

one animal in which 2 rupture points were present, the spinal cord was removed from the 4 T through the 2 L inclusive and caudal to the 6 L segment; both vagi were completely sectioned. In another in which 4 rupture points were observed, the cord removal extended from the 4 T through the 2 L segments and caudal to the 6 L segment; both vagi were sectioned. In a third animal, immediately after vagotomy, 10 cc. of urine from a non-pregnant woman was injected. Twenty-four hours later when an exploratory operation was performed, ovulation had not occurred. Immediately 10 cc. of pregnancy urine was injected. The animal died during the night but one follicle had ruptured. Autopsy showed that the spinal cord had been removed from the 4 T through the 2 L segment and caudal to the 5 L segment; both vagi were cut in the neck. Microscopic observations confirmed the occurrence of ovulation where rupture points had been observed grossly.

These experiments conclusively show that ovulation induced by the injection of pregnancy urine does occur in the complete absence of the visceral afferent and efferent vagal pathways to the ovary, and of those which pass to and from the thoracolumbar and sacral segments of the spinal cord. The efferent pathways were certainly completely removed; thus rendering impotent the effect which any few remaining afferent pathways might exert.

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The Protein-Crystalloid Complex as an Antigenic Unit.*

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It was implied in all classical theories of specific immunity that the alien protein molecule functions as a single antigenic unit, stimulating the production of a single antiprotein substance or function. Within the last decade, however, this early theory has been challenged, several European theorists denying the assumed antigenic unity and postulating that the protein molecule is little more than an immunologically inert mechanical "carrier" of potentially antigenic superficial crystalloids. Each of these superficial "determinants," "coefficients," or "unit characteristics," is pictured as func-

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tioning as a practically independent antigenic unit. There are numerous variants of this theory, differing mainly in the postulated degree of independence or interdependence of the sub-colloidal specificity determinants.

This concept is an apparently logical deduction from the "Landsteiner phenomenon," the well-confirmed fact that immunochemically non-related proteins are more or less homologized if conjugated with the same non-antigenic crystalloid. The resulting antisera apparently have anti-crystalloid functions which can be specifically "absorbed" from such sera.

A critical examination of published data of this type, however, has suggested a possible source of logical error, or at least of a distortion of the logical perspective. Medvecky and Uhrovits,¹ for example, studied the relative specificities of artificial protein-benzoyl conjugates. Quantitative analyses of all wash waters and other waste products in a duplication of their technic suggest that the average colloid of their end-products must have been the "carrier" of no less than 150 to 200 attached benzoyl radicals. Such a mechanical burying of the protein under a unit crystalloid must have given antigenic conditions rarely if ever duplicated in nature. We have, therefore, modified the quantitative relationships of their technic so that our average end-product is the "carrier" of not more than 20 to 30 benzoyl radicals. Typical relative specificities of 3 such partially benzoylated antigens are shown in Table I.

TABLE I.
Heterophile Relationships of Partially Benzoylated Natural Antigens.

Dilution of Stock Solution	Titration with Anti-BEW Precipitin			Titration with Anti-BHS Precipitin		
	BEW	BHS	BDS	BEW	BHS	BDS
1:320	+	+±	0	0	+++	++
1:640	+++	+	0	0	++++	+±
1:1,280	++	+	0	0	+++	+±
1:2,560	++	+	0	0	+++	+
1:5,120	+±	±	0	0	++	+
1:10,240	+	±	0	0	++	+
1:20,480	+	0	0	0	+	+
1:40,960	±	0	0	0	+	+
1:81,920	0	0	0	0	±	±
1:163,840	0	0	0	0	0	±
1:327,680	0	0	0	0	0	±
1:655,360	0	0	0	0	0	0

BEW, benzoylated egg white; BHS, benzoylated horse serum; BDS, benzoylated dog serum; parallel titrations by means of anti-BEW and anti-BHS rabbit precipitin. 0.5 cc. 10% anti-sera, plus 0.5 cc. increasing dilutions of 7.5% stock solutions of the benzoylated antigens; incubator 2 hours, ice-chest over night; quantitative readings by means of a turbidity scale.

¹ Medvecky, A., and Uhrovits, A., *Z. f. Immunitätsforsch.*, 1931, **72**, 251.

It is seen that the 3 partially benzoylated antigens have no invariably common fractional identity, in spite of the presence of an equal number of benzoyl "coefficients" in each antigen. Moreover, the heterophile relationships suggested by titration with one antiserum are not the same as those suggested by a parallel titration with an antiserum of different specificity, both antisera presumably containing the same antibenzoyl fractional antibody or function.

These data are almost impossible to harmonize with the suggested theory that each protein is but a mechanical "carrier" of independent superficial unit "determinants". They can be harmonized, however, with the classical postulate that each protein-crystalloid complex functions as a single antigenic unit.

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Emetic and Fatal Doses of Digitalis at High Altitudes.

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For over a hundred years, there has been some knowledge of changes in effects of drugs at high altitudes. However, some scientific studies, according to a summary of Loewy,¹ indicate conflicting tendencies. Nevertheless, it would seem that changes in certain pharmacological actions might be expected from known or assumed changes in circulatory and respiratory functions, although the degree or character could not be exactly predicted, owing to the adjusting influences of compensatory mechanisms. The interest attached to any possible changes is both fundamental and practical, the latter especially with reference to dosage, toxicity and unexpected actions in medication of persons at high altitudes. Macht² has recently claimed that digitalis is more toxic at high altitudes in the Blue Ridge Mountains, Rocky Mountains, and the Tyrolean Alps than at Baltimore. The continued studies of digitalis along different lines in this laboratory prompted us to include determinations at high altitudes of the emetic and fatal doses in pigeons and of fatal doses in cats. The results obtained are generally consistent with Macht's

¹ Loewy, A., *Physiologie des Höhenklimas*, 1932, 414, Springer, Berlin.

² Macht, *Am. J. Physiol. (Proc.)*, 1931, **97**, 540.