THE UNIVERSITY OF MINNESOTA

GRADUATE SCHOOL

Report

of

Committee on Examination

This is to certify that we the undersigned, as a committee of the Graduate School, have given Harold Leroy Goss final oral examination for the degree of Master of Science in Ophthalmology.

We recommend that the degree of Master of Science in Ophthalmology be conferred upon the candidate.

W. J. Bundick
Chairman

A. H. Sanford

J. L. McCartney Jr

F. E. Gaffen

W. R. Murray

Date Dec. 2-1922

10-20 5M

Graduate School, University of Minnesota.

Date: November 11, 1922.

This is to certify that Harold Leroy Goss, a candidate for the degree of Master of Science in Ophthalmology, has passed the final written examination for the major in the Department of Ophthalmology.

W. S. Bundick

For the Major Department.

Graduate School, University of Minnesota.

Date: November 11, 1922.

This is to certify that Harold Leroy Goss, a candidate for the degree of Master of Science in Ophthalmology, has completed the requirements for the minor in the Department of Anatomy.

C. M. Jackson

For the Minor Department.

REPORT

of

Committee on Thesis

The undersigned, acting as a Committee of the Graduate School, have read the accompanying thesis submitted by Harold Leroy Goss for the degree of Master of Science in Ophthalmology. They approve it as a thesis meeting the requirements of the Graduate School of the University of Minnesota, and recommend that it be accepted in partial fulfillment of the requirements for the degree of Master of Science in Ophthalmology.

W. L. Benedict

H. B. Gifford

A. B. Sanford

Wm. F. Murray

10-20 5M

THESIS

THE EFFECT OF BLOOD TRANSFUSION UPON THE RETINITIS OF PERNICIOUS ANEMIA.

Harold Leroy Goss, B.S., M.D.

Submitted to the faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Master of Science in Ophthalmology.

October, 1922.

The purpose of this study was to determine the effect of blood transfusion given as a part of the treatment of pernicious anemia upon the retinitis of that disease.

The occurrence of retinitis in cases of pernicious anemia was recognized shortly after Thomas Addison first described the disease in 1855. Biermer in the first German report of the disease in 1874 calls attention to the retinitis as one of the important findings in the disease. As early as 1884 Stephen Mackenzie[27] remarked on the tendency of all anemias, but especially pernicious anemia, to develop retinal hemorrhages as soon as the hemoglobin fell below 50 per cent. The percentage of cases in which retinitis occurs varies according to the investigator, most of the early investigators stating that they found a retinitis in all cases examined at the height of the disease. Later authors, however, state that it occurs in from 44 to 62 per cent of the cases. Woltman of the Mayo Clinic, reported 63 per cent of 150 cases of pernicious anemia had a retinitis. Thirty-three per cent of these had a low grade retinitis while the remaining 30 per cent had retinitis with hemorrhages.

The retinitis of pernicious anemia consists of a pallor of the disc or of the whole retina, edema of the retina, hemorrhages which may be superficial or deep, exudates or plaques, and changes in the vessel walls. Of these the most constant findings are the pallor of the disc and retina, and edema. The hemorrhages, once they appear, do not remain indefinitely, but may become absorbed, and the retina remain free for sometime, or a new crop of hemorrhages appear in addition to the old ones.

The hemorrhages appearing in the retina correspond to the hemorrhages found in other parts of the body in this disease for example in the skin, spinal cord, brain, and serous membranes. Biermer, Bramwell, Horner, Müller and Quincke found them in almost all of the cases they investigated at the height of the disease. Retinal hemorrhages have also been found in secondary anemia and chlorosis. Thus they alone are not of significant diagnostic importance. The typical hemorr-

hage of pernicious anemia has a white center surrounded by a red halo. They may be either superficial, having a flame-shaped appearance, due to their location in the nerve fibre layer, or deep, being more rounded and with more regular edges. They may lie either in the neighborhood of the papilla or in the periphery. Their size varies from small punctate hemorrhages up to the diameter of the disc rarely exceeding this in size although Bondi claims to have found one three disc diameters in size. Pathological anatomical researches have shown that the hemorrhages are limited as a rule to one thickness of the retina, usually the nerve fibre layer, less often lying in the outer molecular layer, and occasionally in the two granular layers.

The mode of origin of retinal hemorrhages is apparently not uniform. Manz explained the various stages in the development of hemorrhages by the development of aneurysms in the small vessels. Eichhorst agreed with Manz, but in one case he explained it by diapedesis. Others explained it by rhexis. In a number of cases fatty degeneration was found in the walls of small and middle sized vessels. Embolism of the retinal capillaries was also found in some cases of Sgrosso.

The bright center of single hemorrhages has been explained in various ways by different investigators: (1) Through an accumulation of white blood corpuscles. Manz attributed this to small aneurysms in the vessel wall while Eichhorst and Nykamp claimed that they were in the lymph sheath of the vessels. Many investigators have not found these small aneurysms, however. (2) A regressive metamorphosis of these accumulated cells, combined with a change in the surrounding tissues. (3) Varicose hypertrophy of the nerve fibres. These varicose areas may lie in the center of hemorrhages or be separate. Bettman found both the varicose hypertrophy of the fibres and also collections of lymphoid cells surrounded by hemorrhages. Bettman followed these varicosities through from a first stage of varicosity to a final stage with a deep staining nucleus in this varicose area, which may explain some of the difference in opinion. Colloid masses in the outer molecular layer are also seen analogous to those found in albuminuric retinitis.

The plaques occurring in pernicious anemia are distinguished from the cotton-wool exudate of Bright's disease by their lack of luster, and their more saturated gray color.

The retinal vessels, both arteries and veins, may be dilated and tortuous. In this case there is generally a marked retinal edema. The color of the vessels may be almost uniform so that arteries are distinguished from veins with difficulty. As a rule, however, the arteries are much lighter in color and have a broader light reflex because of their flattened condition. In other cases the arteries may appear to be small with an increased light reflex. This is usually the case after the retinitis subsides. The smaller vessels may show the small aneurysms described by some authors. Bettman and Bondi both lay great stress upon disease in the walls of the smaller and middle sized vessels. They found the vessel walls thickened, and the lumen narrowed with proliferation of epithelium and collections of round cells in the walls. Immermann and Mackenzie[27] held that the hemorrhages were due to the fact that the blood did not contain enough oxygen and therefore the capillary walls became diseased. Bettman brings all of the phenomena (edema, hemorrhages, varicosities of the nerve fibres) into close relationship with disease of the vessel walls, and to such extent that the degree of pathology appearing is dependent upon the degree of change in the blood vessels. Ulrich and Natanson, however, did not find these vessel changes.

The amount of edema of the retina varies. There may be little or none, or a large amount extending out into the periphery of the retina. One observer even reported a detachment of the retina due to a serous exudate interposed between the retina and choroid.

The cases studied were examined ophthalmoscopically the evening before transfusion, and again within three to six hours following transfusion. Following this an ophthalmoscopic examination was made at intervals of twenty-four to forty-eight hours as long as the patients remained in the hospital. Several of the patients left the hospital at the end of twenty-four hours following transfusion,

and no further study was possible. All of the cases were examined with pupils dilated with four per cent cocaine at each examination. The dilated pupils permitted an examination of the retina as far as the extreme periphery, and allowed an accurate estimation of edema and light reflex. Nine of the cases had a retinitis with hemorrhages or exudates. The remaining four cases showed a pallor of the discs, but no hemorrhages or exudates.

Case A344104, a man, aged 59 years, normal weight 225 pounds, present weight 195 pounds. His chief complaints were weakness and dyspnea. He showed glossitis, and no free acid in the stomach. The skin was lemon-yellow in color. The red blood count was 1,880,000,hemoglobin 34 per cent,color index .9+, leukocytes 5200, with polynuclear neutrophiles 60 per cent,lymphocytes 33 per cent, large mononuclears 1 per cent,eosinophiles 4.5 per cent,basophiles 1.5 per cent,anisocytosis moderate, and poikilocytosis moderate. June 9, 1922 ophthalmoscopic examination showed slight pallor of discs,rather full retinal veins,somewhat full retinal arteries,and one rather large retinal hemorrhage.The diagnosis was pernicious anemia.

August 9, 1922 ophthalmoscopic examination showed slight pallor of the discs, slight retinal edema, and both retinal arteries and veins somewhat dilated.

August 10, 1922 he was transfused with 250 c.c. citrated blood. Ophthalmoscopic examination showed the condition of the fundus to be the same as on August 9, 1922. The patient left the hospital the morning of August 11, 1922, and no further examinations were made at this time.

September 21, 1922 ophthalmoscopic examination showed pallor of discs, moderate edema of the retina, and full and tortubus retinal arteries and veins. There were four superficial hemorrhages in the right eye and two superficial hemorrhages with the central white spots in the left eye. The red blood count was 1,140,000, hemoglobin 20 per cent, and the color index .9+.

September 22, 1922 he was transfused with 300 c.c. citrated blood. Ophthalmoscopic examination showed the condition of the fundus to be the same as on September 21, 1922.

September 23, 1922 ophthalmoscopic examination showed slightly less edema of the retina, and the retinal arteries less dilated, otherwise there was no change in the condition of the fundus.

Case A372040, a man, aged 36 years, weight 176 pounds. His chief complaints were weakness, dyspnea and palpitation. He showed some atrophy of the tongue, systolic murmur at apex, and no free acid in the stomach. The skin was of the typical lemon-yellow color. The red blood count was 1,430,000, hemoglobin 27 per cent, color index .8+, leukocytes 5300, with polynuclear neutrophiles 59 per cent, lymphocytes 34 per cent, large mononuclears 4.5, eosinophiles 1.5, myelocytes 1, normoblasts 8, anisocytosis marked, poikilocytosis moderate, polychromatophilia moderate, and granular degeneration slight. September 13, 1921 ophthalmoscopic examination showed pallor of the disc and retina, numerous hemorrhages in the retina of varied type, a few with the central white spot characteristic of pernicious anemia. The diagnosis was pernicious anemia. The patient received three transfusions of citrated blood and returned home in October 1921.

July 24, 1922 the patient returned for further observation. He had felt well since leaving until March, 1922. Since that time he has had several vomiting spells, and has a feeling of a "dead weight" in his stomach. His red blood count at this time was 780,000, hemoglobin 18 per cent, and color index 1.+.

August 11, 1922 ophthalmoscopic examination showed some pallor of the discs with a superficial hemorrhage in the left eye.

August 12, 1922 he was transfused with 500 c.c. citrated blood. Ophthalmoscopic examination that evening showed the condition of the fundus to be the same as at the previous examination.

August 14, 1922, ophthalmoscopic examination showed apparently less pallor of discs. There were at this examination two deep diffuse hemorrhages about one disc diameter in size along the inferior temporal artery right eye. The centers of these hemorrhages were dark red.

August 17, 1922 he was transfused with 400 c.c. citrated blood. Ophthal-

moscopic examination showed the condition of the fundus to be the same as on August 17th. At this time his red blood count was 2,320,000, hemoglobin 45 per cent, and color index .9.

Case A398071, a woman, aged 56 years. Her chief complaints were weakness, dyspnea, stomach trouble, and numbness of lower part of body for the past two years. She showed glossitis, edema of lower extremities, systolic murmur at the apex, and a subacute combined sclerosis. The skin was colored lemon-yellow. The red blood count was 1,100,000, hemoglobin 30 per cent, color index 1.3+, leukocytes 2200, with polynuclear neutrophiles 63 per cent, lymphocytes 35 per cent, eosinophiles 2 per cent, anisocytosis marked, poikilocytosis marked, and platelets 214,000. Ophthalmoscopic examination showed a slight retinal edema, no vasoular changes, and a few scattered retinal hemorrhages which suggested pernicious anemia. The diagnosis was pernicious anemia.

August 7, 1922 ophthalmoscopic examination showed pallor of the discs with slight retinal edema. The retinal arteries showed an increased light reflex. There was one deep diffuse hemorrhage in the right eye, and two superficial flame-shaped hemorrhages in the left eye. The red blood count was 2,260,000, hemoglobin 45 per cent, color index .9+.

August 8, 1922 she was transfused with 350 c.c. citrated blood. Ophthalmoscopic examination showed the condition of the fundus to be the same as on August 7th.

August 10, 1922 ophthalmoscopic examination showed pallor of the discs, and no edema of the retina. The retinal arteries had an increased light reflex. The hemorrhages in both eyes were apparently smaller and thinner than on August 8, 1922. The red blood count was 3,200,000, hemoglobin 55 per cent, and color index .8+.

August 14, 1922, ophthalmoscopic examination showed the condition of the fundus in the right eye to be the same as on August 10, 1922, with the hemorrhage still present. The left eye showed one of the two hemorrhages to have been ab-

sorbed, and a fresh hemorrhage with a white center to have appeared since the last examination.

The patient died on August 15, 1922. Autopsy showed miliary tuberculosis left pleural cavity, bilateral chronic tuberculous bronchitis, partially healed tuberculous ulcers of ileum, bilateral hydrothorax with atelectasis, degeneration of posterior sensory columns of cord, moderate edema of brain, subendocardial petechial hemorrhages, brown pigmentation of the myocardium, atrophy of the tongue, and lemon-yellow tint to the skin. The principal cause of death was pernicious anemia; the contributory cause, tuberculous pleuritis with effusion.

Case A398146, a man, aged 53 years. His chief complaints were weakness, dyspnea, and palpitation of the heart. He showed edema, a systolic murmur heard best at the apex, and no free acid in the stomach. The skin was a pale lemon-yellow. The red blood count was 1,930,000, hemoglobin 39 per cent, color index 1.14, leukocytes 5400, with polynuclear neutrophiles 51 per cent, eosinophiles 6 per cent, normoblasts 1, anisocytosis moderate, poikilocytosis moderate, and polychromatophilia slight. July 15, 1922 ophthalmoscopic examination showed some appearances of anemia with a few hemorrhages and an area of localized edema in the left eye, and two absorbing hemorrhages in the right eye. The diagnosis was pernicious anemia.

August 9, 1922 ophthalmoscopic examination showed a pallor of the disc and retina with slight edema of the retina in the peripapillary region. The retinal arteries showed an increased light reflex, and the calibre of both arteries and veins was increased. There were three hemorrhages in the right eye which were superficial, and had the white centers. There was one deep, diffuse hemorrhage and two areas of exudate slightly less than one disc diameter in size surrounded by a narrow halo of hemorrhage in the left eye. There was one area of localized edema in this eye.

August 10, 1922 he was transfused with 400 c.c. citrated blood. Ophthalmoscopic examination showed two fresh hemorrhages in the right eye. These hemorrhages were deep, round, and diffuse and did not have the central white spots.

August 15, 1922 ophthalmoscopic examination showed the hemorrhages still present but apparently absorbing.

September 4, 1922, ophthalmoscopic examination showed no hemorrhages or exudates in the right eye. The vascular calibre was now normal in this eye. The left eye still showed some venous engorgement with one hemorrhage with a white center which was absorbing and one thin plaque-like exudate.

September 5, 1922, he was transfused with 500 c.c. citrated blood. Ophthalmoscopic examination showed the condition of the fundus to be unchanged. At this time the red blood count was 2,000,000, hemoglobin 37 per cent, and the color index .9+.

Case A399786, a man, aged 36 years, normal weight 175 pounds, present weight 153 pounds. His chief complaints were weakness and dyspnea. He showed glossitis, a systolic murmur at the base, paresthesias, and no free acid in the stomach. The skin was lemon-yellow in color. The red blood count was 2,100,000, hemoglobin 38 per cent, color index .9+, leukocytes 2200, with polynuclear neutrophiles 48 per cent, lymphocytes 47 per cent, large mononuclears 1.5 per cent, transitionals 1 per cent, eosinophiles 2 per cent, normoblasts 8, microcytes few, megalocytes many, anisocytosis marked, poikilocytosis moderate, basophilic stippling slight, and platelets 152,000. July 31, 1922 ophthalmoscopic examination showed a slight retinal edema with dilated and tortuous retinal arteries and veins. There were a few scattered retinal hemorrhages in each eye. The diagnosis was pernicious anemia.

August 11, 1922 ophthalmoscopic examination showed the discs pale with a slight retinal edema. The retinal arteries and veins were dilated and tortuous. The retinal arteries showed a broad light streak. There were a few areas showing arteriovenous compression. There was one thin plaque-like exudate in the left eye but no hemorrhages present in either eye.

August 12, 1922 he was transfused with 400 c.c. citrated blood. The ophthalmoscopic examination showed the condition to be the same as on August 11,

1922.

August 14, 1922 ophthalmoscopic examination showed the plaque-like exudate still present in the left eye. There was slightly less edema, and less dilatation of the retinal arteries and veins.

August 16, 1922, he was transfused with 450 c.c. citrated blood. The ophthalmoscopic examination showed the condition of the fundus to be the same as on August 14, 1922.

August 17, 1922 ophthalmoscopic examination showed the condition of the fundus to be the same as before.

August 21, 1922 ophthalmoscopic examination showed the condition of the fundus to be unchanged.

August 23, 1922 he was transfused with 450 c.c. citrated blood.

August 24, 1922 ophthalmoscopic examination showed that the plaque-like exudate was not present and had apparently become absorbed, otherwise the condition of the fundus was the same as on August 14, 1922.

August 31, 1922 ophthalmoscopic examination showed a pallor of the discs, a slight edema of the retina still present, and the retinal arteries and veins still slightly dilated and tortuous. No hemorrhages or exudates were present.

September 1, 1922 the red blood count was 2,520,000, hemoglobin 48 per cent and the color index .9+.

Case A400266, a woman, aged 38 years, normal weight 125 pounds, present weight 79 pounds. Her chief complaints were weakness and diarrhea. She showed glossitis, edema of the extremities, and no free acid in the stomach. The skin was pale yellow. The red blood count was 990,000, hemoglobin 25 per cent, color index 1.2, leukocytes 2500, with polynuclear neutrophiles 16 per cent, lymphocytes 80 per cent, large mononuclears 2 per cent, transitionals 1 per cent, basophiles 1 per cent, anisocytosis marked, poikilocytosis marked, basophilic stippling slight, polychromatophilia slight, and platelets 640,000. August 4, 1922 ophthalmoscopic examination showed anemia with slight edema of discs, arteries slightly

bright and an appearance of arteriovenous compression in places, one diffuse retinal hemorrhage in the right eye, and an exudate in the left eye. The diagnosis was pernicious anemia.

August 9, 1922 ophthalmoscopic examination showed slight pallor of discs and slight retinal edema. There was a large, flame-shaped retinal hemorrhage in the left eye. No hemorrhages were seen in the right eye. There was an increased light reflex from both arteries and veins.

August 10, 1922 she was transfused with 500 c.c. citrated blood. The ophthalmoscopic examination showed the flame-shaped hemorrhage in the left eye to have developed a white center thus forming a hemorrhage typical of pernicious anemia. There was slight pallor of the nerve heads, and slight edema in the region of the disc.

August 14, 1922 ophthalmoscopic examination showed that the hemorrhage in the left eye had disappeared, otherwise the condition of the fundus was unchanged.

August 15, 1922 she was transfused with 350 c.c. citrated blood. The ophthalmoscopic examination showed the condition of the fundus to be the same as on August 14th.

August 17, 1922 her red blood count was 2,840,000, hemoglobin 55 per cent, color index .9+.

Case A401357, a man, aged 50 years, weight 155 pounds. His chief complaints were weakness, dyspnea, diarrhea, epistaxis and hearing noises. He showed some glossitis, no free acid in stomach, and a subacute combined degeneration of the spinal cord with paresthesias and incoordination. The skin was lemon-yellow color. The red blood count was 1,450,000, hemoglobin 30 per cent, color index 1+, leukocytes 6200, with polynuclear neutrophiles 68 per cent, lymphocytes 30 per cent, large mononuclears 1 per cent, transitionals .5 per cent, eosinophiles .5 per cent, normoblasts 2, megalocytes few, anisocytosis moderate, poikilocytosis moderate, basophilic stippling slight, and polychromatophilia slight. August 12, 1922 ophthalmoscopic examination showed anemia of discs with some edema of the

surrounding retina, dilatation of both retinal arteries and veins. There was one diffuse retinal hemorrhage in the left eye, and two small diffuse hemorrhages in the right eye, one of which had the characteristic central white spot. The diagnosis was pernicious anemia.

August 16, 1922 ophthalmoscopic examination showed the discs pale with moderate edema of the surrounding retina. The retinal vessels, both arteries and veins, were dilated and tortuous with a broad light reflex over the arteries. There was one hemorrhage still remaining in the right eye. The left eye showed that the diffuse retinal hemorrhage noted at the previous examination was still present.

August 17, 1922 he was transfused with 400 c.c. citrated blood. Ophthalmoscopic examination showed two fresh diffuse hemorrhages situated deep in the retina in the left eye. They did not have a central white spots.

August 19, 1922 ophthalmoscopic examination showed the two fresh hemorrhages noted in the left eye on August 17, to be more superficial and to have lighter centers.

August 21, 1922 ophthalmoscopic examination showed the two fresh hemorrhages noted on August 17 to have white centers at this time forming typical pernicious anemia hemorrhages. The right eye showed a fresh hemorrhage with a white center located at the side of the hemorrhage previously seen in this eye. The edema still remained about the same, and the retinal vessels were still dilated and tortuous.

August 23, 1922 ophthalmoscopic examination showed one new hemorrhage in each eye, a large superficial (one disc diameter by 1.5 disc diameters) one in the right, and a smaller (.5 disc diameter) deep and more diffuse one in the left.

August 28, 1922 ophthalmoscopic examination showed the hemorrhages smaller, and apparently absorbing. There was some decrease in the amount of retinal edema.

August 29, 1922 he was transfused with 250 c.c. citrated blood.

October 2, 1922 ophthalmoscopic examination showed one absorbing superficial hemorrhage in the right eye, and one absorbing hemorrhage in the left eye. There was one fresh hemorrhage in the left eye. There was still some retinal edema extending out towards the periphery, and the retinal arteries and veins were still somewhat engorged and tortuous although this was not as marked as it was in the early examinations. The blood count at this time was 2,300,000, hemoglobin 40 per cent, and the color index .8+.

Case A402554, a man, aged 44 years, normal weight 155 pounds, present weight 133 pounds. His chief complaints were weakness, vertigo, noises in the ears, dyspnea, and palpitation of the heart. He showed a systolic murmur heard best at the left third costal cartilage, and a palpable spleen. The skin showed a lemon-yellow tint. The red blood count was 1,370,000, hemoglobin 32 per cent, color index 1.1+, leukocytes 4500, with polynuclear neutrophiles 64.5 per cent, lymphocytes 34 per cent, transitionals 1 per cent, basophiles .5 per cent, normoblasts 2, megalocytes few, anisocytosis moderate, poikilocytosis moderate, basophilic stippling slight, and polychromatophilia slight. August 24, 1922 ophthalmoscopic examination showed anemia of discs with slight edema of the retina in the peripapillary region. The hemorrhages characteristic of pernicious anemia noted on August 24, had disappeared, and there was only one flame-shaped hemorrhage, which lacked the white center, present in the right eye.

August 30, 1922 he was transfused with 270 c.c. citrated blood.

August 31, 1922 ophthalmoscopic examination showed the condition of the fundus to be unchanged.

September 4, 1922 he was transfused with 150 c.c. citrated blood. The ophthalmoscopic examination showed the condition of the fundus to be unchanged.

September 8, 1922 he was transfused with 450 c.c. citrated blood. Ophthalmoscopic examination showed the condition of the fundus to be unchanged.

September 11, 1922 the red blood count was 1,920,000, hemoglobin 40 per cent, and the color index 1+.

Case A404630, a woman, aged 24 years, weight 93 pounds. Her chief complaints were weakness and diarrhea. She showed glossitis, paresthesias, systolic murmur at base, palpable spleen, and no free acid in the stomach. The skin was pale with areas of deep pigmentation. The red blood count was 1,660,000, hemoglobin 28 per cent, color index .8+, leukocytes 5000, with polynuclear neutrophiles 43.5 per cent, lymphocytes 52 per cent, large mononuclears 3.5 per cent, eosinophiles 1 per cent, normoblasts 10, megaloblasts 1, anisocytosis marked, poikilocytosis marked, basophilic stippling marked, polychromatophilia moderate, and platelets 220,000. The diagnosis was pernicious anemia.

September 14, 1922 ophthalmoscopic examination showed pallor of the discs, slight retinal edema with dilated and tortuous arteries and veins. There were several small punctate hemorrhages in each eye and one deep hemorrhage in the right eye which had an indefinite white center.

September 15, 1922 he was transfused with 350 c.c. citrated blood.

September 16, 1922 ophthalmoscopic examination showed slightly less edema of the retina otherwise the condition of the fundus was the same as on September 14th.

September 18, 1922 he was transfused with 500 c.c. citrated blood. Ophthalmoscopic examination showed the condition of the fundus to be the same as on September 16, 1922.

September 21, 1922 ophthalmoscopic examination showed only one small, punctate hemorrhage remaining in the right eye, and one small, deep hemorrhage remaining in the left eye. The retinal edema and dilatation of the arteries and veins remained about the same. The red blood count was 2,800,000, hemoglobin 55 per cent, and the color index .9+.

September 22, 1922 he was transfused with 450 c.c. citrated blood.

September 23, 1922 ophthalmoscopic examination showed less dilatation of the retinal vessels. Otherwise the condition of the fundus was unchanged.

Case A1403, a woman, aged 51 years, weight 124 pounds. Her chief com-

plaints were weakness, dyspnea, and failing memory. She showed glossitis, edema of hands and feet, systolic murmur over entire precordium, neurologic symptoms suggestive of a combined sclerosis, and no free acid in the stomach. The skin was of the typical lemon-yellow color of pernicious anemia. The red blood count was 1,290,000, hemoglobin 30 per cent, color index 1.14, leukocytes 4700, with polynuclear neutrophiles 60.5 per cent, lymphocytes 34 per cent, large mononuclears .5 per cent, eosinophiles 2 per cent, basophiles 1 per cent, normoblasts 3, microcytes few, megalocytes few, anisocytosis moderate, poikilocytosis moderate, basophilic stippling slight, and polychromatophilia slight. March 3, 1922 ophthalmoscopic examination showed some anemia of the discs with numerous and large, mainly diffuse hemorrhages, some of which had the central white spots typical of pernicious anemia. There were some small and punctate hemorrhages. The diagnosis was pernicious anemia. Patient had received fifteen transfusions of citrated blood up to August 7, 1922.

August 7, 1922 ophthalmoscopic examination showed slight pallor of the discs with both arteries and veins slightly dilated. No hemorrhages were seen. At this time her hemoglobin was 40 per cent, red blood cells 1,870,000, color index 1.0, and leukocytes 4900.

August 9, 1922 she was transfused with 350 c.c. citrated blood. Ophthalmoscopic examination that evening showed the condition of the fundus to be the same as the evening before. Patient left the hospital the next morning without receiving more transfusion.

Case A404901, a woman, aged 40 years, normal weight 150 pounds, present weight 114 pounds. Her chief complaints were diarrhea, weakness, dyspnea and vertigo. The skin was described as being "sallow". The red blood count was 1,470,000, hemoglobin 34 per cent, color index 1+, leukocytes 3850, with polynuclear neutrophiles 33 per cent, lymphocytes 63.5 per cent, large mononuclears .5 per cent, plasma cells .5 per cent, eosinophiles 1 per cent, basophiles .5 per cent, normoblasts 4, megaloblasts 1, anisocytosis marked, and poikilocytosis marked.

May 30, 1922 ophthalmoscopic examination showed a couple of small areas of localized edema, or increased glial tissue, otherwise the fundus was negative. The diagnosis was pernicious anemia 85 per cent, chronic cholecystitis 15 per cent.

August 26, 1922 the patient had (1) cholecystectomy (2) splenectomy and (3) appendectomy.

September 11, 1922 the red blood count was 2,570,000, hemoglobin 53 per cent, and the color index 1.04.

September 14, 1922 ophthalmoscopic examination in the morning showed a slight edema of the retina which looked thick and greyish throughout. The retinal arteries showed an increased light reflex. The patient had received four transfusions in addition to the splenectomy up to this time. She was transfused with 400 c.c. citrated blood on this date. Ophthalmoscopic examination the evening of September 14, 1922 showed the condition of the fundus to be the same as in the morning before transfusion.

September 15, 1922 ophthalmoscopic examination showed the condition of the fundus to be unchanged. Patient left the hospital on this date.

Case A395656, a woman, aged 39 years, normal weight 147 pounds, present weight 118 pounds. Her chief complaints were weakness, nausea and vomiting. She showed glossitis, systolic murmur at apex, tenderness and rigidity over upper right abdomen, and no free acid in the stomach. The skin was lemon-yellow in color. The red blood count was 750,000, hemoglobin 10 per cent, color index .6, leukocytes 2600, with polynuclear neutrophiles 40.5 per cent, lymphocytes 57 per cent, large mononuclears .5 per cent, eosinophiles .5 per cent, normoblasts 7, megaloblasts 1, anisocytosis moderate, poikilocytosis moderate, and polychromatophilia slight. Two days later on June 23, 1922 the red blood count was 1,130,000, hemoglobin 11 per cent, color index .4;, leukocytes 2200, with polynuclear neutrophiles 28 per cent, lymphocytes 69 per cent, large mononuclears 1 per cent, transitionals 1 per cent, basophiles 1 per cent, normoblasts 4, megaloblasts 1, anisocytosis moderate, poikilocytosis moderate, and polychromatophilia slight. June

22, 1922 ophthalmoscopic examination showed some edema of the retina with full retinal arteries and veins. There were numerous large retinal hemorrhages with large white areas. The retinitis suggested a primary anemia of some type with many features of a leukemic retinitis. She received seven transfusions of citrated blood. On August 7, 1922 her red blood count was 1,600,000, hemoglobin 25 per cent, and the color index .7+.

September 4, 1922 the red blood count was 1,120,000, hemoglobin 24 per cent, and the color index 1.0+.

September 8, 1922 ophthalmoscopic examination showed pallor of the disc, and an increased arterial light reflex.

September 9, 1922 she was transfused with 400 c.c. citrated blood. Ophthalmoscopic examination showed the condition of the fundus to be the same as on September 8, 1922.

September 10, 1922 ophthalmoscopic examination in the morning showed the condition of the fundus to be the same as at the last examination. Patient left hospital without further treatment.

Case A401154, a man, aged 37 years, weight 155 pounds last March, present weight 128 pounds. His chief complaints were weakness and dyspnea. He showed an atrophic tongue, a systolic murmur over the apex which was poorly transmitted, a mild combined sclerosis, and no free acid in the stomach. The skin was a pale lemon-yellow. The red blood count was 1,460,000, hemoglobin 40 per cent, color index 1.3, leukocytes 4600, with polynuclear neutrophiles 53 per cent, lymphocytes 43 per cent, large mononuclear 1 per cent, transitionals 2 per cent, eosinophiles 1 per cent, normoblasts 2, microcytes few, megalocytes few, anisocytosis moderate, poikilocytosis moderate, basophilic stippling moderate, and polychromatophilia slight. August 11, 1922 ophthalmoscopic examination showed anemia of the disc and retina with some choroidal sclerosis. No hemorrhages were seen. The diagnosis was pernicious anemia. He received a series of five transfusions.

August 16, 1922 ophthalmoscopic examination showed the condition of the

fundus to be the same as that at the first examination.

August 17, 1922 he was transfused with 300 c.c. citrated blood. Ophthalmoscopic examination showed no change in the fundus.

August 19, 1922 ophthalmoscopic examination showed no change in the fundus.

August 21, 1922 ophthalmoscopic examination showed the condition of the fundus to be unchanged.

August 22, 1922 he was transfused with 500 c.c. citrated blood. Ophthalmoscopic examination showed the condition of the fundus to be unchanged.

August 23, 1922 ophthalmoscopic examination showed the condition of the fundus to be unchanged.

August 28, 1922 he was transfused with 500 c.c. citrated blood.

September 4, 1922 he was transfused with 500 c.c. citrated blood. Ophthalmoscopic examination showed no change in the fundus.

September 6, 1922 the hemoglobin was 50 per cent, red blood count 2,400,000, and the color index 1+.

September 8, 1922 patient was discharged from the hospital.

Early in this study it became evident that those cases which showed no hemorrhages before the transfusion did not develop them immediately following transfusion. Those cases which had retinal edema generally showed less edema twenty-four to forty-eight hours following transfusion. One case (A401357) which had a moderate edema of the retina at the first examination did not show any change in the amount of edema for twelve days following the first transfusion. Another case (A399786) showed less edema of the retina in two days, and another case (A404630) showed less edema in one day following transfusion. The retinal hemorrhages disappeared immediately following transfusion in only one case (A400266). Case (A402554)when seen at the office before entering the hospital had many retinal hemorrhages with the central white spots typical of pernicious anemia, but when seen in the hospital five days later he had only one hemorrhage remaining.

He was not transfused during that time.

Four of these cases (A372040, A398071, A398146, A401357) showed new hemorrhages occurring from time to time, even while receiving transfusions, but these same cases showed the older hemorrhages absorbing. Two of the cases (A372040, A401357) showed fresh hemorrhages at the first examination immediately following transfusion. These same cases, however, showed fresh hemorrhages at times remote from the immediate effects of transfusion. Some of the fresh hemorrhages which at first were deep and diffuse became more superficial, and developed the central white spot characteristic of pernicious anemia while other deep hemorrhages went on to absorption without developing the white centers. The superficial flame-shaped hemorrhages also occurred without white centers, or had the white centers when first seen. Some of the white areas generally thought of as being located centrally in the hemorrhages were located at the border of the hemorrhage with only a small margin of hemorrhage on one side, and as much as one disc diameter of hemorrhage on the other. The hemorrhages varied from the smallest visible spot to one and one-half disc diameters in size. In most of the cases the hemorrhages were located near the larger retinal arteries. In one case the hemorrhages were located in the area midway between the superior and inferior nasal arteries in both eyes.

The improvement in the blood picture following transfusion did not seem to effect the appearance of hemorrhages since those showing recurring hemorrhages also showed an improved blood picture. One of the cases (A398071) showing fresh retinal hemorrhages, even with an improved blood picture, died while the retinitis was under observation.

Conclusions:

1. Transfusion does not prevent the further occurrence of hemorrhages in the retina.

2. Transfusion does not cause the retinal hemorrhages to become absorbed any more rapidly.

3. The remote effect of the transfusion is a gradual lessening of the retinal edema and decreased tendency towards the formation of hemorrhages.

4. No change occurs in the retina as an immediate effect of transfusion.

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