Administration officials have been able to suggest analytical problems representative of practical conditions. A few examples are cited:

The qualitative detection of methenamine and cinchophen in mixtures.
The assay of calomel and soda tablets.
The assay of calomel and bismuth tablets.
The assay of phenacetin and salol tablets.
The determination of barbital and related compounds in elixirs.
The assay of ampuls of sodium cacodylate.

SUMMARY.

The Food, Drug and Insecticide Administration, apart from its strictly regulatory functions, aids Pharmacy by maintaining a Unit for collecting, codifying and distributing information on the analysis of drugs; by coöperating with the Association of Official Agricultural Chemists, and with the Combined Pharmaceutical Contact Committee of the American Drug Manufacturers' Association and the American Pharmaceutical Manufacturers' Association in research on methods for the analysis of drugs; by aiding in the revision of the Pharmacopœia of the United States; and by furnishing information to inquirers about new, rare or little used drugs.

L. L. Walton assumed the term "Drug" was used by the author in the legal sense. He also asked the author for a list of the drugs for which assay processes are to be studied.

THE CHEMISTRY OF NATURE.*

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After interesting remarks relating to friends and members of the ASSOCIATION and the section of the country and city in which the meeting convened and a reference to his experience in pharmacy, Dr. Mayo said:

"I am intensely interested in the scientific side of medicine. Long ages ago, the doctor of the period knew such science as was known. As knowledge through investigation progressed, science became specialized along many lines. Linnæus took up botany two hundred years ago, and science gained from the study of his work. When Aristotle had claimed, hundreds of years before, that two bodies of equal size, but of different weight, would not fall with the same rapidity, it was thought true. Long afterward Galileo said they would fall with the same rapidity and he was threatened with being burned at the stake because it was against religious teaching. Under his breath he said, 'It is so, just the same'. I think that showed what kind of a man he was. Some men are pleased to become martyrs, but you need to have a tremendous lot of religion to be a martyr to-day.

"About 1686 study of single cells began. The existence of non-motile bacteria was not appreciated, but there were certain types of single cells that had motion. It was 1818 before any scientist attributed disease to bacteria and recognized that diseases could be reproduced by bacteria. There was no broadcasting of scientific

* Part of an address before the AMERICAN PHARMACEUTICAL ASSOCIATION, Rapid City, South Dakota, August 30, 1929.

thought of that type until Pasteur, in 1857, published his first papers. He had been working on diseases of plants and animals, and finally studied diseases of human beings, reproducing and predicting what would occur. From that time medicine took on new life. Surgery became safe when Lister acquired new ideas as to wound infection and the cause of hospital gangrene. Death following operation was often proved to be caused by bacteria, and it was found that they could be controlled. It is of interest that bacteria were the first chemists of the world, dissolving and acting chemically on soils to develop solutions of those substances needed for growth of plants, and different types of roots were nourished by means of different types of bacteria, although several types of plants might have overriding roots. These bacteria, each particular type depending on the kind needed for the growth of the plant, fed upon the root slime. There are about twelve to fourteen elements in plants, because plants antedate animal life and made animal life possible.

"Chemistry in nature is merely the transforming of one form of matter to another; it is concerned with either the field of activity of life or with any chemical change in non-living substances. Everything that goes on is founded on chemistry; even the action of sunlight on the cell is chemical. Water once covered the earth, and its first action was to hold in solution and suspension the material that could be dissolved. Nature, in building up the outer shell of the earth, has found it easier to split the water to get hydrogen and oxygen than to obtain them any other way; so the water has gradually disappeared, although three-fourths of the earth is still covered with water, so there will be plenty for our time.

"This surface we see in the Black Hills with its calcium and shale, on down to the granite. The types of animal life represented by fossilized bodies, that now are to be seen in the School of Mines, take one back millions of years and add wonderfully to the scientific interest of the present era.

"The first cell in the world had to be a chemical cell. With chlorophyl, came action from light, and everything is dependent on the light and warmth of the sun. It is of interest, to-day, to find limestone in process of formation just as in the Cambrian period of the world's history. Around Australia and the South Sea Islands, and around Florida bacteria may be found working within thirty feet of the surface of the sea, dependent on light and warmth. These colonies of microbes are gathering calcium out of the sea and depositing it as mud. One notes, as one looks at great upheavals of limestone in mountains, or in stone quarries, and sees the thickness of the early layers of it, how much calcium there must have been in solution, and what a nuisance it was becoming, until special bacteria came into the world to gather and deposit it as limestone. As the invertebrate life of the pre-Cambrian period came to die it left the history of its life in these fossilized remains which to-day are found in the limestone. The layers represent periods of growth of the world's surface. When we see lime, we can think of bacterial life. If it is gathered in shell form it is merely the smaller type of shell life; but little of calcium is in crystallization. It is returning to the sea constantly and being formed again and again. There is an interesting area near New Iberia, Louisiana, a half mile from the Gulf of Mexico. Within half a mile of it are round, raised domes fifty feet high and forty acres in extent, each of which is almost pure salt under fifty feet of earth.

"They bored two thousand feet and found only pure salt and beneath the salt found twenty feet of wood. Salt had been deposited at that depth on a forest and had continued there for ages. Beneath the three feet of sand of the Great Salt Lake in Utah are seventeen feet of sulphate of soda, a deposit. North of Duluth are regions of iron. When we realize that salt in masses was gathered from sea water, when we know that calcium is being made by certain types of bacteria, then we can imagine something of bacterial life, acting as a chemical agent taking out the various elements from the sea and gathering masses of them together. Sea water contains gold, one grain to a cubic yard; this gold may be obtained, but it costs too much to get it. It makes us think of the old alchemists who tried to make gold from quicksilver. If quicksilver is bombarded by means of activity from a Crooke's tube and the eightieth electron of quicksilver is knocked out, the seventy-nine left are then gold. It would cost thirty thousand dollars an ounce to make gold in this way and it would be easier to earn it in other ways. Of the ninety-two elements we know all but number 85 and number 87. We know what they are but they have not been found.

"Medicinally, we are largely making use of the bodily elements to-day, and that is what has changed the drug store business to a considerable extent. The old mixtures are more rarely called for in medicine because of the study of the functions of the various glands of the body, the chemical and biologic study of cells and the chemical study of the products of glands. To-day, we work with the material Nature has been using in the production and growth and control of animal life through all ages; only recently have we come to an appreciation of Nature's real method. While these products may be studied through chemical analysis and while they may be synthetically made, and a number of them are so made, we get results that are easy to secure when Nature is the agent, in the use of plant remedies, like belladonna and digitalis. These and other remedies have direct effects. They have been studied longer, we know what to expect from their use, and we are rapidly learning the use of hormones and cellular products.

"The first description of goiter came from Switzerland. Sometime, on one side of those high mountains, apparently the people did not have goiter, whereas on the other side, many had goiter. A priest had the people suffering from goiter move across to the other side of the valley and then goiters disappeared. Now we know that iodine was present on one side of those mountains only. Kendall, who worked about eight years on the analysis of the thyroid gland, found that 65 per cent of the material made by the thyroid gland was iodine. Only a small quantity of iodine is needed daily, but if the body does not deliver it, the thyroid gland cannot carry on its function, and then it makes every effort to get iodine. This effort is manifested by increase in size of the gland, by increase in size of the blood vessels, and the heart beats two or three times faster than normal. A minute amount of iodine must be taken in as food and absorbed from the intestines. To-day, we appreciate that the iodine compounds of plant life probably are split by the common bacteria of the intestines, and a new type of germ might destroy the active microbe that splits the iodine. If the thyroid gland is destroyed by inflammation, persons lose their normal mental and physical states. If they are born without the gland, they remain helpless dwarfs. We see children twelve years old, who are not larger than a three-year-old, start to grow materially,

mentally and physically, when they are given the secretion of the thyroid gland. The thyroid gland is the little boy who reaches out his hand and pulls open the draft of the stove; it makes available the energy of the body cells for use. Epinephrine, which causes contraction of the blood vessels, can be made synthetically; it is used in combinations as a drug. The little parathyroid glands, two on each side, behind the thyroid gland, act like regulators, to control the amount of calcium free in the blood. If we lose the parathyroid glands in an operation, by cutting too deeply in taking out the thyroid glands, and the calcium drops below 7 mg. for each 100 cc., spasms of the muscles result.

"We have enough iron in our body to make an eight-penny nail. A good deal of it is held in the liver. We have enough potassium to make a little paper cap that will make one explosion for the toy pistol. We have enough calcium to whitewash an ordinary sized chicken coop; enough soap to make seven bars and enough sulphur to kill the fleas on a dog. The whole mixture is worth about ninety-eight cents.

"In diabetes, we know that some material is lacking in the pancreas. Banting and Best in Toronto learned how to isolate this material, insulin, from the pancreas. As we look back in history, we find that time and again it was almost discovered; twenty-five years ago, a German wrote about almost the exact discovery of insulin. While iodine is a special agent in the thyroid gland, sulphur is one in insulin. Sugar is held in the muscles. As they move, it produces lactic acid. If we attempt unusual exertion, we finally become almost unable to use the muscles; we must stop and rest because lactic acid has formed. Eventually, a great part of it returns as sugar to the muscle cells; it is the constant change in cellular chemistry that gives power and action to muscle. Sometimes we are almost overcome by what we eat and drink. After all, our control of the body, under normal conditions rests largely with the food we put into it. A great many of us know little about food. Most people think of eating because they are hungry, and not because they are putting fuel in the furnace to be burned. I have watched patients with diabetes who did not use insulin judiciously. One particular patient, the night before an automobile drive, had not eaten much, but had taken the usual dose of insulin. In the morning he took another dose, although he had not eaten much breakfast. The insulin burned the sugar out of the blood and the muscles went into spasms. This person was driving the car, and when I looked at him and saw the condition of his face and body I took hold of the wheel. In the course of half a mile, we came to a place where there was not a drug store, but a soda water fountain. We got some extra sweet orange juice into his stomach, and within three minutes he made a complete recovery. Insulin can be used to burn the sugar to too low a level. It must be used with the greatest care in order to avoid these dangerous conditions; most persons who have need for it appreciate that. One hundred years ago, in this country, we used 12 pounds of sugar for each individual; last year we used 114 pounds. That seems a lot for the babies, but they divide with their big sisters and fat mothers. A great many people eat more candy in a year than their own body weight, and take many sweet drinks as well. The needs of the body put the demand on the action of the glands. We need the secretion of the thyroid gland daily, just enough of it; if we take thyroid substance daily, the demand on the action of the gland ceases. If thyroid substance is

supplied long enough, the thyroid gland temporarily ceases to function. There is an increase in the incidence of diabetes. Is it because we overfeed with the thing the pancreas is making for us and made for men ages before we knew how to produce sugar? Making of sugar from cane is an old process and sugar was made from beet juice in the time of Napoleon.

"We use the pituitary gland at the base of the brain in many cases of disease. The posterior part of the gland produces a chemical agent that acts on the smooth muscles, whereas that of the anterior part of the gland acts on the thyroid gland, and stimulates the reproductive glands. The reproductive glands also are directly used in conditions which it would be difficult to treat by any other method.

"Overweight and underwork help to injure the organs. There is hardly a heart to be found which within itself has a normal circulation in anyone who is seventy years old at the time of death. Although such a person might not have trouble enough to make it evident in the most careful examination, at death changes are found in the blood vessels of the heart. This accounts for many of the sudden deaths, the number of which has doubled in the last forty years. Sudden deaths caused the highest mortality rate last year, namely, 186 in each 100,000. When we think of the startling increase in incidence of sudden death and compare it with that of tuberculosis which thirty years ago, killed 200 out of each 100,000 and which has dropped to 70 or 80, we see how death from tuberculosis has decreased, with better care. We have plenty of tuberculosis, but fewer die of it. We think that the man in the ditch, the farmer and the man using his muscles should be the ones to wear out; they rarely die a sudden death until they retire. The man working with his brain is the one who puts the greatest stress on his heart, the man who overeats and is living and working at the desk. Lack of use of the body leads to degeneration and opportunity for infection. We can put a bandage around the leg or arm and shut off circulation for an indefinite period in our operations on the bones and nerves without injury to the cells. If we shut off circulation of the brain for eight minutes, that is the end of the brain; it undergoes degeneration and death must come. That great brain is the one thing that differentiates man from the animals. We have not learned to use our muscles much better than several types of animals. Consider the kangaroo, weighing 250 pounds; his brain represents $^1/_{240}$ of the weight of his body; yet he has good use of his muscles. Man's brain represents $^1/_{42}$ to $^1/_{40}$ of the weight of his body, and he is not yet using all of it. All life and action is just a question of how rapidly oxidation is taking place. If we check it by an anesthetic for a temporary period, the process acts on the brain and the patient must sleep. We have many types of anesthetics. The newest is a solution of sodium iso-amyl-ethyl barbituric acid. If a certain dose of this solution is injected into a vein in the arm, the man will go to sleep in two minutes. Ethylene gas, a very useful anesthetic, was accidentally discovered to have anesthetic properties through its effect in causing sleep of plant life in a greenhouse in Chicago, where it was used for the illuminating part of the gas and a pipe leaked.

"The liver is our largest organ. We used to think it made the bile; now we know that it takes bile out of the blood. Wherever blood is made, as in bone marrow, or wherever the worn-out cells are destroyed, as in the spleen, there is hemoglobin, and the excess material of which the red cells are made flows back

into the blood stream. One of the functions of the liver is to take this material out. If the liver is not able to function, we have jaundice, which is produced by inability of the liver to take bile out of the blood. The gall-bladder has an action. It is found in types of life that feed off the ground. In animals that live underground, and feed under it, like the pocket gopher, there is no need for a gall-bladder. The elephant, which lives on leaves, must have more potassium or it would die of rickets. Elephants, deer and many other animals must have leaves in order to live well, although they get along fairly well for a period on grass. The gall-bladder filters the water out of the bile; bile in the gall-bladder is ten times stronger than the form in which it is furnished by the liver. The water has filtered out. In a study of liver function, it is found that the liver takes care of heavy metals, such as chlorine. We used to give a great amount of iron; it is better to take it by eating liver or by taking the juice that is squeezed out of liver. Patients with pernicious anemia are benefited and their life is prolonged by giving them the juice of liver which enables the cells to carry on their work. Without hemoglobin, the red blood cell cannot carry oxygen; oxygen must be carried in the blood. The blood must have all the material needed by all the different cells of the body, which live a community life and try to carry on almost like the communities in which we live.

"To-day, instead of using so many drugs, we are making use of greater knowledge of the chemistry of the body. When we run across a deficiency it can be tested out. Phenolsulphonephthalein is put into the blood and will be eliminated by the kidneys; thus we can test the function of the kidney. We can tell, also, what the liver is doing, by testing with certain dyes which are shunted off into the liver; other dyes are used to make the gall-bladder visible by the Roentgen rays. Types of material, such as arsenical poisons, will be shunted through the liver and will produce rapid destruction of it, and, if the substances are in considerable quantity, will cause death. If the patient can survive the injury caused by smaller amounts of these substances, fatty degeneration of the liver will take place.

"Many children have pimples and boils about the face that are due, many times, to the cereals they eat. Your mother, of fifty years ago, said, 'You have pimples because you are eating buckwheat.' The phyloporphyrin of some grains, especially buckwheat, if acted on by light, will bring about these pimply conditions, as the skin is a temporary storehouse for transformation of sugar, through the chemistry of light.

"It is of exceeding interest, scientifically, how nearly different forms of animal life, of course including the human being, are akin and how nearly animal life resembles plant life. Animals must live at the expense of plant life. If the lion and the lamb ever lie down together, the lamb is inside the lion; they are then lying down peacefully. There is no possibility that carnivorous animals can live on grass. There are algæ that feed the small fish, which feed the larger fish.

"Agriculture has progressed by a study of the infinite; that is, of the cell itself, the effect of bacteria, soil content and environment. Still more has been done, and is being done, in the study of human beings, and as side lines the research takes in investigation of the diseases of animals, including fowls and fish. Every year new doorways are opened to such investigations; they are more thorough, and means are discovered for the prevention of much of the misery of the world and for the prolongation of the life of healthier and happier people."