flavin, nicotinic acid, nicotinamide, calcium pantothenate, p-amino benzoic acid, pyridoxine, and vitamin C did not modify the synthesis in low concentrations and increased it in higher ones. 4. Vitamin E increased the synthesis in low and increasing concentrations.

14883

Phlebostatic Axis and Phlebostatic Level, Reference Levels for Venous Pressure Measurements in Man.*

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In the determination of venous pressure both in the clinic and in the laboratory it is often necessary to make the measurements with the subjects in positions (sitting, intermediate sitting, with parts under study in many positions relative to the level of the heart) other than supine. The levels of reference available at the present time fail to fulfill the requirements of practicability and accuracy necessary for clinical and experimental studies. At least 9 different reference levels have been given for the measurement of venous pressure.[1-8] Some have been related to anatomic parts of the body and some to the horizon or examination table. The lack of consistency in the reference or heart levels makes it difficult to undertake studies on venous pressure. The present studies were conducted to find a point of reference for venous pressure measurements which may be applicable to subjects of any build, in many positions, and with the vein under study in any positions necessary for the study of clinical problems concerned with venous pressure measurements in any superficial vein.

Method and Materials. The apparatus, the Phlebomanometer described elsewhere, is accurate to $\pm$ 1 mm of water, and checked satisfactorily at frequent intervals with a water manometer.[9] Approximately 265 determinations were made on 165 normal young adults (ages 16-34 years) of both sexes and negro and white races who rested prior to and during measurements on a firm plywood table with an adjustable head. The veins studied are indicated below.

Results. In 99 subjects of both races and sexes it was found that when a plane passing longitudinally through the body parallel to its anterior surface and midway between the dorsal surface of the thorax and the base of the xiphoid process was used as the reference level the venous pressure measurements in the median basilic veins varied relatively little even though the thickness of the chests varied considerably (78-135 mm, mean 97 mm). That the plane described is a good reference level was further substantiated by the fact that in 10 selected subjects with very thick chests (mean reference level 126 mm from dorsum of trunk) and 10 with very thin chests (mean reference level 89 mm from dorsum of trunk) the venous pressure

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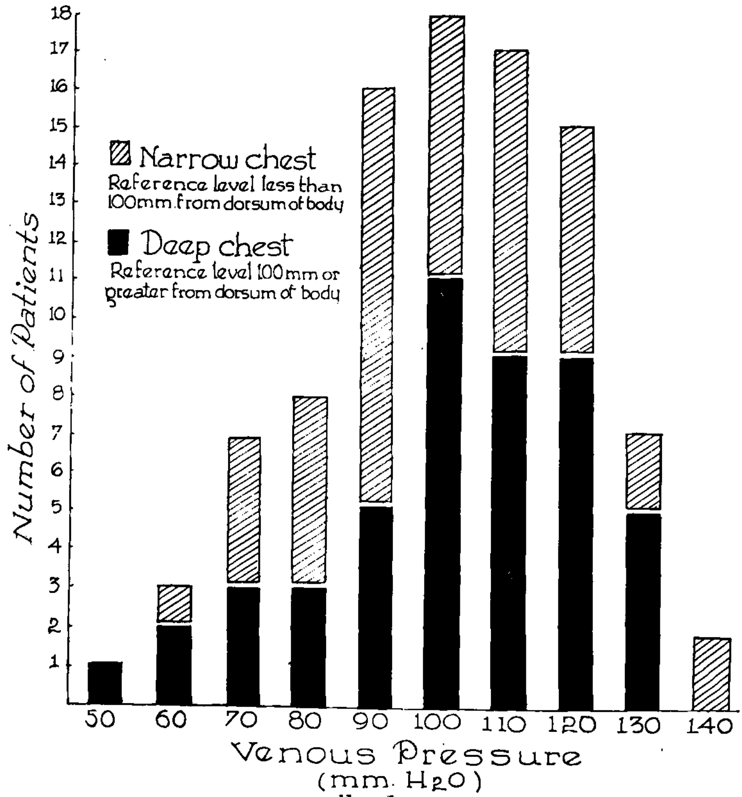

FIG. 1.

Distribution curve of venous pressure measured at the phlebostatic axis (see text) in 99 normal subjects with the axis less than 100 mm from the dorsal surface of the trunk and also in subjects with the axis 100 mm or more from the dorsal surface of the trunk. The ages varied from 16-34 years and included both sexes and the white and negro races. The number of subjects in each venous pressure group may be determined by projecting the length of the columns on the ordinate. For example, the subjects with venous pressures of 70 mm of water consisted of 2 with thick chests and 1 with a narrow chest; of the subjects having 100 mm of water venous pressure there were 5 with thick chests and 11 with thin chests. It can be seen that the distribution of venous pressures was essentially the same for the subjects with thin and thick chests when the phlebostatic axis was used as the level of reference.

measured at the above reference plane averaged 104 and 103 mm of water respectively. Furthermore, when a distribution curve was drawn to correlate venous pressure and chest thickness no significant differences were found in the venous pressure values for chest thickness provided the above reference plane for heart level was used (Fig. 1).

To determine the plane of reference, heart level, for subjects in the erect sitting position the arm was elevated until the venous pressure in the basilic vein reached that previously recorded for the supine position. The level of the vein in relation to the intercostal space was noted. From Fig. 2 it can be seen that in the majority of instances the plane passed through the fourth intercostal space at its junction with the sternum.

The frontal plane described for the supine position and the cross sectional plane for the erect position intersected to form a transverse axis which passed through the thorax from side to side midway between the anteroposterior surfaces at the level of the junction of the fourth intercostal space with the margin of the sternum. In order to determine whether or not this axis can be used as a *universal axis* of reference or heart level for venous pressure measurements with the subject in positions between supine and erect sitting the following studies were conducted:

1. The venous pressures were recorded in a

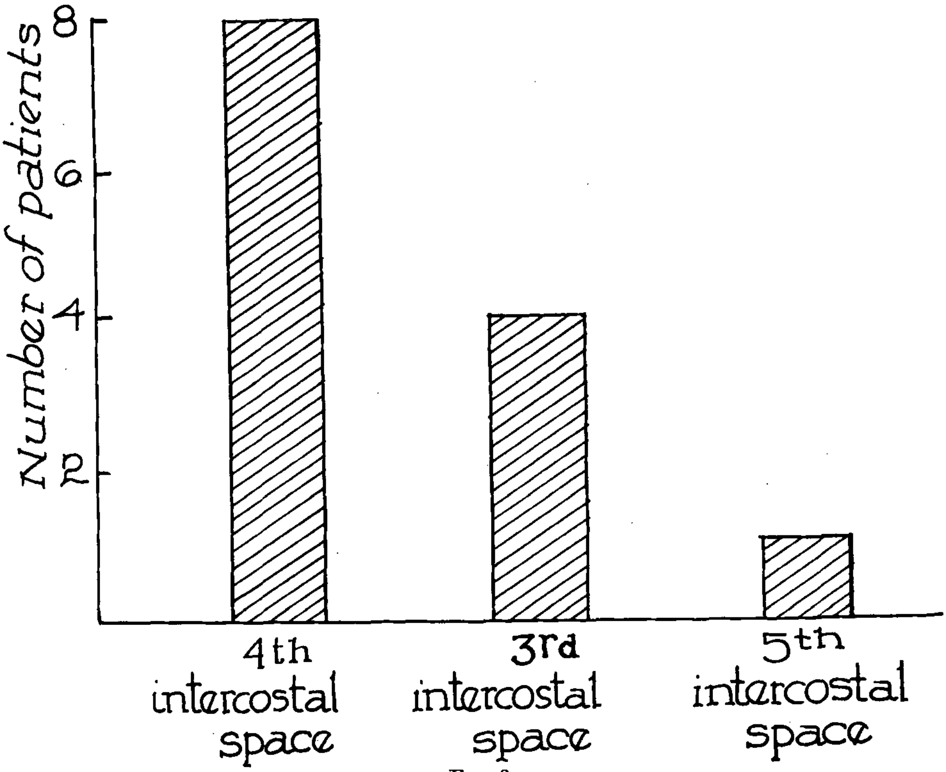

FIG. 2.
In 13 normal young adults the venous pressure in the basilic vein was determined with the subject in the supine position (see text for method). The subjects then sat erect and the vein was elevated until the pressure in the basilic vein reached that recorded in the supine position. In the majority the vein was found to have been raised to the level of the junction of the fourth intercostal space with the lateral margin of the sternum. There were, however, some variations.

dorsal vein of the hand with the subjects in the supine position and in intermediate sitting positions in which the dorsum of the trunk and examining table formed angles of 0, 25, 35, 45, 55, and 90 degrees respectively. Venous pressure measurements were made in each of these positions with the vein under study in the same horizontal plane as the transverse axis of reference. The venous pressure values obtained were essentially the same regardless of the position of the trunk (Fig. 3).

2. Further to test this phenomenon the vein on the dorsum of the hand was kept at the reference level for the supine position and the trunk was flexed to the sitting positions described above. For each position the venous pressure in a dorsal vein of the fixed hand was measured and found to increase by a pressure equal to a column of water extending from the vein of the hand to the new position of the transverse axis of reference.

3. In a third group of studies the trunk was flexed into the above sitting positions and then the hand was elevated until the pressure in a dorsal vein of the hand reached that previously determined for the supine position. Invariably the vein on the dorsum of the hand was found to be at the horizontal level passing through the transverse axis.

A study of widely separated veins important in the evaluation of clinical states concerned with vascular disease and particularly venous obstruction (superficial inferior epigastric, superficial superior epigastric, paraumbilical, cephalic, saphenous, dorsal veins of the feet, thoracoepigastric) indicated that the transverse axis proved to be consistently applicable as a site from which to measure venous pressure.

Comment. The literature shows that most

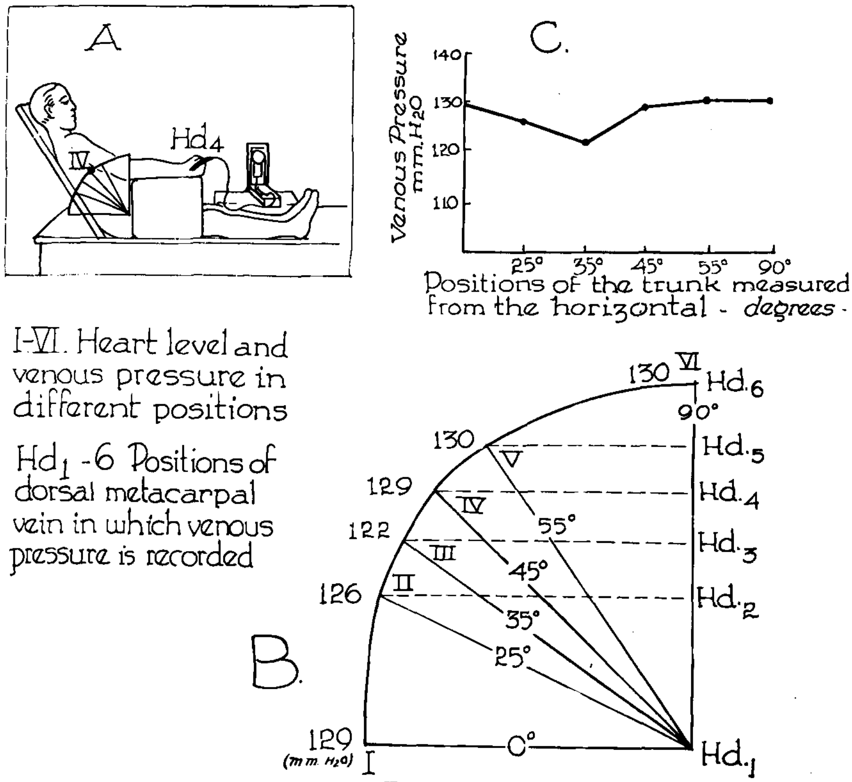

FIG. 3.
The venous pressure in a dorsal vein of the hand was recorded in 10 subjects in various sitting positions varying from horizontal to erect using the phlebostatic axis as the level of reference in all positions. Insert A shows diagrammatically how the trunk was flexed and the hand elevated to the phlebostatic level in the 6 positions indicated. Insert B shows the relative positions of the hand and phlebostatic axis for various intermediate sitting positions. Insert C represents graphically the venous pressure in mm of water for the 6 positions of the trunk. It can be seen that with the use of the phlebostatic axis as the level of reference the 6 positions of sitting did not alter the venous pressure in the dorsal vein of the hand.

observers have employed different reference points for heart level for different positions of the body.[10] Others have limited their studies to one position and employed a reference point suitable only for the one position of study.[11–12] It is obvious that such methods have marked clinical limitations. Furthermore, many observers have tried to determine heart level on an anatomic basis without making a serious effort to correlate the anatomic level with physiologic venous phenomena. Although an anatomic landmark is necessary, the validity of this landmark must be based upon physiologic data. In the observations reported above, it was made certain that the anatomic landmark employed to define the universal axis of heart level correlated and conformed to physiologic venous phenomena. Obviously no one landmark will satisfy absolutely all subjects but the transverse axis described above appears to lead to relatively little variations in results when normal subjects are studied. From roentgenographic studies of living subjects, the transverse axis passes through the openings of the venæ cavæ into the right auricle. When studying venous pressures in any vein with the subject in any position described but always with the transverse axis parallel to the horizon, it is only necessary to refer the vertical level of the vein to the horizontal plane passing through the trans-

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verse axis.

It is proposed to call this transverse axis of heart level the *phlebostatic axis* and any of the horizontal planes passing through this axis used as the reference level the *phlebostatic level* in order to avoid confusion with the many different "heart level" landmarks described previously in the literature.

Summary. It has been found that the reference level or heart level for the measurement of venous pressure is an axis which runs transversely through the thorax at the point of junction of a plane passing cross-sectionally through the fourth intercostal space adjacent to the sternum with a frontal plane passing midway between the posterior surface of the body and the base of the xiphoid process of the sternum. Horizontal planes passing through this axis are the reference levels or heart levels to be used for that particular position of the patient. It is proposed to call the axis the *phlebostatic axis* and the horizontal planes passing through the axis the *phlebostatic level.*

14884

Biological Activity of N-Methylnicotinamide and Nipecotic Acid.*

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The use of microbiological vitamin assays always involves an uncertainty in that the activity of certain related compounds may be different for the test organism than for the animal. In the case of nicotinic acid, no derivative has been found, to our knowledge, which is active for *L. arabinosus* but inactive when ingested by an animal. In fact, it has been established that a number of precursor compounds readily elicit an active response from the animal, but must first be hyrolyzed to be active for *L. arabinosus*.[1-3] It is now generally accepted that autoclaving samples with 1N alkali gives a degree of potency with *L. arabinosus* which agrees closely with the biological vitamin activity for animals. The results given in two recent reports may raise some question about this assumption.

Von Euler *et al.*[4] have reported that hydrogenated nicotinic acid (nipecotic acid) is active for *Staph. aureus* and *Proteus vulgaris.* This is of interest because nipecotic acid has been found inactive for the dog[5] and dysentery bacilli.[6] Najjar *et al.*[7] have reported that N-methylnicotinamide chloride (nicotinamide methochloride) is active in preventing and curing nicotinic acid deficiency in dogs and produces a growth response with *E. coli.* This compound has previously been found inactive for the dog,[5] and *L. arabinosus*.[3] Furthermore, many investigators have tested trigonelline, which is chemically related to N-methylnicotinamide as nicotinic acid is to nicotinamide, and have found it inactive for the dog, man and all microörganisms tested.[1]

In this paper, we wish to present further studies on the activity of N-methylnicotin-

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