grams. The salt produced in this manner melts lower than the anhydrous salt and also lower than heroin hydrochloride. 218°-224° (uncor.).

Three samples of commercial diacetyl-morphine hydrochloride obtained from different manufacturers were examined. (1) The sample melted at 230°-238° (uncor.). Ten grams gave 8.91 grams of precipitated alkaloid and .11 grams extracted. 9.02 grams were recovered while the theoretical for the anhydrous salt is 9.10 grams. The product was therefore the anhydrous salt. (2) The sample melted at 224°-228° (uncor.). From 10 grams there were obtained 8.6 grams of precipitate and .12 grams of extract. The product is therefore the monohydrated salt. (3) The sample melted at 225°-230° (uncor.) and showed a decided loss in weight when treated at 100°. It is therefore the monohydrated salt.

Since the completion of these experiments our attention has been called to a statement by Schaefer (*American Journal of Pharmacy*, 82, 220), that only the monohydrated salt can be found on the market. He found that this salt when dehydrated, regains its water quickly from the air, but we have shown that this is not true of the anhydrous salt which separates from solution.

Assay:—Heroin or diacetyl-morphine may be accurately estimated by dissolving in excess of 1/10 normal hydrochloric acid and titrating the excess of acid with 1/50 normal sodium hydroxide using cochineal as an indicator.

	Weighed Sample.	Found.	Found Per Cent.
Pure diacetyl-morphine.....	.1362 grams	.1354	99.42
	.1735 grams	.1725	99.44
Heroin.....	.1323 grams	.1317	99.53
	.1336 grams	.1328	99.41

For the estimation of the alkaloid in its salts the following method is recommended:—An amount of the preparation representing at least one-tenth gram of the alkaloid and contained in 10 cc. of solution is treated with 20 cc. chloroform and sufficient 10 *per cent.* ammonia to render it slightly alkaline. After shaking vigorously, the chloroform is drawn off into a container suitable for titrating. The extraction with chloroform is repeated three times, after which the combined chloroform extract is evaporated. Add 5 cc. of 1/10 normal hydrochloric acid or sufficient to completely dissolve the alkaloidal residue then add a few drops of cochineal solution and titrate the excess of acid with 1/50 normal sodium hydroxide. The results obtained are very close to the theoretical.

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THE GLANDS OF INTERNAL SECRETION AND THEIR IMPORTANCE AS THERAPEUTIC AGENTS.

CAREY PRATT MCCORD.

The animal body, it appears, manufactures its own drugs. These drugs are the derivatives of the glands of internal secretion. These substances elaborated by the secretory cells of these glands are discharged into the circulation and carried to the various parts of the body. There they react upon the tissues in a manner for the well-being of the body as a whole.

The glands of internal secretion regulate and correlate some of the body's most important physiologic functions and constitute efficient protective and defensive measures against disease. There are, influenced by the glands of internal secretion, such functions as ovulation, pregnancy, muscle tonus, vaso tonus, secondary sexual development, adiposity, skeletal growth, sugar metabolism—on through an extended list. Despite the complexity and intricacy of these manifold manifestations of internal secretory activity the balance is maintained, in health, —in perfect harmony,—that is, the glands regulate and control each other. This interrelation, and interdependence of the glands of internal secretion have given rise to the term "internal secretory balance." Although these several glands are situated in the body widely apart from each other and have no visible connections one with the other, they constitute a unified system of glands, every individual of which having its function or functions, but contributing to the maintenance of a complex interrelation within the entire system. It is now established that there exists not only an organic and functional harmony between all glands but a compensatory interaction as well. Every gland acts, in its peculiar functional manner, upon the blood passing through its tissues, often adding to it bodies of vital importance to the welfare of the individual. If any organic disease or abnormality exists in a particular gland, the missing or altered function appears in some cases to be taken over by some other gland, and disaster is prevented. In other cases the altered metabolism of one gland upsets the normal metabolism of all the others and leads to its impairment and the impairment of the body as a whole. In its deepest significance, it is probable that every cell in the body is a potential ductless gland and has some slight influence on the life and functions of its fellow cells. The terms "ductless gland," "gland of internal secretion" and "endocrinous gland," are, however, restricted to these organs showing glandular tissue and yet having no ducts for discharging the formulated substances.

The tissues producing internal secretions are, pituitary, pineal, thyroid, thymus, parathyroid, pancreas, adrenal, ovaries, testes. There are, in addition, some indications of internal secretion from the tonsils, placenta, and carotid gland.

Glands of Internal Secretion and Disease:—While the ductless glands functionate for the maintenance of the normality of the body, they themselves are subject to disease and traumatism. In many instances, apparently as a prevention against traumatism, the ductless glands are so located that the very shielded and privileged situation of these organs suggests a vital importance. The pituitary gland resting in the saddle of the *sella turcica* of the sphenoid bone at the center of the skull is the best protected organ of the body. Scarcely less protected is the pineal gland near the center of the brain, the parathyroids embedded in and behind the thyroid gland deep in the neck, or the adrenals padded in the fat above the kidney. The removal of the glands experimentally, by accident, or through necessary operative procedures, manifests the absence of the gland by distressing and even fatal symptoms. The removal of the adrenals, for example, leads rapidly to the death of the animal or patient with great prostration and depletion before death due to the loss of the adrenal function of maintaining muscle and vascular tonus. The removal of the parathyroids leads to death from the accumulation of toxic bodies in the circulation, the destroying of which is

the parathyroid's function. The removal of the pancreas leads to diabetes and later to death. Not all glands, however, are immediately essential to life. In adult life the testes, ovaries or pineal gland may be removed without producing any fatal results.

It is not necessary that there be a visible anatomical destruction of the ductless gland to produce a perversion of its secretion and thus a disturbance of the body's equilibrium. They are subject to tuberculosis, to cancer, to infectious diseases, that may lead to a slight or grave impairment, which may manifest itself as an increased or a decreased function. Increased function of the pituitary gland leads to gigantism, acromegaly, while decreased function produces obesity. Increased function of the thyroid causes goitre, while decreased function causes the coarse featured obese cases called "myxoedema," and in young children is termed "cretinism." Even so mild a condition as the so-called "spring fever" may be a condition of decreased adrenal function. All considered, it is very evident that malfunction of these glands may produce very severe pathological states of the body, and it becomes a pertinent matter to inquire as to the efficacy of treating such conditions with preparations of glands derived from cattle, sheep or other animals.

Ductless Glands as Therapeutic Agents:—The conception of using animal derivatives in treatment is by no means new. As early as 6000 B. C. preparations from testes were given in the treatment of obesity. At about the same time there are also mentioned the use of such other animal substances as "swine's fat, dog's dung, fat of a serpent, hair of a virgin goat, and human bone." It is only a step from this, to our present-day desiccated *corpus luteum* and pituitary extracts. It is, however, a far cry from the ancient to the modern point of view regarding such substances. The ancients used these agents, calculating that their vile tastes and nasty odors would drive away the offending disease, while, by us, organ derivatives are employed from our knowing that chemical substances are elaborated and stored by the organs and when given off into the circulation promote the welfare of the body organism. This rational use of glandular derivatives is only 25 years old, but, in these comparatively few elapsing years, a vast amount of work has been performed by scientific workers everywhere, until to-day we are confronted by a bewildering literature filled with contradictions, over-exploitations, speculations and theories, but, fortunately, here and there we find a clear-cut, undoubted fact that stands as a monument of human achievement.

Unrestrained speculation from the very incipiency of organo-therapy has attached stigma to this form of treatment. There has always been the over-optimistic type of worker who has held out greater virtues, as the properties of certain glands, than really existed as facts. Extravagant claims have actually retarded the fuller understanding of the possibilities and limitations of glandular therapy. So, let us recognize that we are surrounded both by existing limitations and by ignorance as to possibilities. Let us at once learn not to expect any panacea that will rejuvenate old men, or which will defer old age beyond a certain physiologic limit, nor can hopelessly anatomically defective minds be brought up to par. On the other hand, nearly every gland has its field of application. In many cases, the application is specific, and neglect to use glandular tissue approaches criminality. Persistence in the treatment on the part of the

physician is essential. Most of the glands, apart from such products as adrenalin and pituitrin, act so as to alter the metabolism. Such changes do not occur at once. For instance, no good results are to be expected from placing a mentally defective child on pineal medication for two weeks. Such treatment must be continued for months and even years.

One of the sources of error accountable for poor results may be ascribed to the chemical manipulation of glandular substances, with the desire to purify them and ultimately to obtain the active constituent in crystalline form. A chemically pure substance, active and freed from attending deleterious qualities due to contamination, is, of course, very desirable, but many glandular products are not standardizable and a mechanically nice-appearing product may be attained at a sacrifice of activity. Except in a few instances, adherence to a product closely simulating the original tissue, is attended with better results, in the absence of any direct data regarding the nature of the substance stimulating the changes. This is especially true of such obtuse agents as the anterior lobe of the pituitary gland and the pineal body.

Very few of the hormones have been isolated in crystalline form, so that, for the most part, the properties of these hormones of the different glands are but meagerly understood. In general, they are the chemical means of correlation of the activities of the different parts of the body. They promote or moderate metabolism. In addition, special functions are attributed to some. Even with so vague a knowledge of the nature and properties of hormones, it is possible to indicate some lines on which with safety we may proceed in the application of these glandular derivatives. They are likely to prove useful in five different ways:

1. The most obvious and natural use is in the treatment of the diseases due to destructive lesions of the glands by which the hormones are secreted. In this substitution treatment glandular derivatives are used in a sound and rational manner. Typical of this use is the employment of *corpus luteum* or ovarian extract in the treatment of artificial menopause due to the removal of the ovaries.

2. Glandular derivatives are serviceable when there is bodily demand for more secretion than the gland supplies. For example, the simple parenchymatous goitre of young women is due to overgrowth of the gland in its effort to supply a greater amount of the thyroid secretion. When such patients are placed upon thyroid medication, these simple goitres in many cases disappear.

3. The derivatives of one gland may be substituted in a deficiency of activity in another gland. For example, where osteomalacia is present and attributable to ovarian malfunction adrenalin preparations are many times useful.

4. A large number of conditions exist where glandular products are beneficial but no connection is established between the pathologic condition and the gland function. Such may be called the "empiric use" of glandular derivatives.

5. The use of these glandular derivatives as drugs, for example pituitary extracts as an oxytocic, or adrenalin as a hemostatic.

In the foregoing pages I have tried to make clear the importance of the glands of internal secretion in health and normal function, the possibility of disaster that may come to the body through perversion of secretory function from disease or traumatism and, in the last paragraph above, it has been my desire to point

out the rationality of combating disease and aiding normal functions by the administration of preparations of these glands. Since the cells of the various organs may be influenced in their functioning by substances procured from other animals, the possibilities at once opened up are immense. Progress to the ultimate control of many complicated conditions, is limited only by the capabilities of the scientific workers to produce satisfactory preparations of established and uniform activity.

This is an all too brief outline of hormone therapy to-day. New pathways in this field of therapy are opening up yearly. The principles of hormone therapy explains in many respects the action of the older drugs and affords solid groundwork for future methods of treatment. For these reasons I commend the glands of internal secretion to your further interest and study.

VOLATILE AND ODOROUS CONSTITUENTS OF HUMAN URINE.

At ordinary temperatures the amount of volatile acids in urine is very small, and the characteristic odor is not due to them, as has been stated. The lower fatty acids occur in such minute traces in normal urine, and are present in salts or in combination, so that they can only slightly, if at all, modify the odor. Sulphuretted hydrogen is given off by all urines, in the cold, when they are treated with dilute phosphoric or sulphuric acid. The volatile substances were obtained by acidifying a large volume of urine with sulphuric acid before distillation. Benzoic acid, derived from the hydrolysis of hippuric acid, was the principal volatile acid found, although in many cases the hydrogen sulphide present was sufficient to account for the total acidity. Fatty acids up to heptylic acid, and possibly hexahydrobenzoic acid, were also present in minute quantity. Phenol and paracresol were present, also notable quantities of higher phenols. Methylamine and indole occur in traces in fresh urine; the amount of these bases increases on fermentation. None of these are responsible for the characteristic odor of urine. This is due to a neutral substance, urinod. It was obtained by acidifying 1,000 litres of urine with sulphuric acid, allowing it to stand for several days, distilling, shaking out the distillate with ether, and removing the acids, phenols, and bases from the ether extract by the usual methods. The residue was then distilled, the distillate again shaken out with ether, the ether extract being shaken with mercury to remove sulphur. The purified ether residue was then fractionated *in vacuo*. Urinod was thus obtained as a yellow oil, slightly heavier than water, in which it is insoluble, with a very persistent, penetrating odor of urine. A drop on a filter paper retained its odor for fifteen months. Its empirical formula is C_6H_8O; boiling point, 108° C. under 28 mm., or 208° C. under normal pressure; but it does not distil under ordinary pressure without decomposition. It is very volatile in aqueous vapor. Urinod is extremely poisonous; its relation to metabolism is not known. It may have some influence as a cause of uræmia. Oxidising agents at once destroy it; hence these are best for use for deodorizing urinals.—W. M. Dehn and F. A. Hartmann (*J. Amer. Chem. Soc.*, 1914, 36, 2,118, 2,136).