one places on animal experimentation. All advances that have been made in the subject of rabies have depended on animal experimentation. It may interest the zoophilists to know that the sacrifice of a few dogs and rabbits in the study and prevention of rabies has been the means of saving the lives of many times their number of dogs, horses, cattle and other animals from this disease.

PLAGUE

The plague bacillus has certain cultural morphologic characteristics, such as a stalactite growth on bouillon, bipolar staining, and involution forms on salt agar; but this organism, which is the cause of the great black death, cannot be recognized with certainty except through animal experimentation. Kolle's method consists in rubbing a little of the suspected material on a shaved patch of skin (about the size of a dime) of a guinea-pig. If plague bacilli are present and virulent the animal contracts the disease in a few days. This method of diagnosing the disease is the foundation on which the preventive measures were carried out in California in the recent successful plague campaign. Animal experimentation is indispensable in the recognition of this disease as it occurs in man, the rats, the squirrel and other animals.

It was entirely through animal experimentation that sanitarians were given the useful knowledge that plague is transmitted from rat to rat and from rat to man through the agency of the flea. With the ability to diagnose the disease with certainty and with a correct knowledge of the channels of infection, suppressive and preventive measures may now be carried out with every assurance of success.

DIPHTHERIA AND TETANUS

The diagnosis of these two diseases may be made tentatively without the use of animal experimentation, but in this, as in many other such instances, appearances are deceiving and we must resort to tests on the lower animals in order to be sure of our diagnosis. The diphtheria and tetanus toxins cannot be recognized except by their effects on animals, and the same is true of the antitoxins. There is a whole group of organisms that look like and grow like the diphtheria bacillus, and are known as "pseudodiphtheria" bacilli. The shape and growth of the tetanus bacillus also is not distinctive enough to be final. We must, therefore, resort to animal experimentation in order to establish the identity of these organisms and the diseases which they produce.

SEPTICEMIA AND PYEMIA

The diagnosis of these conditions, which are commonly known as blood-poisoning, frequently requires animal experimentation. Our knowledge of these conditions, on which is based aseptic surgery and the modern treatment of wound infections, has resulted in large measure from experiments made on animals.

It is not possible in a few pages to specify all the instances in which animal experimentation serves a useful purpose in the recognition of disease; but in addition to the foregoing it plays a more or less important part in the diagnosis and prevention of pneumonia, dysentery, Malta fever, anthrax, glanders, actinomycosis, and a large class of maladies due to microparasites.

Further, it must be plain to anyone who gives the matter careful consideration that animal experimentation has not only been potent in preventing much suffering and saving many a human life, but it has been even more active in the realm of the lower animals. A more

exact knowledge of the causes and channels of infection and the methods of diagnosis of the communicable diseases of the lower animals has resulted in intelligent and humane efforts to conserve the health and comfort of our live stock. A full exposition of this subject is presented elsewhere, and mention is here made of only such epizootics as glanders or farcy, symptomatic anthrax or black leg, actinomycosis or lumpy jaw, anthrax or spenic fever, tetanus, swine plague, chicken cholera, hog cholera, Texas fever and foot-and-mouth disease.

Kipling says:

The doctor is exposed to the criticism of persons who consider their own undisciplined emotions more important than mankind's most bitter agonies; who would cripple and limit research for fear research might be accompanied by a little pain or suffering. But if the doctor has the time to study the history of his own profession he will find that such persons have always been against him—ever since the Egyptians erected statues to cats and dogs on the banks of the Nile.

Present Address: Department of Preventive Medicine and Hygiene, Harvard Medical School, Boston.

THE SIGNIFICANCE OF EHRlich'S ALDEHYD REACTION IN THE URINE*

OSCAR BERGHAUSEN, A.B., M.D.

Member of the Laboratory Staff of the Cincinnati Hospital
CINCINNATI

About eight years ago Ehrlich first noticed that normal urine gave a faintly reddish coloration when treated with a muriatic acid solution of paradimethyl amino benzaldehyd; and that this coloration was remarkably intensified in certain pathologic conditions. To Otto Neubauer¹ is due the credit of having isolated the particular chemical substances causing the reaction, proving that it was caused by pyrrol derivatives present as urobilinogen substances, the product of the metabolism of blood pigments; and, reasoning inversely, he came to the conclusion that the blood pigments themselves were derived from pyrrol derivatives rather than indol substances, as upheld by Nenki. He, furthermore, contended that these urobilinogen substances, mother substances from which the urobilin was formed, were present in increased amounts when there was an increased breaking down of blood pigments, especially in malaria, lead colic, lobar pneumonia, lung infarct, venous thrombosis, liver diseases and some infectious conditions.

The object of the present investigation was to determine the clinical value of the reaction, since it is so readily and easily carried out. Undoubtedly the determination of the urobilin in the urine would be more satisfactory, as recently contended by Hildebrandt,² since by his method of treating the urine with zinc acetate all urobilinogen substances are converted into urobilin, so that both substances are determined at once, whereas the aldehyd reagent shows only the presence of urobilinogen, its action on urobilin causing no change in color. The present investigation was begun some nine months ago, since which time the work of Conner and Roper³ and Hildebrandt² has appeared. My

* From the laboratory of the Cincinnati Hospital.

* Read in the Section on Pathology and Physiology of the American Medical Association, at the Sixtieth Annual Session, at Atlantic City, June, 1909.

1. Neubauer, Otto: Sitzungsber. d. Gesellsch. f. Morphol. u. Physiol. in München., 1903, No. 2, xix, 32.

2. Hildebrandt: München. med. Wchnschr., April 6, 1909, p. 710.

3. Conner, L. A., and Roper, J. C.: Arch. Int. Med., Jan. 15, 1909, ii, 532.

observations so clearly verify many of the observations and predictions of the former writers that their publication seems necessary.

The question of the origin of the urobilinogen and urobilin naturally is brought up, and the various theories for the production of the same called to mind, namely, the enterogenous, hepatogenous, hematogenous, histogenous and renal theories, recently so well summed up by the writers referred to. At the outset it may be stated that my observations would tend to support the enterohepatogenous theory, namely, that under normal conditions the reduction of the biliary pigments into urobilinogen and urobilin takes place in the intestines, in accordance with the views long since expressed by F. Müller and Otto Neubauer, and that a pathologic urobilinuria or urobilinogenuria results when the liver is insufficient; that is, when it is unable to excrete an increased amount of urobilinogen or urobilin when absorbed from the intestines, or when, through disturbances in the liver itself, it is unable to excrete a normal or even deficient amount of these substances. In infections of the liver evidence would point to the fact that these substances may be locally formed in the liver itself. Although the histogenous theory can not be discarded, it would seem that the chief organs concerned ordinarily are the intestines and the liver.

CLINICAL APPLICATION

The reagent used was prepared as follows:

Twenty grams of paradimethyl-amino-benzaldehyd were dissolved in 1,000 c.c. of dilute muriatic acid, made by diluting 150 c.c. of the chemically pure acid to 1 liter with distilled water. To about 5 c.c. of cold urine taken soon after being voided, because long standing causes a conversion of the urobilinogen into urobilin through the action of air and sunlight, 5 to 10 drops of the reagent were added. The mixture was shaken and allowed to stand a minute or two. Normal urine gave a varying coloration, which was intensified to a distinct cherry-red color on heating, usually associated with a peculiar pungent odor. Neubauer asserts that the urobilinogen represents various substances, ranging in structure from $C_8H_{13}N$ (hemopyrrol) to $C_{32}H_{40}N_4O_7$ (urobilin itself) and that the more sensitive give the reaction in the cold, the less sensitive only on heating. When the reaction is distinctly scarlet in the cold, a pathologic condition of the urine is present. Experiment soon showed that the intensity of the reaction varied, even in the normal urine, and the following scheme of recording results was adopted:

A negative result, i. e., maintenance of the original color of the urine, or a yellowish coloration after adding the reagent was reported as —0; a faint reddish color only obtained on looking through the whole columns of urine in the test-tube from above, as +1; when the mixture presented a pinkish or faintly reddish hue, on looking at it from in front, as +2; when a distinctly scarlet coloration was obtained, it was recorded as +3; which intensity of reaction alone is of any pathologic significance.

Examination of my own urine through a period of twenty-five days showed that the reaction varied from one day to the other, but that it never assumed a +3 reaction in the cold, but always on heating. From this it was assumed that an apparently normal individual with a properly functioning liver was able to preserve a urobilinogen balance; that is, the liver was able to excrete these substances derived from the intestines, only allowing a trace to appear in the urine. It may

be possible that in cases of severe constipation, or so-called torpid liver, even in an apparently normal individual, the reaction might approach +3 in intensity, but if this condition persists following free purgation, undoubtedly a pathologic condition is at hand.

The reaction was next applied to the urine of a series of nearly 200 cases taken from all wards of the City Hospital; the tables show the distinct degree of reaction obtained in many of these cases. First, as to the color of the urine: This was recorded in a total number of 107 cases. Of the 74 light-colored urines examined:

13 (17.5 per cent.) reacted + 3
9 (12.4 per cent.) reacted + 2
10 (13.5 per cent.) reacted + 1
42 (56.6 per cent.) reacted — 0

Of the 33 cases of dark-colored urine examined:

13 (39.4 per cent.) reacted + 3
5 (15.1 per cent.) reacted + 2
2 (6.1 per cent.) reacted + 1
13 (39.4 per cent.) reacted — 0

This shows conclusively that the positive reaction was more commonly found in dark-colored urines, 21.9 per cent. more than in light-colored urines, but that it also occurred quite frequently in the latter. In the dark-colored urines a negative reaction was correspondingly less frequent—17.2 per cent. less. On the whole, then, the reaction is independent of the color of the urine, being more common, however, in dark-colored urines.

TABLE SHOWING DEGREE OF REACTION IN ABOUT ONE HUNDRED AND FIFTY HOSPITAL CASES

Clinical Diagnosis.	No. Cases.	Reaction			
		+3	+2	+1	—0
Acute lobar pneumonia.....	17	7	2	1	6
Malaria.....	2	2	.	.	.
Scarlet fever.....	5	.	.	.	5
Acute articular rheumatism.....	12	5	.	2	5
Typhoid fever.....	10	1	3	1	5
Influenza.....	5	2	.	1	2
Erysipelas.....	2	.	.	.	2
Simple pulmonary tuberculosis.....	5	.	1	1	3
Complicated pulmonary tuberculosis.....	2	2	.	.	.
Appendicitis.....	3	.	.	2	1
Pelvic cellulitis.....	2	.	2	.	.
Tonsillitis.....	2	.	1	.	1
Pus tubes.....	4	.	.	1	3
Endometritis.....	1	.	.	.	1
Cystitis.....	2	.	.	1	1
Cirrhosis of liver.....	2	1	.	.	1
Carcinoma of liver.....	1	1	.	.	.
Miliary abscess of liver.....	1	1	.	.	.
Catarrhal jaundice.....	4	2	.	.	2
Myocardial insufficiency + edema.....	8	5	2	.	1
Pleurisy with effusion.....	5	4	.	.	1
Pericarditis + diaph. pleurisy.....	2	.	.	.	2
Pleurisy dry adhesive.....	3	.	2	.	1
Acute nephritis.....	5	1	.	2	2
Uremia.....	1	1	.	.	.
Chronic nephritis.....	5	.	.	.	5
Abortion.....	3	.	.	.	3
Shot wound of chest.....	1	.	.	1	.
Shot wound of abdomen.....	1	.	.	.	1
Shot wound of kidney.....	1	.	.	1	.
Ruptured abdominal aneurism.....	1	.	.	.	1
Fracture femur.....	1	.	.	1	.
Hemorrhoids.....	2	.	.	.	2
Venous thrombosis.....	1	.	.	.	1
Syphilis.....	2	.	.	.	2
Lead colic.....	1	.	.	1	.
Trichiniasis.....	2	.	.	1	1
Diabetes mellitus.....	5	.	1	.	4
Chronic alcoholism.....	2	.	.	.	2
Carbolic acid poisoning.....	1	.	.	1	.
Diabetes insipidus.....	2	.	.	.	2
Burn cases.....	4	.	.	.	4
Morphinism.....	3	1	.	.	2
Senile dementia.....	1	.	.	.	1
Dementia paralytica.....	1	.	1	.	.
Neurasthenia.....	2	.	.	.	2
Melancholia.....	1	.	.	1	.
Acute gastritis.....	1	.	1	.	.
Acute bronchitis.....	4	1	.	.	3

To sum up: The reaction is most commonly obtained in diseases of the liver, myocardial insufficiency with edema, pleurisy with effusion, and acute catarrhal jaundice, all conditions in which the proper elimination of the urobilinogen through the liver after absorp-

tion from the intestines is interfered with; furthermore, in some infectious conditions, as lobar pneumonia, malaria and articular rheumatism. An absence of a pathologic reaction has been conspicuous in more or less localized septic states, as pelvic abscess, pus tubes, tonsillitis, simple pulmonary tuberculosis, acute bronchitis, erysipelas, dry pleurisy and pericarditis, despite the increased temperature.

In this series of cases the absence of the reaction in typhoid fever and scarlet fever is to be noticed. In localized extravasations of blood following shot wounds, or rupture of aneurism, no increase in the intensity of the reaction is to be noticed. Convalescence from a condition in which the reaction was marked was followed by a return to the normal; thus, in both cases of malaria, the quick response to quinin treatment was followed by a disappearance of the reaction. In incipient cases of disturbed myocardial insufficiency, and in suspected cases of gallstone trouble with a clear history and response to treatment, the reaction was not present. Undoubtedly a positive reaction which persists, in these cases, would indicate a marked disturbance, either in the production of the urobilinogen in the small intestines plus increased absorption or a disturbance in the eliminating power of the liver. It must be borne in mind that one section of the liver may be involved and yet the remainder may be efficient, as was demonstrated in one severe case of syphilitic cirrhosis of the liver in which the reaction was negative, though a diminished formation in the intestines may have been present. The reaction is not a constant one, even in those conditions most commonly the cause. That a positive reaction may be of some assistance in suspecting liver involvement was shown in a case of miliary abscess of the liver following infectious thrombophlebitis.

CASE 1.—The patient, a young man, first showed symptoms of appendicitis; later localized peritonitis developed, at which time the reaction was + 2 in intensity. These symptoms subsided, but later increased temperature plus tenderness over the gall bladder made the attending physicians suspect gall bladder or liver involvement. The urine showed a positive aldehyd reaction in cold, and the presence of leucin and tyrosin in the urine. Operation was resorted to for suspected cholecystitis. At operation the gall bladder was apparently normal and cultures taken proved negative. The patient collapsed suddenly on the table.

Autopsy.—This revealed an enlarged liver, studded throughout with miliary abscesses along the portal tract evidently, and an infectious thrombophlebitis. Cultures from the portal vein and abscess areas both showed the presence of diplococci and a colon-like organism, evidently the result of infection following absorption from the originally involved appendix.

Clinically this case beautifully demonstrates what Fischler⁴ showed experimentally on animals, namely, that under certain conditions urobilin can be formed in the liver itself. He made biliary fistulas in dogs draining the bile to the outside, and then injected amyl alcohol and phosphorus into the gall bladder. The liver became involved, and urobilin again appeared in the urine; with the subsidence of the condition, it again disappeared. In my case the liver itself became involved through infection along the portal tract.

EXPERIMENTAL DATA

Since Muller reported the interesting fact that when the common bile duct becomes occluded the urobilin disappears from the urine, the German school has adhered to the enterogenous theory as to the origin of

the urobilin, namely, that when the bile is poured into the intestines and is subjected to the action of the reducing bacteria, urobilin is formed and absorbed from the intestines; it is again excreted through the bile and, to some extent, through the urine. Bile usually contains some urobilin. Neubauer¹ later asserted that occlusion of the common duct would also be followed by absence of the urobilinogen in the urine, bile and intestines, and that this might be shown by a negative aldehyd reaction in the urine, both in the heat and cold. Kimura⁵ showed that normal bile always contained urobilinogen, using the aldehyd reaction and the spectroscopic to detect the absorption band.

With the object of verifying this fact through animal experiment the following investigations were made: It was found that normal rabbit urine reacted toward the aldehyd reagent exactly as does the normal human urine. Rabbits were therefore used, and each experiment conducted under ether anesthesia. Ether was given in minimal amounts, and never exceeded 30 minutes. In two instances the animals died within a few hours following the operation, but no changes beyond the normal were found in the urine.

EXPERIMENT 1.—Male rabbit. The common bile duct was ligated with silk and the operation wound closed. The animal died eighteen hours after operation.

Urinalysis.—Urine before operation, negative in the cold, + 3 on heating. After operating the urine taken from the bladder soon after death was reddish. Aldehyd reagent caused a negative reaction in the cold, the reddish color of the original urine soon disappearing on adding the reagent. On heating a brownish precipitate formed, but no scarlet color developed. The cold urine was then heated, filtered, and the reagent added after cooling. Reaction was + 1, on heating no increase in the intensity of the reaction. The urine, drawn before operation and preserved on ice in the dark, when added to the catheterized specimen immediately caused a scarlet coloration on heating with the reagent.

Autopsy.—This, made about twelve hours after death, showed abdominal wound perfect, no escape of bile, liver enlarged, congested, apparently bile-stained. Common duct ligated, severe congestion from this point upward. The aldehyd reaction negative in the heat and cold, but not confirmed by spectroscopic examination. Kidneys both showed an acutely congested appearance.

EXPERIMENT 2.—Male rabbit; common duct ligated and operation wound closed. The animal died thirty-six hours after operation.

Urinalysis.—Urine after operation showed a negative reaction in the cold, and + 1 on heating. Addition of the urine obtained on the previous day before operation caused intense reddish coloration on heating with the reagent.

Autopsy.—Thoracic organs normal. Abdomen showed an early localized peritonitis, immediately below the operating wound. Liver was bile-colored, gall-bladder dilated.

These experiments both show that occlusion of the common duct is early manifested by a decided alteration in the normal reaction. On heating with the reagent only the faintest trace of a reddish color was noticed. On adding the normal urine, however, the color immediately became scarlet, showing conclusively that the urobilinogen had practically been eliminated; in reality none had been formed, because the action of the reducing bacteria in the intestines had been excluded. The fact that the reaction on heating was still recorded as + 1 would show that, as late as thirty-six hours after the second experiment, there was still a slight trace of urobilinogen present, which no doubt was due to residual urobilinogen in the tissues, this time interval not being sufficient to cause complete elimination from

4. Fischler: Das Urobilin u. seine klinische Bedeutung, Thesis, Heidelberg, 1906.

5. Kimura, T.: Deutsch. Arch. f. klin. Med., 1904, lxxix, 274.

the system. Several experiments were made of infecting the gall bladder above the point of constriction, in order to observe, if possible, the reoccurrence of the scarlet color, due to changes in the liver through bacterial action. No results were obtained, however.

Complete occlusion of the common bile duct is therefore followed by a negative reaction, both in the cold and in the heat, after adding the aldehyd reagent to the urine. There immediately occurs to one the possibility of using this fact as a means of diagnosis in cases of total obstruction of the duct through a stone, through inflammatory changes in the mucosa, or by compression from without through any source. Are these the only conditions which can cause this change in the reaction? Kimura⁵ has shown that in severe diarrheas a similar condition is obtained, owing to the fact probably that no bile can be reduced in the intestines under such a condition, or absorption becomes impossible. We must further conceive of the possibility of a patent ductus venosus, allowing of the discharge of bilirubin into the intestines, although occlusion of the duct be present. In the newly born the same condition is obtained, because bacterial reduction has not as yet begun.

In my list of clinical cases two other conditions were encountered, which gave a similar result.

CASE 2.—Infant, female, aged 17 months, died eight days after acute phosphorus poisoning caused by eating matches. The urine examined before death had unfortunately been standing from thirty to thirty-six hours before the aldehyd reaction was tried. It was, however, found negative both in the heat and the cold. Tyrosin was also found in the urine.

Autopsy.—Made about four hours after death; showed a somewhat enlarged liver, distinctly fatty. Heart showed beginning endocarditis. Intestines were somewhat congested. Microscopic examination of the liver showed distinct fatty changes and round-celled infiltration about the vessels; the liver cells were poorly stained and fat globules numerous. The urine obtained at autopsy showed a negative aldehyd reaction both in the heat and the cold.

CASE 3.—Clinical diagnosis, transverse myelitis. An operation had been performed to relieve any supposed compression of the cord about at a level with the fifth dorsal vertebra, since a distinct traumatic history was given. No relief followed. Immediate operation, however, was successful from a technical standpoint. The patient sank rapidly from incontinence of both urine and feces, and at last refused to eat, so that exhaustion ultimately resulted in death. For several days previous to death profuse hemorrhages occurred from the lower bowel.

Autopsy.—There was found an extremely fatty liver, chronic interstitial nephritis, and hemorrhagic condition of the lower colon. The urine obtained at this time likewise showed a negative reaction in the heat and cold.

In both these cases it may be argued that postmortem changes in the urine caused these variations in the aldehyd reaction from the normal. Among numerous cases examined after death, however, these two cases were the only ones which presented such a condition. Hildebrandt believes that in severe phosphorus poisoning the general destruction of the liver would lead to such findings. He has no direct evidence to support his views, however. Case 2 was undoubtedly one of acute phosphorus poisoning, and tyrosin was found in the urine; bile could not be detected by the nitric acid or iodine tests. Before death, however, the stools were very frequent, quite pale, and grayish in color. To what extent the profuse diarrhea was instrumental in causing the negative urobilinogen reaction can not be definitely told. Likewise, in Case 3, frequent diarrheic stools were present before death, and in addition a severe hemorrhage from the bowel on repeated occasions. In both cases, however, the liver showed marked fatty de-

generation, which would tend to support the views of Hildebrandt. In the future severe anemias may be shown to react in a similar way, because of the lessened destruction of blood pigment in late stages.

In phosphorus poisoning the variety, whether acute or chronic, must also be taken into consideration. Harnack⁶ has recently shown experimentally that in acute cases following injection of phosphorus into the stomach rapid degeneration and fatty changes are produced in the liver. In more chronic cases, as when subcutaneous injections of phosphorus in oil are given, the degenerative changes in the liver are still present, but not so intense as in the more acute cases, inflammatory reactions on the part of the liver being more common. Therefore, it may be possible that in chronic phosphorus poisoning the destruction to the liver substance may not be so intense as to lead to a total absence of urobilinogen in the urine, as indicated by a negative aldehyd reaction in the heat and cold.

The animal experiment was again called into play, to shed, if possible, some light on this subject.

EXPERIMENT 3.—A male rabbit was given phosphorus in oil mixed with the food. About six hours later it began to show signs of being ill, and died some time during the night.

Urinalysis.—Before operation, at which time the bladder was emptied, the urine showed a negative reaction in the cold, and a positive reaction on heating. The urine, withdrawn from the bladder some time after death, showed a similar reaction.

Autopsy.—Stomach full of food, phosphorus fumes still escaping. The most dependent part of the organ showed an escharotic-like condition of the mucosa. The liver was not particularly enlarged, was distinctly mottled on section, but did not present a fatty appearance. Microscopically the liver showed distinct cloudy swelling of the cells, round-celled infiltration about the vessels, and engorgement of the capillaries. No fatty globules could be detected. The kidneys were enlarged and had a congested appearance.

The above experiment did not result in such marked fatty changes as to lead to a complete obliteration of the urobilinogen in the urine. It is possible that the death occurred too rapidly for such changes to be caused, and that a more gradually induced toxemia would have produced the desired result. To establish this point a second animal was used for experiment.

EXPERIMENT 4.—A male rabbit was given phosphorus in oil per mouth. On the three succeeding days the urine was normal in reaction, i. e., negative in the cold and positive on heating. On the fourth day more phosphorus was fed. On the day following the reaction was + 3 in the cold, distinctly positive. This persisted for five days, when more phosphorus was given per mouth. On the following day the reaction was negative in the cold, and a brownish coloration only developed on heating. Twenty-four hours later the reaction was negative in the heat and cold. The animal now showed signs of considerable weakness and suffering, and was killed by chloroform anesthesia.

Autopsy.—The liver was somewhat contracted, pale yellow, with a mottled appearance on section. The liver was still firm. Microscopically there was almost total obliteration of the liver cells; those remaining were pale with poorly stained nuclei. Numerous fat molecules were distributed throughout. There was round-celled infiltration about the vessels, and seemingly a beginning formation of connective tissue. The stomach was full of undigested food. The small intestines were nearly empty, the large intestines packed with ordinarily formed stools. The bile was thin, light greenish in color, and showed a negative aldehyd reaction in the cold and in the heat.

In this instance the destruction of the liver substance had been so great that no bilirubin was offered to the intestines for reduction. All stages of the reaction were also beautifully demonstrated, varying from

6. Harnack, E.: München. med. Wehnschr., March 2, 1909, p. 436.

the normal to a relatively and at last an absolutely deficient liver as indicated on successive days by the changes in the aldehyd reaction.

CONCLUSIONS

The clinical value of the aldehyd reaction obtained by adding the reagent to cold, freshly passed urine, and then noticing the changes in the color, at first in the cold and then on heating, is manifest, though limited at times.

The color reaction in the cold is of pathologic significance only when a distinct scarlet color is obtained.

When the reaction persists following free purgation a pathologic condition is at hand.

The reaction is most commonly present in diseases of the liver and bile passages, severe grades of myocardial insufficiency, and certain infectious conditions, as lobar pneumonia and malaria.

The reaction is not a constant one, even in apparently severe grades of the above conditions, presumably because the liver is still efficient in excreting any normal or increased amount of urobilinogen offered it.

Localized infections are more seldom accompanied by this reaction, and when it does persist in such conditions the condition of the intestines and liver should be taken into consideration.

In early grades of myocardial insufficiency of gall-stone trouble, and of liver disturbances the reaction is often a negative one. The appearance of the reaction in such cases previously negative would arouse suspicions of disturbances in the hepatic function; inversely, the disappearance of a reaction previously positive would indicate improvement.

The positive reaction is not constant in localized extravasations of blood into the tissues.

When the reaction is positive some care must be exercised in the selection of an anesthetic for operations, since it is well known that chloroform, for instance, can be a direct liver poison.

The absence of the reaction, both in the heat and in the cold, would indicate obstruction in the flow of bile into the intestines.

This condition is also obtained in cases of severe diarrhea, in the newly born, and in severe grades of destruction of the liver substance.

In conclusion I wish to express my indebtedness to the medical and surgical staff officers of the city hospital for their kind permission in allowing me to use the material at hand, to the internes—more particularly Drs. Light, Schlanser, Monroe and Mussey—also to Dr. A. E. Osmond, without whose kind assistance and skill much of the experimental work would have been impossible.

19 West Seventh Street.

CRATÆGUS OXYACANTHA *

THOMAS F. REILLY, M.D.

Professor Applied Therapeutics, Fordham University
NEW YORK

Two years ago my attention was called to this agent and since then I have used it rather extensively in order that I might satisfy myself if it had the therapeutic value claimed for it by the sectarian schools. It has been in use by the homeopathic and eclectic schools for some years, but the mass of therapeutic legends sur-

rounding it has deterred physicians of a scientific turn of mind from believing that it was likely to have any efficacy. Originally it was the secret of a quack in the south of Ireland, who by its use is said to have achieved an extensive reputation for the treatment of heart disorders throughout the British Isles. On his death he bequeathed the secret of his successful practice to his niece (if we can believe the romantic story told). She, in a true womanly spirit, could not or possibly would not keep a secret and thus made it known to medical science.

There are only two articles concerning this agent in the regular medical literature. One, Dr. Jennings¹ of Chicago, in 1896 found it such a cure-all for all cardiac complaints that the profession must have judged it to be good for none. Two years later Dr. Joseph Clement² extolled *Cratægus oxyacantha* as a sovereign remedy for angina pectoris; the article attracted no comment. In the homeopathic literature there are a number of small articles in the main grossly exaggerating its virtues and consequently of little scientific value. The homeopathic physicians use it for its drug (physiologic) effect just as they would use digitalis or quinin and not according to their so-called provings, in homeopathic doses.

For that reason the dosage in their literature is somewhat like ours. The eclectic physicians employ it quite extensively and it has been kept prominent largely through their efforts and through the work of the pharmaceutical houses of that school.

It is derived from the ripe fruit of the hawthorn (*Cratægus oxyacantha*). These berries are eaten by some people as a fruit. They must be gathered after the first frost. By some pharmaceutical houses the American species (*Cratægus coccinea*) is used and is thought by some observers to be quite as efficient as the *oxyacantha*. Concerning this the eclectics disagree. A reliable fluidextract or tincture is the best preparation. It has a fruity odor with a rather pleasant taste, is seldom rejected by the stomach, and so far as observed has no cumulative effect. Thus far the active principle has not been isolated, nor have its physiologic properties been determined by animal experimentation.

Some work of this kind is now under way at the physiologic laboratory of Fordham University and will be reported on at a later period. Thus far my own experience with it has been entirely clinical in character and has seemed to warrant its use in some of the cardiac neuroses.

The following cases are illustrative of a type sometimes benefited by this agent:

CASE 1.—*Patient*.—Mrs. M., aged 33, quintipara, negative family history, for the past eight years has had hay asthma. During the last four years she has been having frequent attacks of pain and distress in the cardiac region. In these attacks the patient thinks that she is going to die. At times they are associated with syncope; sometimes they are continuous for weeks. Physical examination during the attack is negative except for a slight lateral enlargement of cardiac dulness and a pulse of 90. There are no evidences of exophthalmic goiter. These attacks bear no relation to disorders of the gastrointestinal tract.

Treatment.—All sorts of cardiac tonics and stimulants seem to increase the trouble. Bromids quiet the nervous system and lessen the apprehension but do not affect the cardiac disturbance. The addition of *cratægus* in 20-minim doses gave the first complete relief in four years. The relief has been permanent as far as the attack was concerned, and whenever the

* Read in the Section on Pharmacology and Therapeutics of the American Medical Association, at the Sixtieth Annual Session, held at Atlantic City, June, 1909.

1. Jennings: New York Med. Jour., Jan. 14, 1906.

2. Clement, J.: Kansas City Med. Recorder, April 7, 1898.