhans to Malacic Diseases of Bone, Am. J. Roentgenol., 30:641-648 (Nov.), 1933.

11. Von Mikulicz: Discussion. Zentralbl. f. Chir., 2:1323-1324 (Nov. 19), 1904.

12. Hunter, Donald, and Turnbull, H. M.: Hyperparathyroidism — Generalized Osteitis Fibrosa, with Observations Upon the Bones, the Parathyroid Tumors, and Normal Parathyroid Glands. Brit. J. Surg., 19:203-284 (Oct.), 1931.

13. Rowland, R. S.: Schüller-Christian Syndrome, Am. J. Roentgenol., 30:649-656 (Nov.), 1933.

14. Schinz, H. R., Baensch, W., and Friedl, E.: Lehrbuch der Röntgendiagnostik mit besonderer Berücksichtigung der Chirurgie. Leipzig, Georg Thieme, 1932, 704 pp.

15. Karshner, R. G.: Roentgen Studies of the Bones in Certain Diseases of the Blood and Hematopoietic System, Am. J. Roentgenol., 20:433-439 (Nov.), 1928.

REACTION FOLLOWING BLOOD TRANSFUSION*

REPORT OF AN UNUSUAL CASE

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AND
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DISCUSSION *by Roy W. Hammack, M. D., Los Angeles; LeRoy Brooks, M. D., San Francisco.*

CASE HISTORY (By J. O. Haman). Mrs. R., thirty-two, was first seen in the Prenatal Clinic in November, 1932, five months pregnant.

The family history and past history were negative, except for typhoid and pneumonia. Catamenia began at seventeen, was always irregular, painful and profuse.

There had been four previous pregnancies, the first in 1927. This progressed normally until one week before labor was due, when headache, diarrhea, vomiting, edema, high blood pressure and albuminuria developed. She was taken to a hospital semi-comatose and in labor; the pregnancy was terminated with high forceps. She had several convulsions after delivery, which were treated by venesection. Later she was given a blood transfusion, her husband being the donor. A mild reaction, consisting of chills and fever, developed immediately, but soon subsided. Blood pressure and urine were normal after the puerperium.

The second and third pregnancies (1928 and 1930) aborted spontaneously at four months, each time with toxic symptoms developing prior to the miscarriage. The fourth pregnancy (1931) was complicated by hypertension and albuminuria throughout. Three weeks before delivery the patient developed oliguria and was under hospital observation for twenty-two days, when she began hemorrhaging. Labor was induced by a Voorhees bag, and a podalic version and extraction were performed. Urine and blood pressure were again normal after this pregnancy.

The present pregnancy was normal throughout, except for a blood pressure which remained at approximately 145/85. Slight traces of albumin were noticed at intervals. Hemoglobin was 65 per cent Sahli. Other laboratory tests and physical examination were negative, except for marked laceration and erosion of the cervix. Twins were diagnosed at the eighth month. Treatment during pregnancy consisted of iron in the form of Blaud's pills, and a low-protein, salt-free diet.

The patient was delivered on March 28, 1933, after a labor of six and three-fourths hours. Fraternal twins were born, each weighing six and one-half pounds. The first was a normal, vertex presentation; the second was in a transverse position, and a podalic version and extraction were performed. The hemoglobin on entry was 62 per cent Sahli, the urine showed nothing abnormal, and the blood pressure was 146/88. As the patient appeared very pale, and her hemoglobin was only 50 per cent Sahli, a transfusion of 400 cubic centimeters citrated blood was given on the third day after delivery, her husband again being the donor. The laboratory report showed both donor and recipient to be Type II (Moss), with the donor's cells showing slight rouleaux formation with the patient's serum. The donor was considered to be suitable if the blood were given slowly. The blood was injected into the median basilic vein at a rate of 7 cubic centimeters per minute, the procedure consuming fifty-five minutes.

Toward the end of the transfusion the patient suffered a severe chill which lasted twenty minutes. The temperature rose abruptly to 40.2 degrees centigrade, dropped to 36.8 degrees centigrade within twenty-four

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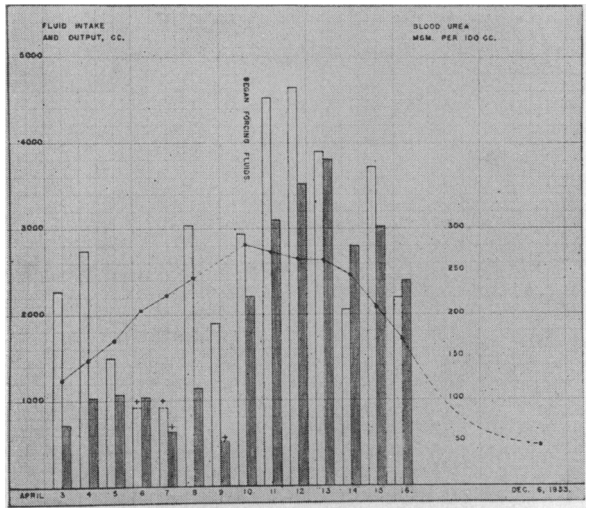

Chart 1.—Showing the daily fluid intake and output, and daily blood urea in milligrams per 100 cubic centimeters.

hours, and remained subnormal throughout her hospital stay.

No other symptoms were noticed for twenty hours after transfusion, at which time the patient was jaundiced and the centrifuged urine specimen showed the field completely full of renal failure casts. Five hundred cubic centimeters of 10 per cent glucose were immediately given intravenously. The urinary output for the next three days averaged about 500 cubic centimeters per day, in spite of a daily fluid intake of over 2,000 cubic centimeters. The blood urea rose daily from 123 to 282 on the eighth day, following which it gradually declined.

The hemoglobin was 42 per cent Sahli two days post-transfusion. Urine examinations showed light clouds of albumin and occasional granular casts for two weeks.

Treatment consisted of daily intravenous injections, saline hypodermoclyses, proctoclysis and iron in the form of iron and ammonium citrate (4 to 6 grams daily).

After a stormy course, the patient gradually returned to normal. On dismissal to a convalescent home, the blood urea was 171, hemoglobin 46 per cent Sahli, and the urine negative except for a very faint trace of albumin.

Eight months later, December 1933, the patient appeared in good health. Physical examination was negative, blood pressure 130/85, hemoglobin 90 per cent Sahli, blood urea 48, and the urine negative.

COMMENT

Study of the Blood of the Donor and the Patient (by C. E. Smith).—As has been stated, the original test of the blood showed no evidence of incompatibility, but after the reaction of the patient, the tests were repeated. The investigation of the recipient's and the donor's blood proceeded in three stages: first, rechecking the type of the donor; second, rechecking the type of the recipient; third, retesting their cross-matching. This last section was expanded to include matching the recipient's serum taken before, and the recipient's serum taken after transfusion, with various types of cells. All tests were performed in triplicate, one set being placed in the ice-box, one set kept at room temperature, one set incubated at 37 degrees centigrade.

First, the donor's type was rechecked. His cells were matched with Type II serum and were entirely satisfactory. They were completely agglutinated with Type III serum. The donor's serum was compatible when checked with Type II cells, but incompatible with Type III cells. Therefore, the donor is unquestionably a Type II.

Second, the recipient's type was retested. Her cells showed no agglutination or rouleaux with Type II serum, while they were completely agglutinated with Type III serum. Her serum agglutinated Type III cells, but showed only slight rouleaux formation with stock Type II cells. A more complete comparison of the recipient's serum compatibility is found in the third part of this study, but she also is clearly a Type II.

The third step was the cross-matching of the recipient's serum with the donor's cells, and simultaneously with stock Type II and Type III

TABLE 1.—*Matching of Recipient's Serum Taken Before Transfusion with Various Cells at Varying Times and Temperatures*

Cells Used for the Cross Agglutination	Ice Box Temperature		Room Temperature		Incubator Temperature 37 Degrees		
	24 Hours	72 Hours	24 Hours	72 Hours	2 Hours	24 Hours	72 Hours
Stock Type II	—	—	—	—	—	—	—
Donor's Type II	—	—	±	±	±	±	±
Stock Type III	Agg.	Agg.	Agg.	Agg.	Agg.	Agg.	Agg.
Type IV (R)	RRR	RRR	RR	RR	RR	RRR	RRR
Type IV (P)	—	—	—	—	—	—	—
Type IV (G)	RRR	RRR	RRR	RRR	RR	RRR	RRR
Type IV (C)	R	R	±	±	±	R	R
Type IV (S)	RR	RR	RR	RR	RR	RR	RR

Types According to the Moss Classification

—	Absolute compatibility.	Agg.	Agglutination.
±	Passable grouping, possibly slight rouleaux.	H	Slight hemolysis.
R	Slight rouleaux.	HH	Moderate hemolysis.
RR	Moderate rouleaux.	HHH	Severe hemolysis.
RRR	Severe rouleaux.	HHHH	Very severe hemolysis.
RRRR	Very severe rouleaux.		

TABLE 2.—*Matching of Recipient's Serum Taken a Few Hours After Transfusion with Various Cells at Varying Times and Temperatures*

Cells Used for the Cross Agglutination	Ice Box Temperature		Room Temperature		Incubator Temperature 37 Degrees		
	24 Hours	72 Hours	24 Hours	72 Hours	2 Hours	24 Hours	72 Hours
Stock Type II	R	R	R	R	RR	RRR HH	HHHH
Donor's Type II	RR	RR	RR	RR	RR	RR HH	RRR HHH
Stock Type III	Agg.	Agg.	Agg.	Agg.	Agg.	Agg. HHH	HHHH
Type IV (R)	RRRR	RRRR	RRR	RRR	RRRR	RRRR HHH	HHHH
Type IV (P)	—	—	—	—	—	HHH	HHHH
Type IV (G)	Agg.	Agg.	Agg.	Agg.	RRRR	HHHH	HHHH
Type IV (C)	RRR	RRR	RRR	RRR	RRR	RRRR HHH	HHHH
Type IV (S)	RRRR	RRRR	RRRR	RRRR	RRRR	HHHH	HHHH

Types According to the Moss Classification
Symbols used are the same as in Table 1.

cells, and cells from five proven universal donors (Type IV, Moss). Fortunately for the completeness of the study, a small amount of the recipient's serum taken for her original typing previous to her transfusion had been preserved in the ice-box. Simultaneous matchings were made using this pre-transfusion serum and post-transfusion serum. The crosses were again in triplicate: at ice-box, room, and incubator temperatures. The results are recorded in tabular form. In Table 1 is recorded the matching with the pre-transfusion serum, and in Table 2 that with the post-transfusion serum.

It is to be noted that the stock Type II cells tested with the patient's pre-transfusion serum showed entire compatibility, remaining entirely separate at all three temperatures for the entire seventy-two hours of observation. However, the post-transfusion serum caused slight rouleaux formation in twenty-four hours at room and ice-box temperature, and moderate rouleaux within two hours at 37 degrees centigrade. Most striking was the hemolysis which took place over night at incubator temperature. The "ghost cells" and remaining unlysed cells showed marked rouleaux formation. By seventy-two hours, although the cells in the ice-box and at room temperatures showed no further change, the incubated cells had completely hemolyzed and the "ghost cells" were firmly clumped.

The donor's cells in the patient's pre-transfusion serum did not show the slightest rouleaux formation after seventy-two hours at ice-box temperature. At room and incubator tempera-

TABLE 3.—*Matching of Recipient's Serum Taken Five Months After Transfusion with Various Cells at Varying Times and Temperatures*

Cells Used for the Cross Agglutination	Ice Box Temperature		Room Temperature		Incubator Temperature 37 Degrees		
	24 Hours	72 Hours	24 Hours	72 Hours	2 Hours	24 Hours	72 Hours
Stock Type II	RR	RR	±	±	—	$\frac{\pm}{H}$	$\frac{\pm}{H}$
Donor's Type II	RR	RR	±	R	—	±	$\frac{\pm}{H}$
Stock Type III	Agg.	Agg.	HH Agg.	HHH	Agg.	HHHH	HHHH
Type IV (R)	RRR	RRRR	RR	RR	RR	RR HH	HHHH
Type IV (P)	±	±	±	±	—	HHH	HHHH
Type IV (G)	RRR	Agg.	RR	RR	RRR	HHHH	HHHH
Type IV (C)	RRR	RRR	R	R	±	±	$\frac{\pm}{HH}$
Type IV (S)	RRR	Agg.	RRR	RRR	RRR	HHHH	HHHH
Recipient's	±	±	—	—	—	H(?)	H
Recipient's	—	—	Substituting normal saline for recipient's serum —	—	—	—	—

Types According to the Moss Classification
Symbols used are the same as in Table 1.

tures there was only a suggestion of rouleaux formation which one would unhesitatingly pass as entirely compatible. Again, the patient's post-transfusion serum caused marked rouleaux formation; and, after twenty-four hours of incubation, a marked hemolysis.

Stock Type III cells showed immediate agglutination with both pre- and post-transfusion serum; but only at incubator temperature, and only with the post-transfusion serum did they hemolyze.

The cells of five proven universal donors showed varying degrees of rouleaux formation. One, P., did not form rouleaux with the patient's pre-transfusion or post-transfusion serum at any temperature. Nevertheless, the cells were completely hemolyzed in twenty-four hours at 37 degrees centigrade by the post-transfusion serum. Another, S., had been typed at least twelve times previously with all types of serum, and had never formed rouleaux. In common with the other three Type IV's (Moss), his cells showed a much more severe rouleaux formation with the post-transfusion serum. Their cells were severely or completely hemolyzed in twenty-four hours at 37 degrees centigrade by this post-transfusion serum. There was no hemolysis with the same serum at the other temperatures, nor with the pre-transfusion serum at any temperature.

It is to be regretted that the patient's own cells were not matched with her pre-transfusion and immediate post-transfusion sera.

The question naturally arose as to whether the recipient's serum would ultimately return to its pre-transfusion status; and on September 6, 1933, over five months after the transfusion, a recheck of the patient's blood was made.

Again, the recipient's serum was matched with the donor's cells, stock Type II and Type III cells, and the cells of the five universal donors who were previously used. In addition, her own cells were matched with her own serum and also observed in normal saline. The results are noted in Table 3. The final readings of the matchings more nearly resemble those of the immediate post-transfusion than of the pre-transfusion matchings. Of all the cross-checks made, the donor's seem to have been most constantly the best. His cells at room and at incubator temperatures fared nearly as well as in the pre-transfusion matching, though a slight degree of hemolysis still occurred. However, in the cross-matching of the patient's own cells and serum, there was a slight hemolysis in the incubator and a suggestion of rouleaux in the ice-box. It is true that the recipient's serum no longer caused severe rouleaux with Type IV (C) except at ice-box temperature. Also, the degree of rouleaux formation with the other Type IV's (Moss) is in a smaller degree than immediately after transfusion, except at ice-box temperatures. Nevertheless, the hemolysis at incubator temperature continued to be severe. However, the most interesting change was found in the two-hour observations. The two-hour incubator temperature readings, as well as two-hour ice-box and room temperature observations, again failed to warn of the danger that doubtless lurks in ever attempting to transfuse this patient.

SUMMARY

A case of transfusion reaction with uremia manifestations and recovery has been described. Preliminary typing had shown apparent compatibility. A recheck of the matching immediately after the reaction demonstrated a marked alteration in which the recipient's post-transfusion serum caused severe rouleaux and hemolysis. A rematching five months later revealed that, although the recipient's blood had not as yet returned to its pre-transfusion state, the methods of typing ordinarily used no longer revealed incompatibility.

DISCUSSION

Roy W. Hammack, M. D. (657 South Westlake Avenue, Los Angeles).—I have read with interest this report of an unusual reaction following blood transfusion. A number of similar reactions have been reported in recent years, among them the reports of Von Daesten and Cosgrove, in *Annals of Internal Medicine,* July, 1933; Stewart, in *Medical Clinics of North America,* September, 1931; and the more extensive report of Bordley, in *Archives of Internal Medicine,* February, 1931. While in some of the cases reported incompatibility of the bloods was later proved, in others no incompatibility could be shown by laboratory methods. In the case reported by Doctors Smith and Haman, hemoglobinuria was not recorded, but jaundice resulted, suggesting hemolysis of the transfused blood. This, with the other phenomena of the reaction, makes it similar to those reactions which follow transfusions with incompatible blood, as were others in which complete compatibility was shown by laboratory studies.

Is it possible that sodium citrate, pure or impure, is a factor? In the reports with which I am familiar, it is stated that the citrate method was used. I refer to those in which compatibility was apparently satisfactorily demonstrated. In a fairly large experience with the multiple syringe method in which uncitrated blood is transfused, I have not known renal insufficiency to occur following transfusion of compatible blood. However, citrated blood is probably used more frequently than uncitrated blood, and renal insufficiency following citrate transfusion is certainly uncommon.

Bordley discusses the attractive theory that the kidneys may be sensitive to some substance in the transfused blood, and "that the renal insufficiency results from a reaction of the nature of an anaphylactic shock." My associates and I have noticed that transfusion reactions, chills or fever, or both, are more likely to occur after the use of donors who have recently eaten a meal, particularly a meal rich in protein, than after the use of "fasting" donors. We have seen, in one instance, hemoglobinuria with chill, malaise and fever following transfusion of blood two hours after a heavy protein meal. In this instance, both the patient and the donor were Group 3 (Moss). Their bloods had been cross-agglutinated, and all tests were repeated after the transfusion, showing complete compatibility. The urine also contained numerous large granular casts and albumin. The casts and albumin disappeared within a few days. Blood nitrogen studies were not made, but there was no suppression of urine and no symptoms suggesting marked renal insufficiency developed.

It is interesting that, in the case reported by Doctors Smith and Haman, the donor was one who had previously given blood to this patient. We have noticed a few times unusually severe febrile reactions,

following the use of a donor the second time for the same patient, after a considerable time interval. However, this has by no means always occurred. I have been told of two severe reactions occurring in the practice of other physicians in Los Angeles following the use of the same donor after a considerable period of time. In one case there was anuria for twenty-four hours, and in the other urinary suppression over a longer period, with development of uremic symptoms. No reactions had followed the first transfusions with these donors. Is it not possible that in such cases the patient becomes sensitized to some unusual constituent of the donor's blood?

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LeRoy Brooks, M. D. (490 Post Street, San Francisco).—Jansky in 1907, and Moss in 1910, classified human blood into four groups. This classification was based on their discovery of two iso-agglutinin substances called A-B in serum, and two iso-agglutinogen a-b, in red blood cells.

Their assumption 'that there were only two iso-agglutinable substances has been shown to be incomplete. Guthrie and Huck in 1923 demonstrated the existence of a third iso-agglutinin D-Q, and a third Iso-agglutinogen d-q. This has been confirmed by others, and forms the basis of the so-called subgroups. These findings furnish a plausible explanation for some of the hitherto unexplained post-transfusion reactions that occasionally occur, even though the rules of selection of donors are followed. It is not an uncommon experience to find by cross-agglutination test that a donor's blood of the accepted group can be demonstrated in the laboratory to be incompatible.

It is also known that the titer or potency of the agglutinable substances varies. After an individual has had one transfusion, their titer is usually strengthened. Theoretically it is just as plausible to assume that the less constant iso-agglutinable substances D-Q, d-q are susceptible of change in titer as the more constant iso-agglutinins A-B, and iso-agglutinogens a-b. This would explain the reactions in the case here reported, as well as the laboratory findings. The first transfusion was followed by a mild reaction; the second transfusion from the same donor by a more severe reaction, due to an increase in the titer of the iso-agglutinable substances probably belonging to a subgroup.

It will be noted that the patient's serum was compatible with stock Type II cells after the first transfusion, but not after the second transfusion. The peculiar and contradictory behavior of her cells with well-known groups, and the fact that the patient's serum after the second transfusion and severe reaction caused a questionable hemolysis of her own cells in twenty-four hours in the incubator, and some definite hemolysis at the end of seventy-two hours, suggest that the last word in groups and subgroups of human blood has not as yet been said. This case demonstrates also the desirability of allowing more time for the laboratory test than is usually practiced when time is available.

It has been my experience that reactions of the character here considered follow transfusions in Type II patients. The literature shows that the experiences of some others have coincided in this respect. This has led to the belief on the part of some that subgroups are more frequently formed in Type II individuals than in other groups. In turn, this experience has led to some clinics and some individuals preferring Type IV (Moss), or universal donors, when transfusing Type II patients. I prefer Type IV (Moss) donors to Type II donors for Type II patients, unless unusually large transfusions are necessary. Grouping of both donor and patient and cross-agglutination testing should be a definite routine.

I think Doctors Smith and Haman should be commended on this case report, and particularly on the follow-up laboratory work which they did after the post-transfusion reaction.

DEAFNESS—ITS HUMANITARIAN PROBLEMS*

A PLEA TO OTOLOGISTS

By George E. Coleman†
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Discussion *by Harold A. Fletcher, M.D., San Francisco; Francis L. Rogers, M.D., Long Beach; Isaac H. Jones, M.D., Los Angeles.*

I WISH to express my great appreciation of the privilege accorded me to address such a representative body of the otologists of the state of California.

From a scientific standpoint many definitions of hearing have been given. It is usual, however, to define deafness simply as a failure to hear. It is true that we respond emotionally in either a favorable or an unfavorable manner to all sensory stimuli normally received, but the entire picture of what happens to a human being whose hearing was once normal, but who has irreparably lost all or a large part of it, cannot be summed up in the single word "deafness."

The understanding of this handicap—it is really an affliction to the unadjusted—and the reaction to it of the normally hearing, of the adventitiously deafened, and of these latter to others who have lost their hearing, differ as widely as do the various constituents which make up the personality complex of each. No one knows all about deafness. However, since the great movement for the economic, social and psychologic betterment of the hard-of-hearing and for prevention began, a far more thorough comprehension of the many problems relating to it has been attained.

ORGANIZATIONS FOR THE HARD-OF-HEARING

This movement, on a broad scale, initiated and maintained almost entirely by the deafened themselves, began in 1906 with the formation of the Nitchie Service League for adult lip-readers, which later became the New York League for the Hard-of-Hearing. In 1919 the nine leagues then in existence (there are now over one hundred) were organized into the American Federation of Organizations for the Hard-of-Hearing. Dr. Wendell C. Phillips is now its honorary president and Mrs. James F. Norris, a specialist in the welfare of the hard-of-hearing child, is president. Several other eastern otologists have had a more or less continuous and active interest in the national work of this federation, and their influence as presidents or members of the board of managers has greatly contributed to its success. I regret that I have not the time to outline the manifold activities, now greatly curtailed because of the depression, of this organization, many of which redound directly to the credit and advantage of otologists.

Conferences, to which the leagues send a large number of representatives, are held annually, and

* Read, by invitation, before the Eye, Ear, Nose and Throat Section of the California Medical Association at the sixty-third annual session, Riverside, April 30 to May 3, 1934.

† The author is not a doctor of medicine, but is himself, one of the deafened, and is a Research Assocate in Medicine in the Hooper Foundation.