This is a strong sulphureted water, and contains sulphate of lime, carbonate of lime, sulphate of magnesia, and sulphate of soda.

Moffatt, south of Scotland.

The waters contain chloride of sodium (28·07), sulphate of soda, sulphate of lime, and sulphureted-hydrogen gas.

Baréges, Hautes-Pyrénées. Altitude, 4,000′. Temperature, 86° to 113° Fahr. Season from July to September.

Waters contain sulphide of sodium, sulphate of soda, chloride of sodium, etc.

These waters are used chiefly for bathing the patients, beginning with the colder and passing on to the hotter waters. These springs have a special celebrity for the treatment of old wounds, diseases of bones, and rheumatic and neuralgic affections.

Cauterets, Hautes-Pyrénées. Altitude, 3,000′, but sheltered. Season, June to September. Temperature of baths, 98° to 131° Fahr.

The composition of the waters is similar to that of those of Baréges, but it is more stimulating, and contains a good deal of iodine. It is especially advised in incipient tuberculosis, bronchial affections, and pelvic diseases of women.

Eaux-Bonnes, Basse-Pyrénées, near Pau. Altitude, 2,000′.

Waters sulphurous and saline, similar to but not so exciting as those of Baréges. This resort is celebrated chiefly for its effects in laryngeal diseases and clergyman's sore-throat.

Challes, Savoy.

This water, according to Macpherson, is one of the most remarkable in Europe, and "is the strongest sulphur-well known." It contains iodine and bromine, sulphide of sodium, bromide of sodium, etc.

Aix-la-Chapelle, Rhenish Prussia. Altitude, 450′. Temperature of air during season, mean, 63° Fahr. Season from June to September.

According to Liebig's analysis, these waters contain chloride of sodium (20 grains), bromide, iodide, and sulphate of sodium, carbonate of soda (4·9 grains), sulphate of soda (2·1 grains), sulphate of potash (1·1 grain), and carbonates of lime, magnesia, strontia, lithia, etc. Used by drinking and bathing, and especially in cutaneous diseases, rheumatism, syphilis, hepatic disorders, etc.

Eilsen, Lippe-Schomburg, Northern Germany.

Neundorf, Prussian Westphalia.

These waters contain the sulphates of soda, magnesia, lime, and chlorides of calcium and magnesium. They are highly charged with carbonic-acid gas and sulphureted hydrogen. They are useful in gouty and rheumatic affections, syphilis, skin-diseases, etc.

Schintznach, Switzerland. Altitude, 1,060′.

This is a highly-sulphurous water, and is charged with carbonic-acid gas and sulphureted hydrogen. It contains sulphate of soda

(9.87 grains), sulphates of potash and lime, chlorides of potassium and magnesium, and carbonates, etc.

Weilbach, Nassau. Altitude, 420′.

These waters contain bicarbonates of soda (3·123 grains), of lithia, of baryta, and of strontia, chlorides of sodium and potassium, carbonates of lime and magnesia, etc. The gases are carbonic acid and sulphureted hydrogen.

THERAPY OF THE SULPHUR-WATERS.—These waters, as a rule, are useful in *liver-disorders;* they diminish *abdominal plethora,* and *congestion* of the *portal circulation.* They are indicated in *malarial affections of the liver and spleen. Rheumatism and gout, tuberculosis in its incipiency, chronic poisoning by the metals,* etc., are certainly benefited by the internal use, and by baths of sulphurous waters. *Affections of the skin, syphilitic diseases, chronic rheumatic affections,* etc., are especially forms of disease remediable by these waters, used internally and in the form of baths.

Authorities referred to:

BRAUN, DR. JULIUS. *Systematisches Lehrbuch der Balneotherapie.*
MACPHERSON, DR. JOHN. *Baths and Wells of Europe.*
MOORMAN, DR. J. J. *Mineral Springs of North America.*
VALENTINER, DR. TH. *Handbuch der allgemeinen und speciellen Balneotherapie.*
WALTON, DR. GEORGE E. *Mineral Springs of the United States and Canada.*

IODINE AND ITS PREPARATIONS.

Iodum.—*Iode,* Fr.; *Iod,* Ger.; *Iodinium,* Latin.

Iodum.—Iodine. In bluish-black crystalline scales, having a metallic luster; very slightly soluble in water (1 in 7,000); soluble in alcohol (1 in 12), in ether, in a solution of iodide of potassium, and in a solution of chloride of sodium. Dose, gr. ss—gr. j.

Iodoformum.—Iodoform. In yellow crystals, having a saffron-odor. Insoluble in water, but soluble in ether, and the fixed and volatile oils. May be prescribed in a mixture, containing at least twenty times its weight of mucilage to render it properly miscible with water. Dose, gr. j—grs. v.

Liquor Iodi Compositus.—Compound solution of iodine. Iodine, 5 parts; iodide of potassium, 10 parts; distilled water, 85 parts. Dose, ♏ v—♏ xx.

Tinctura Iodi.—Tincture of iodine. Iodine, 8 parts; alcohol, 92 parts. Dose, ♏ j—♏ v.

Unguentum Iodi.—Iodine ointment. Iodine, 4 parts; iodide of potassium, 1 part; water, 2 parts; and benzoinated lard, 93 parts.

Unguentum Iodoformi.—Ointment of iodoform. Iodine, 10 parts; benzoinated lard, 90 parts.

Unguentum Potassii Iodidi.—Ointment of iodide of potassium.

Iodide of potassium, 12 parts ; hyposulphite of sodium, 1 part ; boiling water, 6 parts ; benzoinated lard, 81 parts.

Ammonii Iodidum.—Iodide of ammonium. A white, granular, very deliquescent salt, becoming yellowish-brown by exposure. Very soluble in water and in alcohol. Dose, grs. ij—grs. x.

Potassii Iodidum.—Iodide of potassium. In white or transparent crystals, wholly soluble in water (4 in 3), and in alcohol (1 in 6). Dose, grs. v—℥ j.

Sodii Iodidum.—Iodide of sodium. In minute crystals, or crystalline powder, deliquescent, having a saline and bitter taste and an alkaline reaction. Soluble in water and in alcohol. Dose, grs. ij—℈j.

Antagonists and Incompatibles.—Iodine is incompatible with the mineral acids, the metallic salts, the vegetable alkaloids, etc. The chemical antidote is starch, or substances containing it, as flour. These should be given freely diffused in water. It should be remembered that starch is the antidote to free iodine. As, however, the *iodide of starch* is not devoid of activity, in cases of poisoning by iodine, the contents of the stomach should be evacuated. It is obvious that the preparations of iodine, taken after a meal consisting of amylaceous materials, will have their activity impaired by the formation of the iodide of starch, the acid of the stomach freeing the iodine from its chemical association.

Synergists.—Alkalies, and other remedies which increase waste, favor the action of iodine and the iodides. Under some circumstances, mercurials are especially synergistic.

Physiological Actions. — *Iodine.*—When brought into contact with albuminous substances, iodine combines with it and prevents putrefactive change. The vapor of iodine, like chlorine, but in a feebler degree, decomposes sulphureted and phosphureted compounds. It is, therefore, justly ranked among the disinfectants.

Applied to the skin or mucous membrane, iodine, according to the extent of the application, is irritant or caustic. It stains the skin yellow, causes a sensation of warmth in small quantity, or of burning in larger quantity, and excites a superficial inflammation followed by desquamation. In some subjects the application of iodine-paint causes vesication. Pure iodine, kept in contact with the tissues, produces a brown and dry eschar. The vapor of iodine is very irritant to the broncho-pulmonary mucous membrane, causing cough, spasm of the glottis, and increased flow of mucus.

Iodine has a hot, pungent flavor, and excites a sensation of heat or burning in the stomach. In sufficient quantity, it acts as an irritant poison, inflames the mucous membrane of the stomach, and causes superficial eschars. The amount of iodine necessary to produce toxic symptoms varies greatly, and the variation depends in part on constitutional peculiarities, but chiefly on the amount and quality of the

food in the stomach. Whether applied to the surface of the skin or taken into the stomach, it quickly diffuses into the blood, and enters into combination with sodium or potassium, or with both.

Iodides.—The iodides are among the most diffusible substances. They have a bitter, saline, and very disagreeable taste. In a few minutes after being swallowed, the taste of iodide of potassium returns in the mouth, and, during a course of this salt, the saliva is constantly charged with it. In the stomach, in considerable doses, they produce first a cooling sensation, followed by warmth, and even burning. They pass into the blood with great rapidity. It is said that the base is changed in the blood, and the iodides of ammonium and potassium become iodide of sodium. In the blood they probably undergo no further changes, and do not, so far as is known, modify the composition of that fluid. At the points of elimination from the free mucous surfaces (nasal, faucial, and bronchial mucous membrane), the chemical changes which ensue set free ozone, and the irritation there experienced is probably in part due to the iodine, separated from its combinations by the action of that agent (Buchheim). Elimination doubtless takes place by the broncho-pulmonary, faucial, and salivary glands, but chiefly by the kidneys. The diffusion of the iodides into and out of the blood takes place with such rapidity that in fifteen minutes they may be detected in the saliva and in the urine.

Diverse opinions have been expressed in regard to the influence of the iodides over the assimilative functions. By the syphilographers it is held that the iodides promote constructive metamorphosis, and that a gain in body-weight is a result of their use. This opinion is developed in this way : The subjects of syphilis in its constitutional form emaciate, and their forces are depressed ; but, when the iodides are given them, the virus is eliminated, and the organism at once reacts. In the physiological state the iodides increase waste and the elimination of the products of waste, and emaciation with a general depression of the vital functions ensues, when they are administered for lengthened periods.

Iodism.—Iodine and the iodides, when given in large quantity, produce a state termed *iodism*. The quantity which will set up this state of irritation in one subject will affect another but slightly, if at all ; in other words, the susceptibility to the iodine impression varies greatly in different individuals. Iodism is manifested by general *malaise* and rise of temperature, frontal headache, coryza, lachrymation, and sometimes inflammatory swelling of the eyelids, a bitter saline taste in the mouth, soreness of the throat, hoarseness, and difficulty of swallowing—phenomena strikingly similar to summer catarrh. Indeed, patients who experience these sensations for the first time, suppose them to be an acute catarrh. Usually the symptoms of iodism subside, notwithstanding the dose which caused them may still be

taken, or, as it may be expressed, a "tolerance" is established. The quantity which at one time may have caused violent iodism will not necessarily again do so, although a considerable interval may have elapsed. Indeed, it is sometimes difficult to induce iodism in those who have become habituated to the use of the iodides in considerable medicinal doses.

An eruption of acne, especially on the face, shoulders, and thighs, is a very common result of the internal use of the iodides; hydroa on the face and forehead is an occasional consequence, but eczema is more frequent, yet less so than acne, which is usual.

Wasting of the mammæ and of the testes has never been observed by the author, although he has used the largest doses of the iodides, for long periods. There is no doubt about their antaphrodisiac effects, and it has seemed to the author that permanent loss of sexual power has resulted from their long-continued use.

When it is desirable to avoid iodism, large draughts of water should be taken during a course of the iodides. As Rosenthal has shown, large dilution of the salt hastens elimination, and thus prevents the more severe effects of iodism.

Benedict has experimentally studied the effects of iodine and of iodide of potassium on the nervous system. His observations, made on frogs, demonstrated that these agents caused paralysis of the heart and of the respiration, but there are no facts indicating that on man they possess this power. It is true Schule had a case in which such symptoms were induced by injecting the sac of a *spina bifida* with tincture of iodine, but the direct and reflex effects of the injection on the spinal cord may have had much to do with the result. The nervous symptoms which accompany iodism are apparently due solely to the increase in the pulse-rate, the elevation of temperature, and the irritation of the broncho-pulmonary mucous membrane.

Therapy.—A weak solution of the iodide of potassium (grs. j—grs. v—℥ j) is a useful application to the mouth in *aphthæ, mercurial stomatitis, simple sore-throat, tonsillitis, etc.* *Hypertrophy of the tonsils* can usually be cured by the injection of the tincture of iodine into their substance. To execute this little operation, an hypodermic syringe, with a sufficiently long needle, is necessary.

The *vomiting of pregnancy* can sometimes be greatly relieved by drop-doses, every hour or two, of the tincture of iodine. This, like all other remedies for this disorder, is very uncertain, and precise indications for its use have not hitherto been ascertained. *Catarrh of the duodenum, catarrh of the biliary ducts,* and the *jaundice* dependent thereon, are, after the acuter symptoms have subsided, cured by small and frequently-repeated doses of the iodide of ammonium (grs. j—iij in water every two, three, or four hours). This is one of the best remedies for the first stage of *cirrhosis.* The efficacy of the iodide is

increased by combination with arsenic: ℞ Ammonii iodid., ʒ j; liq. potassii arsenitis, ʒ ss; tinct. colombæ, ℥ ss; aquæ, ℥ jss. M. Sig.: A teaspoonful three times a day, before meals.

The preparations of iodine and the iodides are, generally speaking, contraindicated in all inflammatory states of the intestinal canal; but in *passive hæmorrhage,* and *diarrhœa* from atony of the mucous membrane, the tincture or compound solution of iodine in small doses—one or two drops—frequently repeated, renders important service (Schmidt).

Large doses (grs. xv—ʒ ss) of the iodide of potassium, three or four times a day, often afford remarkable relief in *aneurism,* and sometimes effect a cure. This mode of treatment is adapted to internal aneurisms so situated as to be beyond the reach of surgical means. The author has seen several instances in which great relief was experienced, and one case certainly in which a cure apparently resulted. He is, therefore, able to confirm the observations of Chuckerbutty, Roberts, Balfour, and others.

The iodides are unquestionably serviceable in *acute catarrh.* The action is local and substitutive. A grain of the iodide of ammonium every two hours has seemed to the author the best mode of applying the remedy. In *summer catarrh* or *hay-asthma,* the best results are obtained by the use of larger doses, and the efficacy of the iodides is increased by combination with arsenic. ℞ Potassii iodidi, ℥ j; liq. potassii arsenitis, ʒ j; aquæ, ℥ iv. M. Sig.: A teaspoonful every four or six hours. With the internal use of the iodides may be combined the local use, to nares and fauces, of the following solution: ℞ Tinct. iodinii, ʒ j; acid. carbol., gtts. x; aquæ destil., ℥ iv. M. Sig.: Apply with a post-nasal syringe. Local applications will be effective, when the morbid action is confined to the nares and fauces.

The iodide of potassium is one of the most effective remedies which we possess for *spasmodic asthma.* But it is not adapted to all cases arising under various conditions—a fact which explains the difference of opinion on the subject between Williams, Salter, and others. It is most beneficial when the asthmatic seizures are induced by an acute bronchial catarrh, the nervous symptoms being reflex; and when there occurs during an asthmatic attack profuse bronchial secretion. Salter, however, holds that we possess no exact indications for its use, and that cases the most diverse are sometimes benefited in a remarkable manner. As regards dosage, from fifteen to thirty grains every two, three, or four hours, according to the severity of the seizure, is usually the necessary quantity.

Chronic bronchitis, with profuse secretions (bronchorrhœa), is frequently improved by the iodides, more especially the iodide of ammonium. The efficacy of this remedy is increased by the conjoined administration of arsenic. In *capillary bronchitis,* the author has witnessed most astonishing relief by the rapid administration of iodide

of ammonium in small doses. It may be combined with the carbonate, or with the stimulant expectorants. To prevent caseation of the inflammatory exudations of *catarrhal* and *fibrinous pneumonia*, no remedy is more efficient than the iodide of ammonium. To lessen the effect of this remedy on the tissue-changes, arsenic should be combined with it, and every means used to support the body nutrition. The iodide of potassium is one of the remedies resorted to in *chronic pleurisy*, to promote absorption of effusions. In these cases the chest is painted with the tincture, and the iodides are administered steadily for a considerable period.

Affections of the broncho-pulmonary mucous membrane, alluded to above, in which there is profuse exudation, all inflammatory symptoms having subsided, are advantageously treated by iodine inhalations. The method which the author has found most convenient is the following: A small, wide-mouthed bottle, containing a moistened sponge, is placed in a vessel of hot water. The tincture of iodine (gtts. v—gtts. x) is dropped upon the sponge, and as the vapor of iodine rises, is inhaled with the vapor of water. This inhalation is serviceable in *acute catarrh*, *hay-asthma*, and *chronic bronchitis*. The carbolate of iodine (tinct. iodinii, ʒ ij; acid. carbol., ʒ j) may be used instead of the simple tincture of iodine. Ten to twenty drops for inhalation.

But few affections of the brain, non-specific in origin, are benefited by the iodides. According to Niemeyer, the iodide of potassium given to iodism has in few instances cured *basilar meningitis*. The author, who has used it faithfully in various cases, has not been so successful. Trousseau et Pidoux express their disbelief in the reported cures of tubercular meningitis by this agent. Seguin maintains, on the other hand, that remarkably good results sometimes follow the use of large doses of the iodides in other than specific diseases—in the various subacute and chronic inflammatory affections of the meninges and brain.

No remedy is more efficient in the treatment of certain glandular enlargements of the thyroid, spleen, and lymphatic glands. *Goitre* is curable by the internal and external application of iodine, when it consists of simple hypertrophy of the gland-elements. Cystic and calcareous degeneration of the thyroid are unaffected by the use of iodine preparations never so vigorously used. One of the best remedies for true goitre, as will be seen hereafter, is the unguentum hydrarg. iodidi rubri. *Enlarged spleen*, when it consists merely of an hypertrophy of the organ (chronic splenitis), is cured by the internal use of the iodides conjoined with the local use of iodine-paint, or ointment of the red iodide of mercury. The *enlargements* of the *spleen and liver*, with *functional derangement of these organs*, which are caused by malarial disease, are most effectually removed by moderate doses, frequently repeated, of the iodide of ammonium. The author's experience justifies him in strongly urging the combined use of iodide of ammonium and arsenic in *chronic malarial poisoning*.

The prolonged administration of iodide of potassium has appeared in some instances to have retarded the changes which ensue in *chronic Bright's disease* (fibroid degeneration), and to have improved the condition of the patients.

The utility of the iodides is most conspicuous in certain *constitutional states*. The expectations which were at first entertained of the cure of *scrofula* by iodine and its preparations have not been realized. The iodides are unquestionably useful in the *scrofulous* (so called) *enlargements of the lymphatic glands*, but cod-liver oil and suitable hygienic means are more influential in improving the strumous diathesis. The preparations of iodine are effective only when simple hypertrophy of the lymphatic glands has taken place; if they have undergone caseation, or have proceeded to suppuration, no medicine has any influence over them.

The most important therapeutical applications of the preparations of iodine are in the treatment of *constitutional syphilis*. For the primary and secondary stage, mercury is generally admitted to be best; but for tertiary symptoms no remedy at all approaches the iodide of potassium. In the secondary affections of the skin, mercury, especially if it have not been given for the primary troubles, is to be preferred in the papular, tubercular, squamous, and pustular syphilides; iodide of potassium in the ulcerating, especially if the patient is cachectic. It may be stated in general that the preparations of iodine are indicated when the patient is under the mercurial cachexia. On the other hand, it is well known that sometimes, even when the tertiary symptoms have not been relieved by a thorough course of iodides, mercury will quickly remove them. But this fact does not invalidate the rule that the iodides are specially serviceable for the tertiary period.

No therapeutical fact is more conspicuous than the cure of *syphiloma of the nervous system* by iodides. *Mental disorders*, *epileptiform seizures*, *paralytic states*, etc., dependent on gummata, nodes, etc., are usually removed in a manner little short of magical. *Neuralgia of the fifth* (*tic-douloureux*), the pain being nocturnal chiefly, or *nocturnal pain in the head*, is similarly promptly cured. In syphilitic affections of the brain, more imperatively than in the same affections of other organs, are large doses of the iodide of potassium required. The limitation of the dose depends entirely on the physiological susceptibility of the patient, and the influence exerted over the progress of the case. Hence the dose may vary from ten grains to a drachm every four hours, or three or four times a day. The symptoms of iodism—the use of the agent to saturation—should be induced; for this effect is the only measure of the therapeutical power of the remedy. The more promptly iodism can be induced, the better, for the soft nervous tissue may

be quickly and irreparably damaged by syphilitic deposits and new growths. *Syphilitic paraplegia* is equally amenable to the same means; but, as above remarked, much depends on the promptness with which the iodide is used.

Recent experience has conclusively shown the curative power of iodine in *malarial fevers*. Thus three hundred consecutive cases were, with few exceptions, promptly arrested (Anderson). In some cases no paroxysm occurred after the medicine was administered; sometimes the attacks persisted for two or three days, but then the relief was complete. The official compound tincture of iodine may be prescribed —for adults, ten to fifteen minims, three times a day, well diluted, and before meals. Carbolic acid, itself having considerable anti-periodic power, may be combined with the compound tincture of iodine. ℞ Tinct. iodinii comp., ℥ ij; acid. carbolic., ʒ j. M. Sig.: Ten to fifteen minims three or four times a day. The official tincture of iodine is given by many practitioners. If quinine be necessary to break up the paroxysms, iodine is highly useful in the interim, as has been indicated. Some recent experiences by Dr. Atkinson, of Baltimore, throw doubts on the previous statements. He found that iodine failed in two thirds of the cases of intermittent fever.

The use of the compound solution of iodine during the course of the first and second week of *typhoid fever* is known in Germany as the "specific treatment." A very considerable reduction in mortality appears to have followed this method. The solution of iodine or the tincture is administered regularly three times a day, well diluted with water. When it does good, the temperature falls, the nausea lessens, and the diarrhœa is restrained within safe limits.

Chronic rheumatism, when there are present thickening of the fibrous tissues, and inflammatory depositions about joints, tendons, periosteum, and nerve-trunks, is often very signally benefited by the iodides. The cases in which these remedies prove so serviceable are most probably due to syphilitic, mercurial, saturnine, or other constitutional causes. There are, in our modern life, many ways in which these mineral poisons enter the organism, and it is probable that they are often undiscovered and even unsuspected causes of rheumatic symptoms. *Lumbago*, *sciatica*, and *paraplegia*, apparently of rheumatic origin, and curable by the iodides, may not unfrequently be caused by syphilis, mercury, copper, tin, or lead.

The *various accidents caused by the metals above named*, especially the *mercurial* and *saturnine*, are removed by the use of the iodides, notably by the iodide of potassium. With regard to the dose necessary, what is true of syphilis is equally true of the mineral poisons: in order to remove them, the organism must be saturated by the remedy. From fifteen grains to a drachm, three or four times a day, should be given; but the measure of the quantity required is the effect produced. The iodides penetrate into every tissue, convert the deposited metal into soluble combinations, and cause them to be discharged by the various organs of excretion, chiefly by the kidneys. It has been repeatedly asserted that salivation may be induced, and existing salivation increased, by the use of the iodides for the removal of mercurial salts from the organism; but the author has not witnessed any facts which support this statement.

In *skin-diseases of syphilitic origin* there can be no question as to the utility of the iodides. But these remedies are more especially curative in the tertiary affections, especially in destructive syphilitic ulcerations. Hebra insists, and with justice, that the preparations of iodine are only useful in *lupus*, whether syphilitic or scrofulous, and do not permanently improve other cutaneous diseases. Mr. Hutchison calls attention to the fact that the various skin-diseases classed as hydroa may be produced by the iodide of potassium. The author has certainly had one case illustrating this action of the iodide.

Local Uses of the Preparations of Iodine.—The tincture of iodine is in universal use as a counter-irritant. It is applied by means of a camel's-hair brush to *goitre*, to *enlarged glands*, and to superficial *inflammatory swellings* before the formation of pus. Painted over the neck, it is a useful counter-irritant in *acute affections of the pharynx and larynx*, and to the chest to relieve the *chest-pains* which occur in *phthisis*. It is the most serviceable counter-irritant to promote absorption of inflammatory products in *catarrhal* and *fibrinous pneumonia* after the acuter symptoms have subsided. The same application appears to possess the power to promote the absorption of *pleuritic effusion*. It is a good plan in these affections to paint, on successive days, the tincture over the front, the lateral, and the posterior wall of the chest, so that one surface has time to recover from the irritation before it is again attacked. As the susceptibility to the action of the iodine varies in different subjects, it is always prudent to make a slight application in the beginning. If extreme burning follow the applications, the iodine may be dissolved off by a solution of iodide of potassium, by alcohol, or ether.

The tincture and the ointments of iodine are also used to remove the *induration of the breasts* which results from attacks of inflammation. It must be remembered that the integument in this situation is extremely sensitive to irritating applications. *Splenic and hepatic disorders of a chronic kind* are frequently treated locally by the application of tincture and ointment of iodine. Enlarged spleen of malarial origin is more speedily cured by the application of the official red iodide-of-mercury ointment, and, as regards hepatic disorders, the only affection which has seemed to the author to be benefited by iodine applications is the engorgement due to malarial attacks.

After the acute symptoms have subsided, tincture of iodine will re-