386, Statutes of 1935. Under that law certain responsibilities were placed upon the California State Board of Health, and Director Dickie's communication was a request to the Attorney-General for clarification.

The legal principles involved in the interpretation of laws are well exemplified in this statute. The State Board of Health must govern itself by the opinions of the State's Attorney-General, unless such opinions are overruled by the proper courts. In the present instance, Deputy Browne points out the difficulties involved in having the office of the Attorney-General render an opinion on an abstract proposition, when, as a matter of fact, some of the legal points must be settled by the courts on separate and specific cases, and then only "upon a consideration of all the facts adduced and of the law applicable thereto." The letter of Deputy Browne, printed on page 243, should be read, not only by members of the profession associated with the specialties mentioned, but by all physicians who seek to orient themselves on the medical-legal principles under discussion.

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Roster for 1935.—The roster of membership of the California Medical Association for the year 1935, with additions and changes of membership up to the date of printing of the March CALIFORNIA AND WESTERN MEDICINE, is given place on the opening pages of this number. During the last several years, the Council has been printing the State Association roster in condensed form to provide members with a list which they could easily check with the additional information to be found in the Directory of the California State Board of Medical Examiners. The publication of the roster in this new form, as a part of the official JOURNAL, means a saving in printing expense of more than one thousand dollars.

Last year's roster was printed in CALIFORNIA AND WESTERN MEDICINE of September, 1935. It is gratifying to note, that in spite of the hard times, there has been no decrease in State Association membership. And further, that in the largest county unit of the State—in Los Angeles—where the application fee must be accompanied by a one hundred dollar pledge, this fee has not been a deterrent in securing new members; an indication of what a headquarters building and broad society activities can do for an organization. Let us hope that the coming year will be marked by a numerical and percentage increase in members greater than that to the credit of the last several years.

Other State Association and Component County Society News.—Additional news concerning the activities and work of the California Medical Association and its component county medical societies is printed in this issue, commencing on page 208.

EDITORIAL COMMENT†

VITAMIN D TOXICITY

Physicians, in company with the general public, have become conditioned during the past two decades to considering vitamins as "accessory food factors." The implication of this conception, which is strongly supported by extensive commercial and advertising interests, is that vitamins are completely harmless and nontoxic, even in the highest conceivable dosage. Hints to this effect are not wanting in medical literature. The recognition of the chemical constitution of vitamins A, B, C, and D during the last five years has put an entirely different complexion on the matter. It must now be recognized that vitamins are drugs and that, in common with all drugs, they do have a definite toxicity in high enough dosage, and that there is a limit to the amount that may be used without invoking dangerous symptoms. The effective dosage of these drugs is very small. For pure crystalline vitamin D, for example, an effective daily dosage is about one-tenth of a milligram. That is, its dosage is less than any other drug now ordinarily employed. It is very important that physicians get away from prescribing vitamin D in terms of obscure units of variable biological activity, and insist that solutions or preparations of it be furnished in such a manner as to indicate clearly the percentage concentration of the pure crystalline material, so that it may be prescribed in milligrams of the pure drug.

Vitamin D has recently been recommended in high dosage in the treatment of arthritis.[1] Dreyer and Reed state that they have treated 700 patients with massive doses of vitamin D, and they admit that sixty-three showed signs of toxicity. This is a relatively high percentage of untoward reaction, and it raises the question as to whether the disease hazard justifies such a pronounced therapeutic hazard. The signs of vitamin D toxicity appear about two weeks after the high daily dosage treatment begins. The patient is nauseated, becomes dizzy, and has tingling in the extremities; and there may be vomiting, diarrhea and polyuria. A patient recently admitted to a California hospital with these symptoms, which were definitely attributed to excessive vitamin D intake, died in coma three days after admission. There is a very definite risk of clinical toxicity with vitamin D, of which all physicians should be aware.

There has been much scientific discussion of vitamin D toxicity. This has been complicated

† This department of CALIFORNIA AND WESTERN MEDICINE presents editorial comment by contributing members on items of medical progress, science and practice, and on topics from recent medical books or journals. An invitation is extended to all members of the California and Nevada Medical Associations to submit brief editorial discussions suitable for publication in this department. No presentation should be over five hundred words in length.

1 Dreyer, I., and Reed, C. I.: Arch. Phys. Therapy, 16: 537 (Sept.), 1935.

by the confusion between various preparations of irradiated ergosterol with vitamin D. The differences between vitamin D and other irradiated ergosterols is best determined by the study of the absorption spectra of the solutions of the materials. An excellent review of this matter has been prepared by Bills.[2] Vitamin D (calciferol) shows a maximum absorption band at 265 mμ. This material has antirachitic potency of 40,000 international vitamin D units per milligram. Too intense or too prolonged irradiation of ergosterol produces a series of substances with maximum absorption spectra below 250 mμ, which are definitely toxic, and which have only weak antirachitic effects. One such agent is called "toxisterol," because of its high toxic calcifying properties. This shows a maximum absorption band at 248 mμ, and must carefully be excluded from irradiated ergosterols offered for clinical use. The only protection at present afforded the medical profession or the public against the presence of this toxic agent in vitamin D preparations is the care with which manufacturers control their products.

There is as yet no evidence to indicate what the chronic toxicity of vitamin D preparations may be, especially if contaminated with "toxisterol." This poisonous ingredient, which may be present in any irradiated ergosterol product if the irradiation is not carefully controlled, *is a powerful calcifying agent, but has no significant antirachitic properties.* This introduces a peculiar danger in the clinical use of vitamin D preparations containing it, since failure to obtain desired results from such preparations may lead the physician to use larger amounts, thus increasing the dose of the toxic factor. Long-continued administration of relatively small amounts of vitamin D preparations, contaminated with "toxisterol," may lead to gradual abnormal calcifications, whose presence may not be suspected for many years. There is clinical evidence indicating that excessive vitamin D itself, or even the natural crude drug containing it, cod liver oil, may promote cardiac disturbances or vascular abnormalities.

When one considers the extent to which the public is subjected to utterly uncontrolled irradiated food products, and the extent of the current fad of self-irradiation, equally uncontrolled, one is justified in expressing a word of caution in connection with the additional prescribing of, or self-medication with, high doses of an extremely potent drug formed by such irradiation. That such a word of warning is not out of place is apparent from the vitamin D deaths reported from England, and the recent one occurring in our own state.

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2 Bills, C. E.: Physiol. Rev., 15: 1 (Jan.), 1935.

GENES, HAPTENES AND AUTOCYTOTOXIC HORMONES*

During the last ten years immunologic research has led to the discovery of four basic physiologic facts:

(*a*) The colloidal and particulate permeability of mammalian epitheliums.

(*b*) Differences between the immunochemic specificity of different organs, tissues and body fluids of an individual and, at different stages of development, maturity and senescence.

(*c*) The "fractional antigenicity" of certain environmental crystalloids ("haptenes").

(*d*) "Heterophile antibodies" (anti-haptenes) that function as autoallergic or autocytotoxic hormones.

To clinical science the new facts suggest plausible explanations for numerous research failures of the past. General biologists may find the new data equally suggestive, particularly in their bearing on current theories of genetics and organic evolution.

CLASSICAL THEORIES OF EPITHELIAL DEFENSE

Belief in the colloidal impermeability of normal skin and mucous membranes was originally deduced from studies of osmotic interchange through sausage-skins, fish-bladders, and parchment membranes.

If egg-white, serum, milk or other proteinaceous material is thus dialyzed, the various simple salts and other non-colloidal components of the material are readily demonstrated in the dialyzate. Protein molecules, however, are apparently retained quantitatively by the membrane, the most delicate colorimetric test failing to detect a trace of protein in the diffusate.

It seemed obvious from such evidence that normal skin and mucous membranes were perfectly designed for the prevention of internal tissue contamination by environmental colloids.

This perfectionist theory became a major premise in practical clinical logic. It followed logically, for example, that food proteins must be hydrolyzed to peptones, amino-acids and other simple crystalloids before they can be absorbed from the gastro-intestinal contents into local capillaries or lymphatics.

Certain individuals are hypersensitive to one or more food proteins. These individuals give no allergic reactions with the final split products of protein digestion. Obviously, therefore, they must have an hereditary or acquired hyperpermeability of the gastro-intestinal mucosa.

RECENT PROOF OF EPITHELIAL PERMEABILITY

Experimental paradoxes and clinical inconsistencies, however, eventually led to a restudy of colloidal diffusion through animal membranes. It was found, for example, that measurable amounts of egg protein can be demonstrated in fish-bladder dialysates, by the simple device of evaporating the

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Presented before the Sigma Xi Club, University of California, Davis, October 16, 1935.