The lead soaps which were insoluble in ether were decomposed with acid in the presence of ether and the fatty acids obtained by removal of the ether. The residue was liquid indicating a very incomplete removal of the unsaturated acids. The fatty acids were taken up in a small amount of alcohol and placed in an ice-salt mixture. A few crystals came out of solution, however, not in sufficient amount to determine the melting point.

Extraction of Fatty Oil with Ether.—Four hundred and forty-six Gm. of seeds supplied by Prof. Richtmann were finely pulverized, sifted and repulverized in an iron mortar. The powder was then placed in a large Soxhlet extractor and exhausted with ether. After recovery of the ether, the extract was found to weigh 132.5 Gm. = 29.7 p. c. S. V. 206.0 and 207.8, respectively. Specific gravity determined with a pycnometer 0.9217 at 25° C. The refractive index (Zeiss) was 1.4840 at 23° C.

The U. S. P. method for the I. V. determination having given unsatisfactory results a larger amount of iodine was used; in the first experiment 40 cc. in place of 25 cc. and in the remaining determinations 50 cc. In this manner concordant results were obtained, *viz.* 207.0, 207.7, 207.4 and 207.3, respectively.

X-RAY CONTRAST MEDIA.*

BY BERNARD FANTUS, M.S., M.D.

The miracle of looking into the interior of the body, of examining and photographing almost each and every one of its major structures has been accomplished by reason of the selective absorption of the Roentgen rays by various tissues of the body; and, where this is insufficient, the introduction of contrast media. These latter are of interest to the pharmacist, as he may be called upon to prepare and supply a number of these.

The great difference in the absorptive power of various materials can best be comprehended by an understanding of the law, that *the absorption of X-rays by media is approximately proportional to the fourth power of the atom number of position of the element in the periodic system.* Table I may serve as a basis for the illustration of the truth of this "law."

TABLE I.—ATOM NUMBERS OF ELEMENTS OF PRACTICAL IMPORTANCE.

Hydrogen	1	Chlorine	17
Carbon	6	Bromine	35
Nitrogen	7	Iodine	53
Oxygen	8	Barium	56
Phosphorus	15	Lead	82
Calcium	20	Bismuth	83

Hence an atom of calcium with its atom number of *20*, absorbs about 40 times more X-rays than an atom of oxygen with its atom number of *8* for:

$20^4 : 8^4 :: 160{,}000 : 4{,}096$, equals approximately *40*.

From this it will be seen that the absorptive power increases enormously as we proceed down the scale.

* October meeting of Chicago Branch, A. PH. A.

The great difference in absorptive power of various elements in accordance with this proposition may also be visualized by noting (Table II) how many atoms would be required to produce the same degree of absorption as one atom of oxygen.

TABLE II.

1 atom of chlorine equals	20 atoms of oxygen.
1 atom of iodine equals	2,000 atoms of oxygen.
1 atom of barium equals	2,400 atoms of oxygen.
1 atom of bismuth equals	10,000 atoms of oxygen.

The absorptive power of a chemical compound may be calculated by the addition of the atom number of the various elements composing it. Hence most of the tissues of the body, composed as they are of various proportions of the light elements: carbon, oxygen, hydrogen and nitrogen—which do not differ much from each other in atom number—show no difference in absorptive power among each other, or from wood or other organic material. The bones, on the other hand, containing calcium, show a marked difference in absorptive power as compared with the soft parts. Calcium is the natural contrast medium of the body. The artificial contrast media take advantage of the absorptive power of elements of high atom number, such as iodine and barium.

The absoptive power of a body is, of course, not only dependent upon the kind of atoms it is composed of; but also upon the number of atoms per unit space: its density or specific gravity. Hence gas absorbs much less than fluids or solids. Table III gives some idea of the differences in specific gravity:

TABLE III.

Air	0.0013
Fat	0.94
Water	1.0
Soft parts, blood, bile, urine	1.01 to 1.06
Cartilage	1.09
Bone	1.9

From this it will be seen that the difference between the absorptive power of water and the soft tissues is so slight that layers of equal thickness would be practically indistinguishable. The difference between bone and the soft parts is greatly increased by the atomic absorptive power of calcium. The difference between air and the soft parts is enormous: approximately 1000. Hence air or other gas is a good contrast medium.

AIR.

The presence of air in the lungs makes it possible to visualize most of the contents of the chest without the artificial introduction of contrast medium. By reason of the air contained in it, the normal lung is transparent; and, against this background, the heart can be seen with startling distinctness beating away for dear life. Sufficiently advanced diseases of the heart or lung can now be seen, thanks to X-rays, as distinctly as deformities or blemishes on the face. The root structures of the lung—bronchi, large blood vessels and lymph glands—cast somewhat of a shadow because they contain less air; and, when diseased, can be seen much more plainly than when normal, because of the thickening of the tissue. We can see the diaphragm ascend and descend in respiration by reason of the heavy shadow cast by the liver; and adhesions of the diaphragm can be readily made out by irregularity in its naturally well-rounded dome. As "seeing is believing" the actual demonstration of abnormalities to the eye makes us feel so much more certain about them than the indirect methods of percussion and auscultation we formerly had to rely on.

The air cavities or sinuses in the head stand out so clearly against the denser bone, that it is possible to detect accumulations of pus or filling up by tumors in any of them.

Bold indeed must have been the mind that first conceived the idea of blowing air into the ventricles of the brain, as contrast medium, to make photography of the interior of the living human brain (ventriculography) possible. Though not frequently resorted to, it is at times an important means of localizing brain tumors.

The Roentgen rays have shown us that there is generally a large bubble of gas in the human stomach. People who complain of "having gas on the stomach" merely feel what the rest of us have without feeling, just as people who complain of palpitation merely feel the heart beat, when ordinarily we do not feel this motion. We all know there is gas in the bowel; and by means of it portions of intestine become outlined in normal, X-ray pictures. Particularly extensive accumlation of gas may suggest intestinal disease or obstruction; and this can, at times, be verified by inflation of the bowel with air introduced into it through the rectum. Should rupture of the stomach or bowel occur with escape of gas into the peritoneum, the presence of free gas above the liver may be detected by Roentgen rays when its quantity would not be sufficient for detection by other means. At times oxygen is intentionally introduced into the peritoneum to demonstrate the presence of adhesions and other abnormalities. When this is done properly, the gas is soon absorbed, without untoward results.

Sometimes air is injected into the tissues around a solid organ, for instance the kidney, which may be of considerable help in the diagnosis of kidney tumors.

BARIUM SULPHATE.

At the other extreme of opaqueness stands barium sulphate, which has become so important as a Roentgenographic medium that it is now official in the United States Pharmacopœia. It finds its chief use in the outlining of the shape and location and in the study of the functions of the alimentary tract.

When a person drinks a barium suspension, one can see, by proper posturing before the Roentgen screen, how the gob slides down the gullet with surprising rapidity. Hesitation at any one point means abnormality there. By making the paste thick enough so that it goes down *very* slowly, one can obtain a silhouette of the esophagus which may demonstrate disease in it or its surrounding structures.

To see the intact human stomach working on a meal is a sight our grandfathers dared no more think feasible than flying. It is, nowadays, commonplace in the X-ray laboratory. We can see its size, shape, location, movements and rate of emptying. One can see deep constriction waves pass over it, forcing the contents toward the pylorus and beyond; flicking, at short intervals, a small portion of them into the first part of the duodenum which generally assumes the shape of a little cap, and is therefore spoken of as the "cap of the stomach." Ulcers and cancers and other abnormalities in these tissues can now at times be recognized with almost the same certainty and clearness with which we can see ulcer or cancer of the skin.

The rate of progress of the meal through the bowel can be followed with scientific precision. By the sixth hour, the meal has normally left the stomach, most of it has passed through the small intestine excepting the last portion of the ileum and has entered the cecum and ascending colon. It is just as surprising how rapidly the meal passes through the small intestine, about 4 or 5 times the length of the body, as it is how slowly it travels through the colon, which is only about as long as the body. Normally within 24 hours most of it, and within 48 hours all of the barium has been eliminated. Abnormally, we find it sticking in the cecum for two or three or more days. This is frequently due to adhesions in the vicinity of the appendix from previous attacks of apppendicitis, or adhesions at the hepatic flexure from gall-bladder or pyloric inflammation. Stagnation here is often associated with spasm of the distal colon, due—no doubt—to the contents in the proximal colon becoming so irritating as to stimulate the distal colon to spasmodic contraction. This establishes a vicious circle in that spasm of the distal colon, increases stagnation in the proximal colon, and the more the contents stagnate the more rotten and irritating they become. To remedy this condition is one of the problems of intestinal housecleaning, we call catharsis. When I was a pharmacist, I thought I knew all about securing operations of the bowel. Now I hesitate to prescribe a cathartic in cases of chronic constipation without a preliminary X-ray examination, because only in this way can I decide with a moderate degree of confidence what remedy to employ. Sometimes there is no delay anywhere excepting in the last part of the large intestine, the rectum; and for this form of constipation enemas are the proper treatment. Even though the bowels move every day, constipation, *i. e.*, retention in the proximal colon, may be present.

The appendix can often be visualized. The place where it is attached to the bowel, the cecum, can always be seen; and the question whether a pain or a tenderness is located in the appendix or elsewhere decided. The appendix should empty itself; when it does not, a "potentially pathologic appendix" is reported.

Barium suspension is also used as an enema; and with it the large bowel can often be filled from beginning to end; and the filling defects from tumors and other abnormalities accurately determined.

The best mode of administration of barium sulphate for stomach and bowel visualization is a strictly pharmaceutical problem. As this heavy substance tends to sediment rapidly, a gum or other colloid is required to keep it in suspension. There is no general agreement, as yet, as to which suspending medium is best. Many roentgenologists administer the barium in buttermilk or in malted milk. Neither of these is ideal from the standpoint of pleasantness. It is poor technic to inflict an unpleasant dose upon a patient, when it might be given in really palatable form. The most pleasant vehicle for the barium, I know of, is a hot cup of cocoa. There seem, however, to be practical difficulties in having this ready at the right temperature at just the right time. So we have experimented with other disguises, and are now giving it sweetened with sugar and flavored with orange; and patients seem to take it without dislike.

An interesting modification of the problem of introducing contrast medium is in connection with fistulas, *i. e.*, abnormal passages leading to some focus of pathology, the body is attempting to eliminate, but often unable to do so. Injecting fluid or semi-fluid contrast medium may succeed in satisfactorily outlining the tract. More convenient because dispensing with the necessity of a syringe; and often more efficient, because injection is less likely to reach the all important end of the passage, is the introduction of bougies of contrast medium that pharmacists may prepare in accordance with the following formula:

Bismuth Tribromphenate (Xeroform) 5%	1.0
Barium Sulphate	10.0
Cacao Butter	10.0

Make into bougies 8 mm. long and 2 to 3 mm. wide.

One after the other of these little rods is gently and cautiously inserted into the fistula by means of a sterile forceps; the attempt being made to push the previously inserted one further in by means of the next one. This is continued until the melted contrast medium escapes liberally from the fistula opening, which is then sealed with a small wad of cotton and a bit of adhesive plaster.

HALOGEN COMPOUNDS.

Because of their high absorptive power for the X-rays and their relatively low toxicity and irritative action, iodides and bromides, most especially of sodium or potassium, have been used as contrast media, *e. g.*, for showing the interior of the kidney, ureters or bladder. At present, 15 per cent solution of sodium iodide and 25 per cent sodium bromide solution seem to enjoy preference, and give at times remarkable results in clearing up the nature of abdominal or lumbar pain.

A number of halogenated oils, such as lipiodôl, iodipin, bromipin, etc., are advantageously used as contrast media for the demonstration of abnormalities in various cavities, passages and tubes of the body. Brominized oils are less liable to give rise to undesirable side effects than iodized oils; but, they do not give as dense a shadow.

Spectacular is the effect of injection of halogenated oil into the trachea, while posturing the patient so that the fluid flows by gravity into that portion of the bronchial tree one desires to explore. It is possible in this way to obtain pictures of lung cavities and of dilated bronchi for the guidance of lung surgery.

Even more heroic is the injection of halogenated oil into the spinal canal. Lipiodol (poppy seed oil containing 54 per cent of iodine) has been used with success in the diagnosis of tumors or obstructions of the spinal canal. Injection of 3 cc. of lipiodol into the upper end of the spinal canal (cisterna magna injection) with the patient in the sitting posture is followed by the prompt fall of the substance to the bottom of the spinal canal. If there is an obstruction in the canal, *e. g.*, by a tumor, the lipiodol will stop at the upper border of the obstruction. By combining lipiodol with olive oil, a so-called light lipiodol is obtained, which, upon injection into the lumbar region of the spinal canal, flows upward. The lower border of the spinal tumor may also be outlined; and surgical removal of it directed most precisely.

Halogenated oil has been injected into the urethra to help in the diagnosing of strictures and other obstructions there. It is also possible to inject it into the seminal vesicles and to obtain pictures of these.

In the diagnosis of sterility in the female, injection of such oil into the uterine cavity and tubes is of great help. One can detect thereby, whether the Fallopian tubes are patent: as, when they are, drops of oil escape into the peritoneal cavity from which they are absorbed without harm.

Oil of this kind has been injected for the purpose of ascertaining the point of obliteration of the blood vessel in thrombosis or embolism. It has also been used for injection into fistulas, wound cavities, and into the accessory sinuses of the nose.

TETIOTHALEIN.

The very acme of romance in achievement is the visualization of the human gall-bladder by means of the Roentgen-rays after introduction into the system of a substance that circulates through the blood, is picked out of it by the bile which thereby becomes opaque to the Roentgen-rays. The reason this is possible is the fact that the bile is a very good solvent for fats and substances soluble in fats. When a body of just the right degree of lipoid solubility gets into the circulation, it is picked out by the liver and eliminated in the bile, no doubt, by a mechanism similar to that which the chemist uses when alkaloids are "shaken out with ether." Of quite a large number of substances that might qualify for this service and have been tried, tetraiodophenolphthalein has been found the best; and the Council on Pharmacy and Chemistry has adopted the abridged name, "tetiothalein" for it, by which it had better be known rather than some of the proprietary names such as "iodeikon."

This is a very feeble acid insoluble in water which like other phenolphthaleins becomes soluble in alkali with which this compound strikes a beautiful purple color. The administration of the free acid in its ordinary form has merely a cathartic action analogous to that of phenolphthalein. When it is dissolved in alkali, it is so strongly irritating by reason of free alkali as to cause vomiting. It is for this reason that Graham who deserves most credit for the development of this method has resorted to intravenous administration of the dye for the purpose of securing gall-bladder visualization. As the intravenous injection is not only somewhat troublesome, but also very liable to cause undesirable and sometimes alarming side effects, a good deal of experimentation has been undertaken to make its oral administration possible. Enteric coating was the first attempt in this direction. Unfortunately absolutely dependable enteric coating has not yet been devised. Sometimes some of these capsules do not dissolve in the intestines and at other times open up in the stomach and are rejected by vomiting. In either case, the purpose of the administration is defeated, no gall-bladder shadow being obtained. It was at this stage that I undertook experiments with the view of freeing the dye from its irritant qualities which I believed and now know to be due to the alkali required to keep it in solution. I reasoned that a preparation of the substance in the form of a colloid which is the next thing to a solution might at one and the same time give us a non-irritating and still readily absorbable administration form. By precipitating a dilute solution of the dye with a very feeble acid, such as carbonic acid, such colloid precipitate can be obtained and I found that it met the requirements very well. The result of my studies at this stage were published in the *Journal of the American Medical Association* of July 16, 1927, where a formula for the preparation of the colloidal tetiothalein may be found. Unfortunately this preparation was unstable and I have since then experimented upon ways and means of securing a more stable preparation, and I was efficiently helped in this endeavor by the Abbot Laboratories. We have finally succeeded in reducing the bulk of the dose to the size of a two-ounce bottle and in giving it sufficient stability for practical purposes.

In the course of our experiments we tried a powder form of such composition that the tetiothalein was precipitated upon admixture with water. We found that, under these circumstances, the precipitate was not sufficiently colloidal to secure satisfactory absorbability and good gall-bladder shadow. Nevertheless, since the publication of my experiments on this substance, two powder preparations appeared upon the market, both of which make use of extemporaneous precipitation, which, unfortunately is hardly more than 50 per cent efficient. It may be of interest in this connection to state that we had an opportunity to experiment with mechanically produced colloidal tetiothalein and that this proved practically unabsorbable.

When tetiothalein is injected intravenously or has been successfully administered by mouth and the subject fasts, in course of hours the gall-bladder becomes filled with bile that casts a denser and denser shadow—the density increasing due to absorption of water from the bile and consequent thickening of it. In this manner pictures of the gall-bladder can be obtained by means of the X-rays and not only the size, shape and position of the gall-bladder determined or the presence or absence of gall-stones ascertained, but also its functional quality studied. For, when a meal rich in fat is taken, the shadow disappears normally more or less completely in two hours. Persistence of the shadow, therefore, much beyond this period means abnormality of the function of the gall-bladder.

From all this it will be seen that Roentgenography, the infant among the diagnostic medical procedures, is bidding fair to outstrip all others; and that artificial contrast media have increased its extent of applicability to an almost unbelievable degree.

METHOD FOR TESTING ANTISEPTIC DYES.

BY GEORGE F. REDDISH, PH.D.

In a previous publication, the writer (1) outlined laboratory methods for determining the efficiency of various kinds of antiseptic preparations. The methods described constituted an attempt to simulate to some degree at least the conditions met with in practice. It is, of course, impossible to duplicate practical conditions closely, but these methods do constitute a distinct attempt to approximate practical use as nearly as reasonably possible and consistent with laboratory practice. In devising these tests, the use for which the various antiseptic preparations are intended, the character of the preparation and the method of application were deciding factors in determining the laboratory procedure for each. All that is required of an antiseptic is that it render the pathogenic microörganisms innocuous when it is applied to infected tissue surfaces.

In the paper referred to above (1), page 495, the writer made the following statement:

"There are types of antiseptic preparations and methods of application by means of which infective organisms are merely held in check and not actually killed by the chemical agent used.