

rum the fatality was only 3 per cent. He attributed this reduction to the use of the serum. The seven fatal cases had either peritonitis, hemorrhages or perforation.

Professor Tavel¹⁰ of Berne has also used an immune serum in the treatment of typhoid fever, which is prepared by incubating 1.5 liters of a bouillon typhoid culture for two weeks, and then adding 0.5 per cent. of carbolic acid. This kills the bacilli and releases the intracellular poisons. Two horses were injected with gradually increasing doses of this bouillon until 150 c.c. could be taken. Later mixed dead cultures of four different races of typhoid bacilli were used, and at last living mixed cultures were injected. The serum was thus made polyvalent.

Tavel¹⁰ has recorded 4 cases in which he used from three to six injections of his serum. In all of these cases the plateau stage of the fever was greatly lessened, and this was rapidly followed by the stage of decline. The pulse and respiration also fell with the temperature, and no unfavorable symptoms were noted. These four cases reached a normal temperature in 18, 20, 18, and 13 days respectively. He noted a fall of temperature often twenty-four hours after the injection of the serum, but found that a future rise of temperature had to be again combated by further injections.

Our series included 23 cases with two deaths. Autopsies were not obtained in either of the fatal cases.

CASE 1.—The first was a boy of 14, who had been in the hospital ten days when the injections were begun. He received eight doses of 10 c.c. each in four days. After the serum treatment began the boy developed a bullous dermatitis. The injections appeared to cause some decline in temperature, but in the middle of his third week in the hospital he developed otitis media followed by streptococcus septicemia, which proved fatal. (Chart 1.)

The other fatal case was seen in private practice.

CASE 2.—Man, aged 44, overfat, a civil engineer. He was seen in the beginning of his attack, having a temperature of 100 degrees.

Treatment.—Two days later his blood gave a distinct and prompt Widal reaction, and on the following day serum treatment was begun. His urine was not examined before the first dose of serum was injected, but was found to contain albumin and casts immediately after. He received in five days six doses of serum, 90 c.c. in all. After the third injection of serum the temperature began to drop and we were inclined to think that good results were to follow, but the temperature rose to 103 degrees on the thirteenth day in bed and the fifth day after the last injection. Intestinal hemorrhages appeared on the fourteenth day in bed. There were several copious losses on this day. Two days later hemorrhage reappeared, and on the night of the nineteenth day in bed he died.

Among the 21 cases ending in recovery, there were 15 in which we considered that the influence of the serum contributed to the favorable result. The temperature charts of 10 of these cases are shown. The cases in which no effect for good or evil was observed were 6 in number, and one of these is illustrated by a temperature chart.

One of the distinctly favorable cases was that of a young married woman of 23, who was six and a half months' pregnant. She aborted on the evening of the day when the first injection was given, but completed her defervescence in fourteen days. (Chart 2.)

One of the cases admitted to Johns Hopkins on the fourth day in bed was defervescing in ten days after admission, or on the fourteenth day in bed. No unfavorable effects on the kidneys or blood were reached

by urinalysis or blood counts in any of the cases. The average period from admission to defervescence was in thirteen favorable cases, 12.6 days.

The laboratory experiments coincided with the clinical observations that the immune hog serum is not hemolytic for human blood. In one or two instances we encountered discouragement from associated clinicians who feared injury to the kidneys or hemolysis from the use of such large amounts of serum. In one case we stopped the serum in deference to the suspicion that it caused collapse. This patient was a sailor who came to the City Hospital in an exceedingly feeble state, having had diarrhea on ship board for two weeks. He was exceedingly depressed after each bath. The use of serum was, however, resumed after an interval of days, though tubbing was not resumed. The case appeared to be one of those favorable to the use of the serum.

CONCLUSION.

In conclusion, we believe that by the use of this serum the febrile period may be shortened, and the daily variation may be favorably modified.

DISCUSSION.

DR. CHARLES C. YARBROUGH, Detroit—In the experiments on hogs, was any air injected? If so, what results were observed from it?

DR. WILLIAM ROYAL STOKES—As we could not always shut off the injection just at the moment because it went in under rather heavy air pressure, air certainly got in; we noted an emphysematous condition of the tissues at times, but we did not see the slightest unfavorable results. It is hard to kill a hog.

DR. CHARLES C. YARBROUGH—The general opinion among the profession is that the injection of air is very dangerous. The average physician is very careful when he makes hypodermic injections, especially injections of serum, to see that every particle of air is expelled from the syringe before making the injection. A large number have a great dread of injecting even the minutest quantity of air. This dread, I believe, is wholly unfounded.

DR. JOSEPH MCFARLAND, Philadelphia—I have intentionally injected air under the skin of 16,000 guinea-pigs without noticing any unfavorable result. I did that in order to drive out of the hypodermic syringe every particle of mixture of diphtheria toxin and antitoxin in order to test the value of it.

LEAD POISONING.

A STUDY OF THE GASTRIC CONTENTS IN TWELVE CASES.*

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Last winter during my service at Blockley a patient was admitted suffering from severe intestinal colic due to chronic lead poisoning. In the hope of obtaining some information on the nature of the colic, a test-meal was obtained, and the findings were so interesting that, at my suggestion, my resident physician, Dr. John Speese, obtained test-meals of all the cases of lead poisoning that were available during the rest of the winter. The results were so nearly uniform that it seems unlikely that a more extended series of investigations will show any material difference. The technic was as follows: Usually with, sometimes without, a preliminary washing, the patient was given a test-meal of two slices of bread and about twelve ounces of water. One hour after the patient commenced eating, the stomach contents were withdrawn by aspiration, measured

10. Tavel: Schweizerisches Serum und Impf.-Inst., März, 1899.

* Read before the medical section of the College of Physicians.

and tested for free acid with Congo red, then filtered and examined. The total acidity was tested with decinormal soda solution, using phenolphthalein as an indicator, the first permanent pink being employed to determine the degree of acidity. Free hydrochloric acid was tested for qualitatively by Congo red and phloroglucin vanillin, and quantitatively by dimethylamidoazobenzol occasionally using Günzberg's reagent as a control. Lactic acid was tested for with Uffelmann's reagent, using the reaction produced in another tube with a dilute solution of lactic acid for comparison. Pepsin was estimated by a slight modification of Hammerschlag's method, as follows: The white of one egg (about 30 cm.) was dissolved in 1,000 c.c. of 0.4 per cent. HCl. To 10 cm. of this solution 5 cm. of filtered gastric juice were added, and to another 10 cm., 5 cm. of distilled water. The tubes were plugged, placed in the incubator for one hour, and the percentage of albumin estimated by centrifugation after precipitation with acetic acid and potassium ferrocyanid, according to Purdy's method. Hammerschlag's method has been subjected to a considerable degree of criticism, and has been as warmly defended. Undoubtedly, it does not give accurate, merely approximate results, but no method hitherto devised for the estimation of pepsin that is clinically applicable does any more than this. As a clinical test it certainly seems satisfactory. Dr. Speese and Dr. Lvenson performed it nearly 200 times last winter on different cases of gastric disease, and in nearly all instances it conformed very closely to what would theoretically have been expected. Most conservatively estimated, it suffices to show at least three degrees of peptic digestion, i. e., "none," "little" and "much," and its most enthusiastic supporter will hardly claim that the range of error is less than 10 per cent. in either direction. It can not, therefore, be considered scientifically accurate, but absolute accuracy is not essential. In all cases microscopic examination was made for the presence of the Oppler-Boas bacillus, and wherever possible the blood stained for basophilic degeneration, but this, unfortunately, could not be done in every case. The cases are as follows:

CASE 1.—J. S., male, aged 26, Russian, a painter. A satisfactory history was not obtainable. The symptoms were a blue line on the gums, constipation, abdominal pain and vomiting. Blood: Hemoglobin, 68 per cent; white blood cells, 5,000; red blood cells, 3,100,000. Granular degeneration of reds present.

GASTRIC ANALYSIS.		
	First.	Second.
Total acidity	17	10
Free HCl	Absent	Absent
HCl deficit	10	13
Lactic acid	Present	Present
Pepsin	50%	20%
Oppler-Boas	Negative	Negative

CASE 2.—P. C., male, aged 40, leadworker. He had lead colic four years ago, when he stopped working in lead; he returned to it three weeks ago, with a recurrence of symptoms. These were constipation, pain in the abdomen, blue line on the gums and nausea.

GASTRIC ANALYSIS.		
	First.	Second.
Total acidity	10	
Free HCl	Absent	
HCl deficit	10	
Lactic acid	Present	
Pepsin	8%	
Oppler-Boas	Negative	

CASE 3.—T. M., aged 44, white, paint mixer. He had had lead poisoning in 1899 and a second attack in 1902, with wrist-drop, which became bilateral in 1904. There was abdominal pain, constipation, fetid breath, a blue line on the gums, and wrist-drop. After one hour's digestion of an Ewald meal,

3 ounces were recovered containing some undigested food, mucus and blood.

GASTRIC ANALYSIS.		
	First.	Second.*
Total acidity	10	16
Free HCl	Absent	Absent
HCl deficit	18	14
Lactic acid	Present	Present
Pepsin	Absent	Absent
Oppler-Boas	Negative	Negative

CASE 4.—F. R., aged 44, white, Ireland, a painter. He had had several previous attacks of lead colic and on admission complained of pain in the abdomen and constipation. There was a blue line on the gums and anemia. The blood showed granular degeneration of red blood cells. The Ewald meal was given; one hour's digestion; two ounces withdrawn containing a few particles of undigested food, no blood nor mucus.

GASTRIC ANALYSIS.		
	First.	Second.*
Total acidity	10	16
Free HCl	Absent	Absent
HCl deficit	18	14
Lactic acid	Present	Present
Pepsin	Absent	Absent
Oppler-Boas	Negative	Negative

* Second admission with same symptoms.

CASE 5.—W. R., aged 43, white, leadworker. The symptoms were anemia, constipation, a blue line on the gums, and, in addition, acute mania. The blood showed granular degeneration of the red cells.

GASTRIC ANALYSIS.		
	First.	Second.*
Total acidity	6	
Free HCl	Absent	
HCl deficit	8	
Lactic acid	Present	
Pepsin	6%	
Oppler-Boas	Negative	

CASE 6.—J. C., aged 42, white, painter. The symptoms were a blue line on the gums, constipation, abdominal pain, anemia and weakness in the muscles of the arms.

GASTRIC ANALYSIS.		
	First.	Second.
Total acidity	13	
Free HCl	Absent	
HCl deficit	18	
Lactic acid	Present	
Oppler-Boas	Negative	

CASE 7.—T. R., painter, aged 26, Philadelphia. The patient had never had symptoms of lead poisoning, although he had worked at this trade for several years. He was somewhat anemic, slightly constipated, and had a blue line on the gums. He was admitted with pneumonia, and a test meal was given as an experiment. It was retained for one hour and two and a half ounces withdrawn; it was white in color and the digestion was complete. There was no blood but some mucus.

GASTRIC ANALYSIS.		
	First.	Second.
Total acidity	34	
Free HCl	25	
Lactic acid	Absent	
Pepsin	100%	
Oppler-Boas	Neg.	

CASE 8.—J. C., ward 5. He has been a lead worker for several years, although there is no history of a previous attack. He complained of pain in the abdomen, constipation: there was a blue line on the gums, loss of power in the left arm, with some atrophy of the muscles, but no wrist-drop. There was granular degeneration present in the blood; reds, 3,600,000; whites, 6,000. Toast and water, one hour's digestion, one and a half ounces recovered, partially digested, no blood, no mucus. On washing, a considerable amount of food was recovered.

GASTRIC ANALYSIS.		
	First.	Second.
Total acidity	14	9
Free HCl	Absent	Absent
HCl deficit	14	10
Lactic acid	Present	Present
Pepsin	Absent	Absent
Oppler-Boas	Suggestive	

CASE 9.—E. S., aged 34, white, lead burner. He had never had any previous attack of lead poisoning. The symptoms began several weeks before admission. He first noticed constipation, followed by severe abdominal pain centering at the umbilicus. There was a blue line on the gums, loss of power in the left arm and hand, but no wrist-drop. He has worked

steadily at his trade for the past sixteen months. Toast and water given, digestion one hour. About an ounce recovered, consisting of a few particles of undigested food, but no blood or mucus. On washing a small amount of undigested food was recovered.

GASTRIC ANALYSIS.

	First.	Second.
Total acidity	12	11
Free HCl	Absent	Absent
HCl deficit	12	5
Lactic acid	Present	Present
Oppler Boas	Negative	
Pepsin		7%

The blood showed degeneration of the red blood cells.

CASE 10.—M. H., aged 46, white, Ireland. He has worked in lead and brass. He had lead poisoning one and a half years ago. Three months ago he developed pain in the abdomen, weakness in the arms and legs, and a blue line on the gums. The active symptoms of lead poisoning have disappeared, and the chief trouble at present is due to paralysis and weakness of the muscles of the arms. No granular degeneration in the blood. Ewald meal, one hour digestion, three ounces recovered. Some undigested food and mucus, but no blood.

GASTRIC ANALYSIS.

Total acidity	9
Free HCl	Absent
HCl deficit	8
Lactic acid	Present
Pepsin	23%
Oppler-Boas	Negative

CASE 11.—J. F., white, aged 42, Ireland. He had lead poisoning five years ago, and has been a lead worker at intervals for the past seven years. He complains of general weakness, pain in the abdomen, headache, vertigo, anorexia and weakness of the wrists. Ewald meal, one hour digestion; watery contents and undigested food. No mucus or blood.

GASTRIC ANALYSIS.

Total acidity	9
HCl deficit	9
Lactic acid	Present
Pepsin	Absent
Oppler-Boas	Negative

CASE 12.—G. E., white, aged 39, Sweden. He had been a lead worker for three weeks; he had been very careless about his habits. He developed severe abdominal pain, which was present on admission, constipation, and had a slight blue line on the gums. His appearance was anemic. Blood: Hemoglobin, 61 per cent.; red blood cells, 3,290,000; white blood cells, 11,800. Basophilic degeneration of the red cells. Ewald meal, one hour digestion. Slight amount of mucus, some undigested food, and no blood, regained. Two ounces recovered. On washing a considerable amount of food was recovered.

GASTRIC ANALYSIS.

Total acidity	35
Free HCl	8
Lactic acid	Negative
Pepsin	40%
Oppler-Boas	Negative

SUMMARY OF GASTRIC ANALYSES.

No.	Total Acidity.	Free Acid.	HCl Deficit.	Lactic Acid.	Peptic Digestion.	Oppler-Boas.	Granular Degeneration.
7	34	25	0	0	100%	Neg.	
12	35	8	0	0	40%	Neg.	Present.
1	17	0	10	Present.	50%	Neg.	Present.
1	10	0	13	Present.	20%	Neg.	
2	10	0	10	Present.	8%	Neg.	
3	8	0	12	Present.	10%	Neg.	
4	10	0	18	Present.	0	Neg.	Present.
4	16	0	14	Present.	0	Neg.	
5	6	0	08	Present.	6%	Neg.	Present.
6	13	0	18	Present.	0	Neg.	
8	14	0	14	Present.	0	Sug.	Present.
8	9	0	10	Present.	0	Neg.	
9	12	0	12	Present.	7%	Neg.	Present.
9	11	0	5	Present.	0	Neg.	
10	9	0	8	Present.	23%	Neg.	Absent.
11	9	0	9	Present.	0	Neg.	

These twelve cases fall naturally into two groups, the first comprising Cases 7 and 12, and the second, Cases 1 to 6 and 8 to 11, inclusive. Case 7 may be dismissed briefly. It is probably not a case of lead

poisoning, the only symptom being the blue line on the gums, which is occasionally seen on workers in lead apparently as a result of a deposit of dust containing lead on the mucous membranes. His gastric analysis was practically normal. Case 2 was evidently one of acute lead poisoning. The man had only worked in lead for three weeks; the symptoms were moderate, but the basophilic degeneration of the reds may be accepted as proof that intoxication had occurred. The gastric analysis showed a mild degree of subacidity, and a rather pronounced reduction in the activity of the pepsin. The remaining 10 cases are all examples of achylia gastrica, or of subacidity with reduction of the pepsin. Altogether, 14 test-meals were obtained, which gave the following results:

SUMMARY OF TEST MEAL RESULTS.

The total acidity varied from 6 to 17; the average was 11. Free hydrochloric acid was absent in every analysis.

The deficit of hydrochloric acid varied from 5 to 18; the average was 11.5.

Lactic acid was present in every case. No quantitative estimations were made.

The peptic digestion was absent in three cases. It was 50 per cent. of normal in the first test meal of the first case and 20 per cent. of normal in the second test meal of this case. In Case 10 it was 23 per cent. of normal and in the remaining cases it varied between 6 per cent. and 10 per cent. of normal.

The Oppler-Boas bacillus was not found. In Case 8 it was reported as suggestive but the mere finding of a few long, thick bacilli can not be regarded as indicating its existence, at least not in the typical manner that occurs in carcinoma.

The red blood cells were stained for basophilic degeneration in seven cases. In six cases it was present (Cases 1, 4, 5, 8, 9 and 12), and in one case it was not found (Case 10).

In the cases of achylia and subacidity abdominal pain was noted in every case excepting the fifth.

The blue line on the gums was present in every case excepting the eleventh.

Constipation was present in eight cases; anemia in four.

One patient had vomiting, and one complained of nausea.

Unfortunately, the absence of symptoms was not noted, and it is impossible to be sure that these statistics are accurate. Lead encephalopathy was present in one case; weakness of the arms, sometimes amounting to wrist-drop, was present in six cases.

The duration of these cases was fairly long. Four of them had had previous attacks at various intervals up to nine years. In two cases the duration was not noted excepting the statement "for some time;" in all the others the duration was a year or more.

I have made a careful study of the literature in order to discover confirmation of these investigations, and have been unable to do so. I have gone in vain through the *Archiv für Verdauungskrankheiten*, including the abstracts from the literature, and through most of the recent text-books on the subject. Von Jaksch fails to mention it. It seems to me curious, in view of the pronounced digestive symptoms produced by lead, that this is the case.

Of course, a small series of cases is not decisive, but it seems fair to expect that in the majority of cases of chronic lead poisoning, or intoxication, disturbance not only of the gastric secretion, but (when they can be tested) of other forms of secretion, will be found. It is one of the misfortunes of the present day in clinical medicine that we have no means of obtaining the pancreatic secretion; but the salivary secretion may be obtained, and I hope to investigate it in a subsequent series of cases.

The mechanism by which this alteration of secretion is brought about is not clear. Whether it is merely a

functional disturbance of the glands, or whether there is actually some anatomic alteration, is not known. I have been entirely unable to obtain portions of the stomach from a fatal case of lead poisoning in order to determine this point, but the opportunity will certainly arise in the course of time.

The only conclusions that are at present justifiable appear to be:

1. In a series of 12 cases of lead poisoning, or suspected lead poisoning, there was deficiency in the secretion of HCl in 10 of the chronic cases, and no deficiency in 2, one of which was doubtful and the other acute.

2. This deficiency in the secretion of free HCl in the majority of cases is associated with an extreme reduction in the percentage of peptic digestion, and with the presence of lactic acid.

3. It is not justifiable at present to regard it as an indication for treatment, at least not until the effects of the ordinary treatment for achylia gastrica in cases of lead poisoning have been tested.

BRAIN HEMORRHAGE.*

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While brain hemorrhage is not of common occurrence, it happens with sufficient frequency to make its discussion of more than passing interest to the general practitioner. In this paper I shall take into consideration only those cases which are the result of degeneration of the arterial tunics.

Degenerative changes in the coats of the blood vessels were noticed and commented on in the early days of medicine by Lobstein, who gave it the name by which it has since been known—arteriosclerosis. Morgagni and Senac also speak of it. To Rokitsky and Virchow and, more recently, to Thoma we are indebted for a thorough investigation of the nature of the process, which I shall not take the time to discuss. I shall assume that the pathologic changes in arteriosclerosis and atheroma are practically the same—differing only in degree. In the small arteries of the brain substance we find minute aneurismal pouches caused by the gradual giving way of the diseased coats. As these blood vessels possess no true outer coat, their dilatation under the combined influence of disease and increased blood pressure becomes an easy one. Of capillary hemorrhages following the plugging of a vein I shall not speak, and while hemorrhage from a vein may occur, hemorrhage is practically always from an artery. It will not be amiss, I think, but profitable to notice at the outset some of the causes that lead to changes in the coats of the blood vessels. These alterations may result from a multiplicity of conditions, some of which are fairly well understood, while others are decidedly obscure. When we think of arterial degeneration, we are too prone, I fear, to picture to ourselves an old man who has lived his allotted time on earth and in whom decay and deterioration are plainly visible in every body cell. This is a fatal error. Arterial degeneration may and often does take place, from causes we can not well fathom, in those who are comparatively young; and that it does

occur in these cases is patent to all who have had a fairly wide clinical experience.

That the consumption of large quantities of alcoholic beverages is a potent factor in bringing about this degeneration has been recognized for years. It is true that not all who use alcohol in its various forms have disease of the arterial coats, but it is found too frequently in this class of cases to be more than a mere coincidence. Not only does this poison affect the blood vessels, particularly of the brain, but also, in consequence of the effect of the alcohol on the glands and mucous membrane of the stomach and liver, poisons of varying degrees of intensity and non-oxidizable in character are found circulating in the body fluids, and we have this secondary cause added to the primary, with greater or less disease in the coats of the blood vessels.

I am satisfied that among business men, weighted with the responsibilities of large enterprises, who think long and persistently and yet drink constantly, these phenomena are most marked and come on earliest. At the last session of the American Medical Association, Cabot¹ of Boston read a paper in which he brought forward statistics to prove that alcohol is not the potent factor in the production of arterial degeneration that it is supposed to be; and yet the experience of the profession as a whole lends color to the belief that alcohol is, both directly and indirectly, a cause of this condition. Indeed, those who do not use alcohol in any of its forms but who lead a strenuous life, with but little freedom from worry and anxiety and with practically no exercise, become prematurely old and have premature vascular decay. In these cases, in some mysterious way, chemic or otherwise, toxins are developed which slowly but nevertheless surely bring about arterial degeneration. Or it may be, as has been suggested by Romberg, that the irregular blood pressure caused by an unstable and overwrought nervous system is the cause.

Next to alcohol as a factor in the production of these pathologic changes stands syphilis, and like alcohol its evil effects are seen in a most pronounced way in the blood paths of the brain. The syphilitic poison, whatever it may be, interferes with the nutrition of the walls of the blood vessels, destroying in a measure their elasticity, and thereby allowing them to become weakened and dilated. In some cases we may find both alcohol and syphilis operating as causes, as in a case I have under observation now.

In brain hemorrhage, chronic interstitial nephritis with its unknown antecedents should always be thought of and looked for, and is next in importance to the causes I have already assigned. In this disease, as prominent symptoms there are marked changes in the walls of the blood vessels, increased peripheral tension, followed by cardiac hypertrophy with its augmented potential energy. Whether the degeneration of the blood vessels is primary and the kidney lesion secondary or vice versa, I can not say. It is certain that toxic substances circulating through the blood and not eliminated by the kidneys, must sooner or later produce this form of degeneration. Indeed, these poisons bring about destructive changes in the kidneys in the same manner as in the coats of the arteries.

It is within the range of possibility that an increased activity on the part of the suprarenal glands may be a cause of greater or less intensity in the production of arteriosclerosis. Just to what extent this is operative as a cause can not be definitely stated, as it will require

* Read at a meeting of the Northwestern Ohio Medical Association at Tiffin, 1904.

1. THE JOURNAL, Sept. 17, 1904, p. 774.