per day. The pain in the right foot and leg was severe at this time. Injections of the nerve by Dr. Byars, during the absence of Dr. Oatman, gave relief.

Blood counts around 8,000,000 led us to think he was improving, but apparently it was only one of the oscillations common in these cases, as the polymorphonuclears remained about 80 per cent.; lymphocytes, 12 per cent.; eosinophils, 3 per cent., and February 7 the count was 10,000,000.

The benzol was reduced on account of the poor appetite of the patient. A Wassermann test on this date was negative. His cells formed eight-ninths of the total blood mass, instead of 50 per cent., normal. The patient's corpuscles showed no hemolysis against two units of antihuman amboceptor (twice the amount necessary to hemolyze normal corpuscles) in equal volume percentage (5 per cent.). The following day on titrating the patient's corpuscles against antihuman amboceptor, in order to hemolyze his corpuscles, it was found necessary to use five times the quantity of amboceptor used to hemolyze normal corpuscles (details in accompanying table). The resistance to hypotonic solutions was found to be normal, hemolysis beginning at 0.48 per cent. saline and complete in 0.30 per cent. saline. (Corpuscles added to solutions from 0.20 per cent. salt to 0.60 per cent. by 0.01).

RESULTS OF TITRATION *

Amboceptor Units	Complement Units	Patient's Corpuscles, 5% C.C.	Result†	Normal Corpuscles 5% 0.1 C.C., Complement 1 Unit	
1	1	0.1	0	Ambo. Units	Result
1.5	1	0.1	h/2		
2.5	1	0.1	h		
4	1	0.1	hhh	4/5	hhh
4.5	1	0.1	hhhh	1	hhhh
5	1	0.1	hhhh	6/5	hhhhh

* No hemolysis with antishoop amboceptor.

† Complete hemolysis is indicated by hhhh.

‡ 2 units, hhhh, etc.

Although the theory of a greater resistance of the cells has been advanced, previous reports have not detailed any work tending to prove or disprove the idea, with the exception of the work of Guinon, Rist and Simon,¹¹ whose patient had cells showing a slightly greater resistance to hemolysis in hypotonic solutions, and the cases reported by Weber,¹² and by Lutenbacher, which were normal. However, the cell resistance in these cases was tested against dilute salt solutions, against normal serum, and antishoop amboceptor. No one tested the cell resistance to *antihuman* amboceptor. Since our case was examined, Freund and Rexford¹³ have reported a case of polycythemia in which this test was made and the cell resistance found normal.

February 16, apparently on the up curve of the red count, raw spleen was administered, from 25 to 30 gm. per day, and continued until February 25. From March 2, splenic extract, 1.3 gm. daily, was administered.

A hemolysis test, March 6, showed a resistance to antihuman amboceptor of over four times that of normal corpuscles. By March 13 only two times that amount of amboceptor was required. As the red count was stationary, the splenic extract was increased to a dose of 2 gm. a day. March 24, the hemoglobin dropped to 120 per cent., reds 8,680,000. The dose of spleen was reduced to 0.6 gm. daily until March 28. The cyanosis was almost gone, mental condition and general condition were greatly improved, and memory was good. A cystitis had become troublesome, hematuria was said to have occurred March 27, but urine examination, March 28, showed no blood, uropheins or urohematin (blood destruction). The differential count was normal.

During the time the splenic extract was not obtainable, the red count rose to over 7,000,000. April 17, 1.3 gm. of dry spleen were given daily again, the hemolytic test showed a normal resistance to antihuman amboceptor, hemoglobin was normal, and the cell count likewise. The treatment was

then discontinued for a month in order that results might be watched.

Blood examination, June 27, two months after the last examination shown on the chart (April 29), without treatment, was as follows: hemoglobin 106 per cent.; red count, 4,580,000; whites, 9,200; blood pressure, systolic, 170; diastolic, 90; differential count, normal; hemolytic resistance, normal.

COMMENT

In this case with a small spleen, the destruction of the red cells was evidently at fault, although the hyperactivity of the marrow is shown in the blood picture. The inactivity of the spleen is shown in the effect of administering extract of spleen, and in the increased resistance of the red cells to destruction by a hemolytic agent (antihuman amboceptor). It is possible that Metchnikoff's theory of causation is correct in this case, namely, that minute doses of hemolysin are being taken into the circulation, possibly from an atrophic spleen, in quantity sufficient only to stimulate the formation of red cells, and in our case, the genesis of cells of increased resistance to the hemolytic agent. This theory is supported by the fact of the several tests, and by the result of the therapy with spleen, with the idea of stimulating this organ. First there is a flattening of the curve of the red count, and the absolute reduction of the count with larger dosage of spleen; a slight increase on suspension of the extract, and prompt reduction on its resumption. Further observation will clear up this point.

Polycythemia is a very rare disease, but the opposite blood picture, pernicious anemia, is common. The present case is suggestive of new lines of work in anemia.

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THE CONTROL OF THE NAUSEA AND VOMITING OF PREGNANCY

BY INTRAMUSCULAR INJECTIONS OF CORPUS LUTEUM EXTRACT

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A preliminary report on this subject has already appeared.¹ Herewith is presented the result of further experience.

THEORY

Every woman, during the period of sexual activity, is constantly absorbing corpus luteum. No sooner is the corpus luteum of one menstruation disposed of, than another appears to take its place. With the onset of pregnancy, this absorption ceases. The corpus luteum of pregnancy constantly increases in size, until it reaches its acme about the third month. From this time on, it is gradually absorbed. The nausea of pregnancy, beginning during the period of nonabsorption, disappears about the time that the corpus luteum begins to decrease in size. Is it not reasonable to assume that this is not coincidence, but cause and effect, and that the corpus luteum plays an important part in relation to the nausea?

Based on this idea, corpus luteum extract was administered intramuscularly, with the results shown below.

CASE RECORDS

It has now been used in twenty-five consecutive cases, taken without any attempt to choose the favor-

1. Hirst, J. C.: Corpus Luteum Extract in the Nausea of Pregnancy, THE JOURNAL A. M. A., Feb. 26, 1916, p. 645.

11. Guinon, Rist and Simon: Bull. et mém. Soc. med. d. hôp. de Paris, 1904, Series 3, xxi, 786.

12. Weber, Lancet, London, 1906, ii, 1433.

13. Freund, H. A., and Rexford, W. K.: Serologic Examinations in a Case of Polycythemia, Arch. Int. Med., March, 1916, p. 415.

able or eliminate the unfavorable. It was successful in controlling the nausea and vomiting in twenty-one of the twenty-five. In four it proved a complete failure, and did not in any way check the vomiting. The essential points regarding the successful cases will be presented under the heading of dosage, as I think it unnecessary to detail the histories of the twenty-one successes. The failures offer a more interesting field:

FAILURE 1.—Primipara (Case 4 in the preliminary report), aged 24, with severe nausea, received four doses of 1 c.c. each, and was worse than ever. The nausea was finally controlled by lavage and large doses of bromid, but there was no effect from the corpus luteum. This patient has a large goiter, which may or may not be a factor in her case. She was delivered, Aug. 9, 1916.

FAILURE 2.—Quadripara with severe nausea, eight weeks pregnant, received five doses of 1 c.c. each with absolutely no beneficial effect. This patient is the only one who showed any reaction to the extract. The reaction took the form of severe hives, with intense itching, all over the body. She had had a similar reaction to an immunizing dose of diphtheria antitoxin two years previously. When she was ten weeks pregnant, she suddenly developed dysuria. On examination, a retroversion of the gravid uterus was discovered. This was replaced, and the nausea ceased almost at once. This was evidently a case of the reflex type, and certainly was not influenced by the corpus luteum extract.

FAILURE 3.—Primipara, nine weeks pregnant, farmer's wife, received twelve doses of 1 c.c. each, with no good effect. She then refused further treatment, and the nausea persisted until the fourteenth week. In this patient, there does not seem to have been any palliative of the failure, such as might be suspected at least in the first two.

FAILURE 4.—Tertipara with severe nausea, who had had similar nausea in the other pregnancies, received twelve doses of 1 c.c. each, and then treatment was discontinued as no good effect was noted. The nausea was not in the least relieved. Here also there are no palliating circumstances.

Of the successful cases, two were of the pernicious type, in which the vomiting was so severe that the termination of pregnancy was seriously considered. In one of these, fourteen doses were given (two daily, 1 c.c. each) and in the other, seventeen (also twice daily). In both, the vomiting was entirely controlled.

The smallest number of doses in any successful case was four. This patient showed such a prompt response that I am confident her vomiting was neurotic in type and would have been controlled by any method of treatment which made a similar mental impression.

The largest number of doses was forty-two. This was in Case 5 in the preliminary report. The patient had previously had two hydatid moles, so that this was her third pregnancy. There was no need of further treatment after the tenth dose, as the nausea had ceased. The treatment was continued on the chance that it might have some effect in preventing a third mole. The patient was delivered at term of a female child, Aug. 8, 1916.

The average number of doses required in successful cases was eleven.

DOSAGE AND METHOD OF ADMINISTRATION

In the average case of nausea, in which it amounts only to discomfort, and the vomiting is limited to one or two morning attacks, the patient will usually respond to a dose of 1 c.c. every other day for five or six doses. Particularly is this true in the cases in which the nausea has begun to decline. In these cases the effect is almost immediate. In the more severe cases, when nausea is constant, and the patients are

subject to frequent paroxysms of vomiting at any time during the day, the dose should be 1 c.c. daily for from twelve to fifteen doses. During the period of treatment, the patient's activity should be curtailed, and as much rest as possible is essential.

In the pernicious cases, I have given 1 c.c. twice daily, and should not hesitate to give more than this. These patients are confined to bed, of course.

The doses suggested above are average only, and I should not hesitate to give 2 or more cubic centimeters to a dose in severe cases in which a decision as to the value of the method must be reached without delay.

The site of the injection is prepared by cleansing with tincture of green soap and alcohol. The deltoid is my preference. The syringe used is glass, and it and the needle are boiled, and allowed to cool before the extract is drawn up from the ampule.

Alcohol is not a safe antiseptic to prepare a syringe for injection of any animal extract.

The site of the injection is gently massaged for a minute or two after the needle is withdrawn.

All injections are given deep, into the muscle, and *never* subcutaneously.

MATERIAL

The material used is in ampules, containing $\frac{1}{3}$ grain of soluble corpus luteum powder in 16 minims of physiologic salt solution saturated with chlorbutanol for its local anesthetic effect. This amount is equivalent to $2\frac{1}{2}$ grains of desiccated corpora lutea.

As to the sterility of this preparation, I have no misgivings. In several hundred injections, there has not been a single abscess. There is sometimes a red area around the site of the injection, for twenty-four hours, which is slightly tender, and this is less common the deeper the injection is given. A compress of alcohol and water, equal parts, promptly relieves this. Except in one case (Failure 2) there has been no general reaction and no anaphylaxis. The reaction in the case mentioned was of short duration, and occurred in a person evidently markedly susceptible. Not one of the patients aborted. This is somewhat remarkable. With the normal ratio of 25 per cent., it would not have been unusual if six had done so. Theoretically, at least, there should be some risk of abortion in the use of luteum extract, but the facts do not confirm the theory. At the very least, it can be stated definitely that the method does not add to the risk of abortion.

Another curious fact is the sedative action in markedly neurasthenic cases. Not only was the nausea improved, but also the patients' nervous phenomena. The dizziness, headache and other nervous manifestations of early pregnancy seemed to be remarkably controlled.

The percentage of success in this series (84) coincides with that of the preliminary report (80). As the cases were not selected, but taken consecutively, I see no reason why the results in a much larger number should vary far from this. It is too much to claim, in a subject so complex as the nausea of pregnancy, that any single agent should prove specific. Based on the foregoing results, however, it seems justifiable to assert that here is an important factor which heretofore has not received the attention it deserves, and it is my hope that more extended trial by the profession at large will prove that this assertion is not unfounded.

Since preparing this article additional cases have been observed, making a total of thirty-two successful cases of thirty-six studied.

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