PHYSIOLOGICAL ADAPTATION AND NUTRITIONAL STATUS DURING AND AFTER PREGNANCY

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TWELVE FIGURES

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INTRODUCTION

The meager existing knowledge regarding the physiological requirements, adjustments and readjustments of the human mother during and following the gravid and lactating states indicates that deprivations owing to restricted or imbalanced diet, disease or injury should be a grave concern of all authorities charged with protecting and improving the health of this and other nations. The cumulation of salient scientific observations demonstrates the urgency for extending fundamental research in all fields relating to human reproduction, for the current benefit of mothers and infants, for their benefit when they become adults, and for the benefit of generations to follow. Developments in obstetric, pediatric and geriatric care; in food production, preservation and preparation; in dietetic and nutritional practices; and in public health measures and elimination of world needs for economic aid — all may be profoundly influenced by the scientific facts being brought into focus in the field which Adair ('43) so aptly designated "The Frontier of Human Welfare."

Pregnancy may precipitate malnutrition through: (1) the sudden inability of food intake to satisfy augmented nutritional requirements; and (2) the interference of physiological adjustments with the consumption of an adequate food intake or with its absorption and utilization. Poor nutritive state at conception, owing to underfeeding or to misfeeding, enlarges requirements and may create demands for greater physiological adjustments than the dietary permits and growth and development continue to exert nutritional demands. Darby et al. ('48) believe that the biochemical assessment of the nutritional level during pregnancy and lactation permits objective quantitation of individuals, but with present knowledge the problem "is one of *investigation, not of interpretation* of observed changes."

Various methodologies have been used in evaluating individual and group differences in metabolic function and in physiological adaptation to increased nutritional needs during pregnancy, parturition, the puerperium and lactation. The quantitative chemical procedures for evaluating nutritional status have included: (1) metabolic balances, analyses of food and excreta for corresponding time intervals, and determination of body gains and losses of protein, minerals and vitamins; (2) measurement of the urinary excretion of the metabolites of protein, minerals and vitamins by mothers and their newborn infants; and (3) determination of the distribution and concentration of blood proteins, minerals and vitamins (Research Laboratory, '53). While chemical analyses provide fundamental information, the procedures are not practical for studies of large numbers of individuals. Some of the complex problems encountered in the evaluation of nutrition survey data and the necessity for careful appraisal have been discussed (Dann and Darby, '45; Garry and Wood, '46; McHenry and Leeson, '47; Sinclair, '48; National Research Council, '49; Pett and Angus, '49).

This report summarizes the results of an investigation of the nutritional status of mothers and their infants (Moyer et al., '54). The subjects studied were healthy, non-pregnant white women and pregnant white and Negro women who received, prenatal, natal and postnatal care from public and private sources in an urban community. Emphasis in this communication is placed upon nutritional aspects of pregnancy, and major reliance for evidence rests upon the results obtained for a group of women "selected" as representative of typical, uncomplicated gestation.

Nutritional status and progressive physiological adaptation to the stresses of reproduction were assessed on the bases of clinical observations, medical histories, food intakes and seriatim microchemical determinations of hemoglobin, sera total protein, vitamin C, vitamin A, carotenoids and alkaline phosphatase. The blood components determined represent various developmental and functional metabolic processes and involve several body systems. The tripart results with several hundred patients indicate the presence or absence of relationships between nutritional status and health in pregnancy.

SUBJECTS

In the investigation, almost all of the subjects were obtained from three sources. Group A included 109 white and 544 Negro women who were seen in the public prenatal clinic maintained at Herman Kiefer Hospital by the Detroit Department of Health. These women represented the low-income and indigent populations of Detroit. Group B consisted of 33 white and 131 Negro subjects who were served by the private prenatal clinic at Henry Ford Hospital, Detroit. In general, the women in Group B represented families with moderate incomes. In Group C were 230 white private patients of an obstetrician who is a surgeon in the Department of Obstetrics and Gynecology, Harper Hospital, Detroit. The husbands of the majority of the women in Group C were professional men and the group would be characterized as middle-class with a few wealthy individuals. In the total number of subjects were 6 white and 11 Negro women who were not in Groups A, B or C.

Infants were considered delivered at term if any two of the following criteria were met: gestation of 37 weeks or more; birth weight of at least 2,500 gm; birth length of at least 47 cm. If records for only two criteria were available, classification was not made unless the data agreed. Length of gestation was calculated by assuming that the estimated date of delivery represented a pregnancy of 40 weeks and any variation of the actual date indicated the difference of the gestation period from 40 weeks. Length of gestation was not calculated if the date of last menstrual period was not known.

Inasmuch as the data in this study are not always normally distributed, median values rather than means are presented since they are a truer measure of central tendency.

Men; non-pregnant women

As a check on analytical procedures, and to obtain comparative seriatim blood data for individual physiological variability, seasonal influence, sex differences and other factors, a group of 48 healthy, non-pregnant white women and a group of 24 white men of comparable ages also were studied. These subjects were professional people associated with the laboratory and the hospitals.

Selected subjects

After records for all subjects were completed, those were "selected" who would represent gestation and delivery uncomplicated by unusual disturbance or disease, and who were delivered of healthy, term infants weighing at least 2,500 gm. The criteria for selection included consideration of the medical history, the clinical course during pregnancy and the outcome of gestation with respect to both mother and child. Excluded from the group were women with physical structural defects, congenital or acquired, and those in whom malnutriture or disease had left clinical recognizable effects so serious that the pathological process might permanently have impaired health. Both mother and infant were omitted for reasons which would exclude either of them. Such conditions as active tuberculosis, syphilis and toxemia during the current pregnancy were bases for categorical exclusion from the Selected Group. In other instances, obstetrical judgment combined with pediatric [1] consultations in relation to the condition of the infant were determining factors. Women whose deliveries involved operative procedures other than low forceps or caesarean section after an estimated 37 weeks of gestation were excluded, as well as those who were in labor over 24 hours. Of 1,064 women (378 white, 686 Negro), only 427 women (160 white, 267 Negro) and their babies met the criteria for inclusion in the Selected Group. Subsequent reports will discuss groups of subjects who were excluded from the Selected Group.

Group characteristics

For the white and Negro women in Groups A, B, C, Selected and Total, averages are given in table 1 for age, physical characteristics, pregravid weight, weight change during gestation, infant birth weights, race, diet rating and estimations of prenatal care.

Differences in averages for stature (162 to 164 cm) and for weight change during pregnancy (23 to 25 lb.) among the several groups were slight; however, group averages for age (23 to 29 years) and for pregravid weight (54 to 59 kg) showed more variation. White women in each group were older, on the average, than Negroes in the same group. White private patients (Group C) were older, weighed less and were slightly taller than white women in the public clinic Group A. Despite the difference in physical characteristics, the average weight changes of the several groups during pregnancy (table 1) were comparable.

Median birth weights of infants in the groups ranged from 3,038 to 3,307 gm. White infants in the higher economic Group C had a greater average weight (3,306 gm) than the average for those in the public clinic Group A (3,200 gm). The average birth weight of Negro infants in the private clinic Group B was higher than that of those in Group A.

[1] Donald J. Barnes, M.D., and Otto Grob, M.D. gave generously of their time in pediatric consultation.

TABLE 1

General characteristics of study groups

	WHITE WOMEN					NEGRO WOMEN			
	Selected	Group A	Group B	Group C	Total	Selected	Group A	Group B	Total
Number of subjects[1]	160	109	33	230	378	267	544	131	686
Age, median (yrs.)	28	26	27	29	28	24	23	26	24
Stature, median (cm)	163	162	162	164	163	163	163	163	163
Pregravid weight, median (kg)	56	58	54	56	56	57	57	59	58
Weight change, median (lb.)	23	23	23	25	24	23	23	25	23
Gravidity									
Primigravidas, %	28	25	42	37	34	21	31	42	33
Multigravidas, %	72	75	58	63	66	79	69	58	67
Infants' birth weight,[2] median (gm)	3307	3200	3290	3306	3282	3089	3038	3295	3078
Diet rating,[3] median, %	74	63	75	77	73	64	63	63	63
Prenatal care									
Good, %	71	14	91	98	71	34	30	80	40
Poor, %	18	53	0	0	17	21	22	2	18

[1] Other values given in the table may be based upon slightly smaller numbers of subjects.

[2] In Group A 10 white and 52 Negro infants; in Group B, 4 Negro infants and in Group C, 6 infants were born prematurely.

[3] Based upon average values for weekly servings of food in the Seven Basic Food Groups which would supply the Recommended Allowances for pregnancy.

The median pregravid weights of Selected white and Negro women were 56 and 57 kg, respectively. According to the Metropolitan Life Insurance Company Standard Tables of Height and Weight, in the Selected Group 5.7% of the white and 11.9% of the Negro women were more than 20% overweight (pregravid): 1.9 and 2.3% of the white and Negro women, respectively, were more than 20% underweight. Thus, a greater percentage of the Negro women fell within the extreme weight group.

Periodic dietary records of sufficient length and accuracy, accompanied by dietary histories carefully cross-checked and evaluated, have given basic information on what pregnant women eat (Burke, '47). Dietary records, obtained by experienced personnel, complement clinical observations effectively in relating prenatal nutrition to health of the infant (Burke et al., '43a). Weighed diets for determining protein intake combined with determinations of urinary nitrogen excretion have contributed additional information in evaluation of the effects of nutritional factors upon the health of mother and infant (Dieckmann et al., '51a, '51b). For this study, qualitative procedures for estimating the dietary intake of large groups of individuals were developed and tested for reliability. Better mixed diets with higher nutrient value were indicated for the white women in the Selected Group, in private patient Group C, and in the private clinic Group B by median diet ratings of 74, 77 and 75, respectively. In contrast, the white women in the public clinic Group A and Negro women in all three groups had diet ratings averaging only 63 or 64% (table 1).

Relative evaluation of prenatal care in terms of good, fair and poor as judged from the clinical records, was based on the personal impressions of the obstetricians. The major considerations were the time at which the patient sought prenatal care and her dependability and cooperation in following instructions.

The women in groups of higher socioeconomic status received better ratings for prenatal care; 98% of the private patients (Group C) and 91% of the white and 80% of the Negro private clinic patients (Group B) were graded "good." In the Selected Group, 71% of the white subjects were rated good but only 34% of the Negro subjects; however, almost equal proportions of the two races were rated "poor," 18 and 21% respectively. That over 50% of the low-income white women had poor prenatal care is accounted for by their seeking medical aid late in pregnancy.

Data for the total groups of white and Negro patients were similar to the respective values for the Selected patients of the two races.

Since differences in gestational weight change were not appreciable among the groups of white and Negro women, we have assumed that the blood volume changes for all groups were similar. This assumption is necessary to comparisons of the concentrations of several blood components from the various groups at equivalent stages of pregnancy. The characterization of the various groups (table 1) suggests that in the interpretation of the data on the bases of nutritional status, racial characteristics, inequality of nutrient intake and of prenatal care should be considered.

Longitudinal study

Of the subjects in the Selected Group, 70 white and 30 Negro women provided seriatim blood samples in pregnancy and postpartum. One hundred women were included in the longitudinal study. Each woman supplied at least one blood sample in three of the 4 study intervals: first, second and third trimesters of pregnancy and postpartum (one to 8 days). These longitudinal data permitted study of trends in the same individuals during the progression of pregnancy versus those indicated by cross-sectional data. Trends indicated by group average concentrations of blood components may not always agree with those shown by concentrations in seriatim blood samples collected from the same individuals at various stages in the cycle. Consecutive observations have been demonstrated to have greater scientific value since the same individuals are observed at intervals during the physiological transformation (Macy and Mack, '52).

MEDICAL RECORDS

Medical records from the clinics, hospitals and physician's office were compiled and evaluated by the obstetricians (J.P.P., H.C.M., P.C.D.). These records have the advantage of representing the interpretation and judgment of a single team in their evaluation. The information obtained consisted of: (1) medical and gestational histories (2) clinical data concerning the current gestation, including diet; (3) pertinent facts about delivery and the puerperium; and (4) data pertaining to the physical status and health of the infant. The number of subjects involved in the survey and the length of time involved in the study of an individual throughout pregnancy and postpartum made it impossible to obtain complete information regarding every subject. The greatest factors in incompleteness of data were failure to seek prenatal care early in pregnancy and patients moving away from the area prior to delivery.

BLOOD SAMPLING

Peripheral blood samples were collected and analyzed by the microchemical methods developed by Bessey and Lowry and previously used in this laboratory in a study of the nutritional status of children (Moyer et al., '48). Approximately 0.3 ml of blood was drawn from women by finger puncture and from infants by heel puncture after cleansing the skin with alcohol. Hemoglobin and serum protein were determined immediately after collection and preparation of the samples. Samples and protein-free filtrates of serum were prepared and measured into microtubes which were stored at — 30°F. for determinations of vitamin C, alkaline phosphatase, vitamin A and carotenoids.

Blood samples usually were taken in the morning but were not necessarily representative of the fasting state. All groups were equally subject to unstandardized conditions, such as traveling, waiting to see the physicians, and anxiety over physical condition. It is known that hemoglobin may be increased due to anxiety, fatigue and diurnal influences (Kenyon and Macy, '38) and that the blood levels of some nutriments are readily influenced by recent food consumption.

Of the 1,064 women enrolled in the study, 378 white mothers and their infants provided 1,761 maternal and 265 infant blood samples; 686 Negro mothers and their infants gave 2,005 maternal and 467 infant blood samples — a total of 3,766 maternal and 732 infant samples. Some patients who entered the study early in pregnancy provided as many as 13 samples.

Capillary versus venous samples

Microdeterminations of hemoglobin and sera protein, vitamin C, alkaline phosphatase, vitamin A and carotenoids were made on samples of blood collected coincidentally by venipuncture and by finger prick from 20 women (Di Loreto et al., '52). Venous samples were collected with minimum stasis and capillary samples were obtained from a free-flowing wound. The determinations showed that the samples of venous blood contained greater amounts of hemoglobin and serum protein. Consistent differences, however, were not found for sera vitamin C, alkaline phosphatase, vitamin A and carotenoids. Although data from chemical determinations on peripheral blood samples may not duplicate those for venous samples, the differences between results for the two types of blood samples would be constant and the trends obtained by either procedure would be similar.

Postpartum blood changes

Whether the levels of blood constituents vary appreciably in an individual mother or infant during the first few days after delivery also was investigated (Moyer et al., '54). Five white and 7 Negro women and their infants were chosen for study on the basis of health and absence of complications. The women were selected from those delivered on a single day. The following day and daily for 5 days, blood samples were taken from the mothers and infants. Maternal serum protein values were consistently higher for the 6th than for the second day. For the majority of the subjects, values were higher for the 5th than for the second day — results which are consistent with other observations made in this laboratory (Macy and Mack, '52). There were no consistent differences among the maternal or infant protein values for the second, third and 4th postpartum days. Definite trends were not apparent in the hemoglobin, vitamin C, vitamin A, carotenoid or alkaline phosphatase levels of the mothers or the infants. Because of this finding, in the investigation reported here blood samples were collected from parturient mothers one to 8 days after delivery and from their infants one to 9 days after birth.

Blood volume

Any consideration of physiological trends in the reproductive cycle must recognize alterations in blood volume in the interpretation of results, since blood volume may increase as much as 25% during pregnancy (Dieckmann and Wegner, '34a, '34b; McLennan and Thouin, '48; Tysoe and Lowenstein, '50; Lund, '51) and may even increase during labor (Tatum, '53). If there is no change in the concentration of blood constituents with pregnancy, it is obvious that there are increased amounts available in the bodies of the mother and fetus. An increase in concentration indicates an even greater increase in the supply available for use in the two bodies; on the other hand, a decrease in concentration of a blood component without knowledge of blood volume change is not definite evidence of a decreased supply of that component for the bodies.

Although there is no satisfactory method for determining blood volume change in surveys of population groups, in this investigation the Selected Group permits study of individual characteristics and physiological variability during gestation. Results for the Selected women also provided an average pattern for reproduction with which departures from healthful performance may be compared. Since there were only small differences in the medians for age, height, pregravid weight and maternal weight changes during pregnancy among the 4 groups of women (table 1), we have assumed that the blood volume changes for all groups were similar. This assumption justifies comparison of blood concentration data from the various groups at equivalent stages of pregnancy without knowledge of blood volume.

ANALYTICAL METHODS

Hemoglobin

Hemoglobin was determined by the alkaline method developed by Bessey and Lowry ('45). Ten cubic millimeters of fresh, whole blood were placed in 4 ml of 0.5% solution of concentrated ammonia and the resulting color intensity was measured in a Beckman spectrophotometer at a wave length of 540 μ.

Total serum protein

Serum protein concentration was measured in droplets of serum 2 to 4 cu. mm in size by the method of Lowry and Hunter ('45), employing the gradient tube principle for measurement of specific gravity.

Serum vitamin C

Blood samples were chilled immediately and held under refrigeration until serum could be prepared, after which protein-free filtrates were frozen until analyzed. Serum vitamin C was determined by the micromethod of Lowry et al. ('45) with some modifications described by Bessey et al. ('47). These procedures adapt the dinitrophenylhydrazine method of Roe and Keuther ('43) to the determination of ascorbic acid in 0.01 ml of serum. The method avoids venipuncture and is well suited for mass nutritional status surveys. The term "vitamin C" has been applied to results obtained in this laboratory by methods which determine greater vitamin C activity than would be found by using methods which determine only ascorbic acid.

Serum vitamin A and carotenoids

Serum was prepared and chilled until analyzed for vitamin A and carotenoids by the methods of Bessey et al. ('46b). The measurement of light absorption with a Beckman spectrophotometer adapted to examination of small quantities of solution was described by Lowry and Bessey ('46). This procedure records both total vitamin A and carotenoids: the concentrations for both components are expressed in micrograms per 100 ml of serum.

Serum alkaline phosphatase

For determination of serum alkaline phosphatase, 5 cu. mm. of serum from capillary blood were used according to the method of Bessey et al. ('46a). The procedure employs sodium paranitrophenyl phosphate as the substrate and the released paranitrophenol was measured with a Beckman spectrophotometer adapted as described by Lowry and Bessey ('46). The results are expressed in nitrophenol units, one unit being the amount of phosphatase activity per liter of serum required to liberate one millimole of nitrophenol per hour from sodium paranitrophenyl phosphate under the specific conditions of the test.

Clark et al. ('51) did not find a difference in the alkaline phosphatase activity of plasma and of serum, but in the present study some unusually high alkaline phosphatase values were obtained, similar to those noted by Beck and Clark ('50) without explanation. The high values produced asymmetrical distributions of the data and for this reason the median serum alkaline phosphatase values best represent central tendency.

DIETARY INTAKE

Qualitative 7-day food intake records were obtained from the women in Groups B and C. Records were sought early in pregnancy and at least once during each trimester. Each woman was instructed personally to record on the special form, all information on quantity of food eaten, with descriptions of the food items. Records were omitted for days of illness and other emergencies, and if more than two such days occurred, the 7-day record was discarded.

Nutritionists [2] in the public prenatal clinic routinely obtained 24-hour recall records of the food intakes of women in Group A, supplemented by brief dietary histories. This information was taken at admission and sometimes additional records were secured. The nutritionist tried to determine all the foods eaten the preceding day, both at meals and between meals.

Evaluations were based upon average values for weekly servings of foods in the Seven Basic Food Groups which would supply the Recommended Dietary Allowances for pregnancy. The method was devised in this laboratory (Thomas et al., '54) for making broad comparisons between the dietary intakes of different groups of women and results with the procedure were tested for reliability against analytical values for mixed diets and checked against estimates for pregnant women eating the diets. The method was checked further against diet records and histories of Tennessee women [3] during pregnancy, and rated by procedures in use by Van-

[2] E. Eunice Coy, Director, Nutrition Division, assisted by Jane Todd and Mary Marshall, interviewed the women in the public clinic (Group A) and recorded their food intake.

[3] Diet histories obtained through the courtesy of Dr. Nevin S. Scrimshaw, School of Medicine and Dentistry, University of Rochester, Rochester, New York, were rated by staff members associated with their pregnancy nutrition study. A percentage score was obtained by comparing the calculated nutrient intake with the Recommended Dietary Allowances of the Food and Nutrition Board, National Research Council. Grateful acknowledgment is made of the cooperation of William J. Darby, M.D., and Margaret P. Martin, Ph.D. of Vanderbilt University.

derbilt University and the University of Rochester maternal study groups.

The dietary evaluation procedure employed a scoring technique to obtain a percentage score indicative of an over-all comparison with the Recommended Dietary Allowances of the Food and Nutrition Board, National Research Council ('48). Details of the scoring method and of the reliability and significance of results obtained with it are being published (Thomas et al., '54).

Each diet record also was ranked high, intermediate or low with respect to 6 of the Seven Basic Food Groups. The "low" intake ranking for any food group was arbitrarily established as an intake of less than 60% of the number of servings needed to meet the allowances. Conversely, "high" indicated a number of servings sufficient to fulfill the recommendations. First trimester dietary records were scored on the basis of the allowances for a moderately active, healthy woman; dietaries for the succeeding trimesters were scored on the basis of the allowances for pregnancy. The qualitative evaluations of 473 7-day recordings and 655 24-hour recall records — obtained from 83% of the subjects — are given in table 2.

The short-cut method of rating food intake with average values for servings of a selected list of important foods and food mixtures was necessary to reduce time requirements for interviewing and calculating the values of diets. Regardless of limitations attributed to evaluation methods based upon dietary histories and records (Hunscher and Macy, '51) carefully taken and skillfully evaluated (Burke, '47), qualitative estimations for large population groups provide valuable information on food intake and dietary habits that otherwise could not be recorded. Approximations of nutrient intake for groups possessing racial, socioeconomic and other differentiating characteristics indicate group needs and suggest public health measures and individual instructions for patients aimed at desirable improvements in diets (Donelson and Leichsenring, '45; Burke, '47; Darby et al., '48; Young et al.,

TABLE 2

Ratings of food intake records

	WHITE WOMEN					NEGRO WOMEN			
	Selected	Group A	Group B	Group C	Total	Selected	Group A	Group B	Total
Records, number	216	118	35	284	440	266	551	130	688
Total food intake [1]									
median rating, %	74	63	75	77	73	64	63	63	63
ratings 90% or above, %	10	5	6	12	10	4	5	2	5
ratings below 60%, %	13	42	20	9	19	39	43	42	42
Food groups [2]									
I. Leafy, green, yellow vegetables									
high, %	30	26	20	30	28	29	25	25	25
low, %	48	68	66	42	51	61	67	47	63
II. Citrus, analogous foods									
high, %	64	51	51	71	64	51	53	35	50
low, %	20	40	29	12	21	39	38	46	39
III. Potatoes, other vegetables, fruits									
high, %	1	0	3	2	1	0	0	2	0
low, %	73	96	54	64	72	96	97	89	96
IV. Milk, milk products									
high, %	22	30	14	21	23	21	21	7	18
low, %	36	56	46	30	39	60	60	62	60
V. Meat, eggs, legumes									
high, %	8	4	3	13	9	6	5	8	6
low, %	34	65	37	27	38	47	49	45	48
VI. Bread, cereals									
high, %	49	65	54	33	43	65	68	36	62
low, %	11	11	12	18	15	8	8	15	9

[1] A qualitative dietary procedure tested for reliability was used to evaluate food intake records with respect to the Recommended Dietary Allowances. Records obtained during the first trimester of pregnancy were rated in relation to the allowances for adult women; intakes in the last trimesters, in relation to the allowances for pregnancy. A combination of servings which supplied the recommendations was scored 100%.

[2] Food intakes which included a sufficient number of servings from a food group to meet the allowances were ranked "high" with respect to that food group; if the number of servings provided les than 60% of the allowances the ranking was "low."

'52; Beal, '53). Greater confidence in gross or crude methods than the procedures warrant, however, is unjustifiable.

THE USUAL PHYSIOLOGICAL COURSE DURING REPRODUCTION

Variation of response is inevitable in a complicated chain of metabolic events such as those associated with gestation. The chain involves the symbiotic growth and function of two vitally different organisms, yet information is sketchy regarding the extent to which physiological alterations are compatible with the health of both individuals. Knowledge of the biological changes that occur with regularity following conception and subsequently characterize the progressive stages of the reproductive cycle, and of the ranges of performance to be expected in individuals and among groups of women of different races, is basic to the differentiation and evaluation of nutritional and other influences upon health. Sinclair ('48) emphasized that "the assessment of deviations from the normal demands a knowledge of the range of normality, and of the factors that enlarge or diminish it. Unfortunately, the study of the relevant parts of the physiology, morphology and chemistry of man has not advanced far; man is a neglected animal and the variations that are found and the causes of these should be more carefully studied."

Besides blood volume change, in pregnancy there are equally consequential factors to be considered in evaluating the results of study. There are, of course, variable factors which are offset by obtaining and analyzing blood samples from large numbers of mothers and their infants in widely-scattered clinics and offices. Other variables may not be compensated for, hence, one must constantly bear in mind the reliability of the methods, the individual differences among subjects, individual fluctuations, and the emotional and physical stresses experienced during pregnancy and puerperium.

We endeavored to overcome some of the restricting factors by using two types of control subjects — non-pregnant and

TABLE 3

Maternal and infant levels of blood components — Selected Group

	WHITE SUBJECTS				NEGRO SUBJECTS			
			Percentile				Percentile	
	Samples	Median	10th	90th	Samples	Median	10th	90th
Hemoglobin, gm/100 ml								
Non-pregnant women	524	13.4	12.3	14.5				
Pregnant women								
3rd month	41	12.7	11.4	14.3	4	12.0	10.4	12.8
4th month	59	12.4	11.1	13.7	9	12.4	11.3	13.6
5th month	61	12.0	10.6	13.0	27	11.1	9.2	12.8
6th month	75	11.9	10.9	13.1	54	11.1	9.6	12.8
7th month	83	12.1	10.8	13.0	90	11.1	10.0	12.6
8th month	132	11.8	10.4	13.0	145	11.1	9.6	12.7
9th month	205	12.2	10.6	13.6	176	11.4	9.8	12.9
Postpartum	140	12.3	10.3	14.1	190	12.2	10.2	14.1
Infants	119	19.6	16.6	22.6	182	18.9	16.0	21.8
Serum protein, gm/100 ml								
Non-pregnant women	426	6.95	6.30	7.38				
Pregnant women								
3rd month	43	6.28	5.75	6.94	5	6.60	6.20	7.00
4th month	56	6.25	5.74	6.76	9	6.36	6.07	7.24
5th month	61	6.19	5.71	6.68	28	6.33	5.78	7.12
6th month	74	6.11	5.66	6.71	58	6.34	5.92	6.91
7th month	81	6.06	5.60	6.44	97	6.24	5.71	6.86
8th month	128	5.98	5.51	6.41	166	6.24	5.72	6.84
9th month	208	6.00	5.56	6.55	193	6.23	5.66	6.85
Postpartum	142	5.83	5.26	6.57	187	6.29	5.61	7.10
Infants	116	5.69	5.00	6.59	175	5.87	5.14	6.72
Serum alkaline phosphatase, Nitrophenol units [1]								
Non-pregnant	401	1.36	0.90	1.96				
Pregnant women								
3rd month	43	1.23	0.72	1.87	5	1.25	0.62	2.25
4th month	55	1.28	0.84	1.80	9	1.21	0.72	1.55
5th month	60	1.28	0.73	1.88	27	1.32	1.02	2.32
6th month	75	1.56	1.04	2.29	52	1.62	1.00	2.84
7th month	83	1.96	1.30	3.1[illegible]	95	2.06	1.21	3.55
8th month	131	2.81	1.90	4.82	156	2.68	1.78	4.20
9th month	205	3.49	2.27	6.25	189	3.80	2.37	6.18
Postpartum	142	3.33	2.22	4.99	180	3.43	2.12	5.11
Infants	110	3.42	2.33	5.62	163	4.14	2.78	6.64

Serum vitamin A, μg/100 ml								
Non-pregnant	387	41	22	64				
Pregnant women								
3rd month	39	40	22	55	5	51	28	72
4th month	57	39	22	58	8	45	24	56
5th month	57	40	27	56	22	38	23	53
6th month	72	42	26	61	48	31	13	53
7th month	80	42	23	65	88	30	12	54
8th month	127	36	20	58	148	31	16	54
9th month	198	39	20	63	176	34	16	53
Postpartum	133	44	23	68	163	39	22	56
Infants	87	16	3	33	133	14	3	32
Serum carotenoids, μg/100 ml								
Non-pregnant women	400	165	88	259				
Pregnant women								
3rd month	40	133	87	200	5	137	123	215
4th month	57	157	104	248	8	170	76	344
5th month	60	170	116	252	24	157	96	256
6th month	75	176	108	277	51	163	80	253
7th month	81	175	114	299	90	167	107	270
8th month	127	178	107	288	148	166	106	258
9th month	204	163	102	279	181	168	92	259
Postpartum	135	138	77	230	168	144	89	225
Infants	90	28	8	47	134	28	8	41
Serum vitamin C, mg/100 ml								
Non-pregnant women	464	1.47	0.75	2.00				
Pregnant women								
3rd month	39	1.35	0.53	2.26	5	0.75	0.50	1.15
4th month	55	1.34	0.62	1.85	9	0.90	0.18	1.62
5th month	56	1.26	0.68	1.88	26	0.58	0.32	1.16
6th month	77	1.44	0.74	2.02	56	0.54	0.24	1.24
7th month	78	1.31	0.65	2.01	92	0.59	0.22	1.23
8th month	128	1.17	0.44	1.81	158	0.58	0.24	1.13
9th month	198	1.15	0.45	1.74	178	0.62	0.24	1.24
Postpartum	138	0.56	0.20	1.21	181	0.44	0.14	0.94
Infants	110	1.26	0.78	2.12	166	1.24	0.81	1.97

[1] One unit is the amount of phosphatase activity per liter of serum required to liberate 1 millimole of nitrophenol per hour from sodium paranitrophenyl phosphate under the specific conditions of the test.

Selected pregnant individuals — for checks on methods and procedures and for study of individual variability and racial and environmental influences. Table 3 presents data which characterize the usual physiological course of human reproduction with respect to concentrations of hemoglobin, sera total protein, vitamin A, carotenoids, vitamin C and alkaline phosphatase. Data are included for non-pregnant white

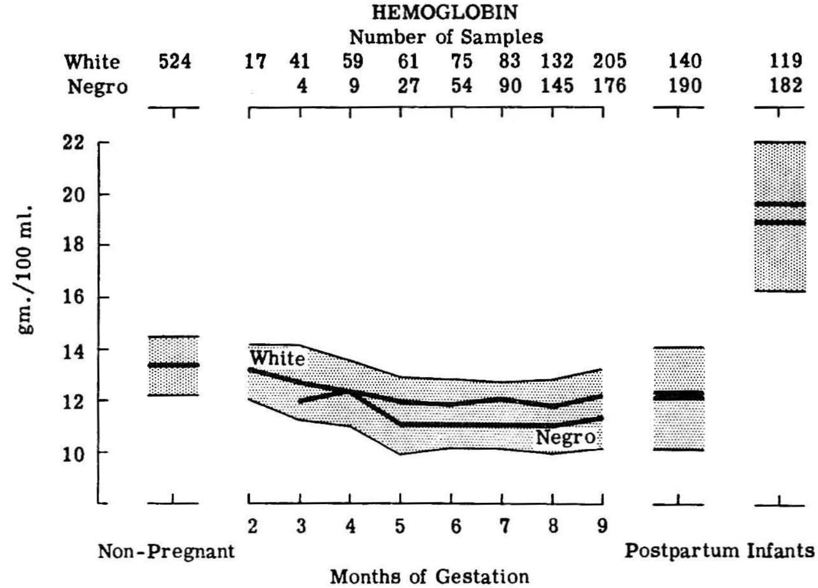

Fig. 1 The median hemoglobin levels of white non-pregnant women, of Selected white and Negro women during gestation, after delivery, and of their respective newborn term infants, portray the trend graphically. The 10th to 90th percentile range for the combined racial groups serves as a standard for normality.

women, for the Selected white and Negro patients at intervals in pregnancy and postpartum, and for their infants. The values for 48 non-pregnant white women provide a basis for observing the physiological alteration from the non-pregnant to the pregnant state; those for the Selected Group of 427 patients, chosen because they were free from clinical manifestation of disease, provide average and range values which may be used as standards for departures from health.

In obtaining data for blood composition, unaccountably high or low results may occur which may be spurious and not true values. Such figures were eliminated from table 3 by including only values between the 10th to 90th percentiles, which characterize the usual physiological course during pregnancy.

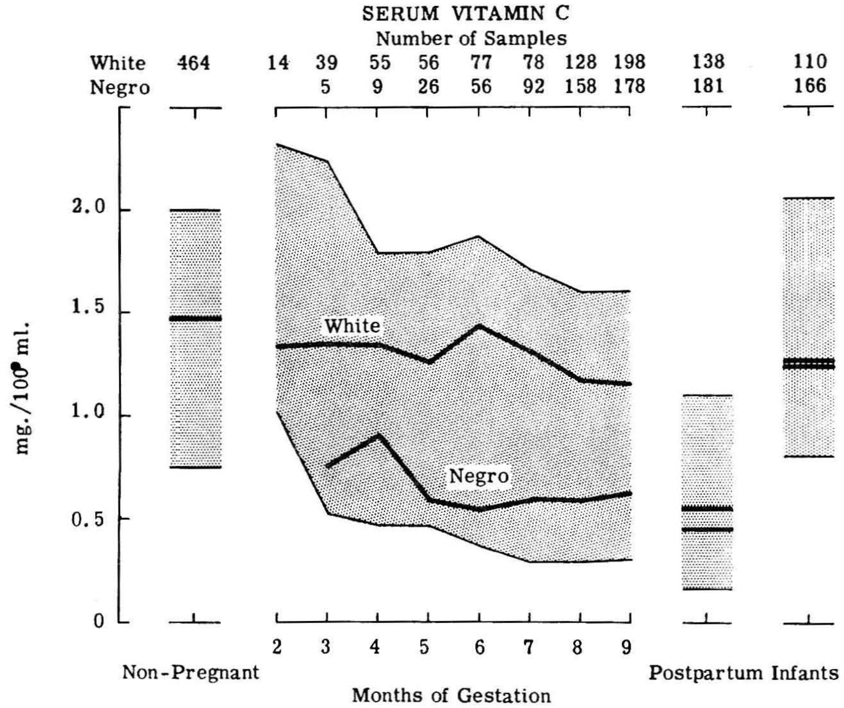

Fig. 2 The median serum vitamin C levels of white non-pregnant women, of Selected white and Negro women during gestation, after delivery, and of their respective newborn term infants, portray the trend graphically. The 10th to 90th percentile range for the combined racial groups serves as a standard for normality.

Figures 1 to 6 present graphically the medians and 10th to 90th percentile ranges for hemoglobin, sera total protein, vitamin A, carotenoids, vitamin C and alkaline phosphatase. Data are plotted for non-pregnant women, for the Selected white and Negro women during pregnancy and one to 8 days postpartum, and for their full-term infants one to 9 days after birth.

The medians and the ranges for hemoglobin throughout pregnancy (fig. 1) were lower than those of the non-pregnant women. The range of hemoglobin levels for white women was higher than the range for Negro women, indicating a true difference in the racial groups. The median hemoglobin val-

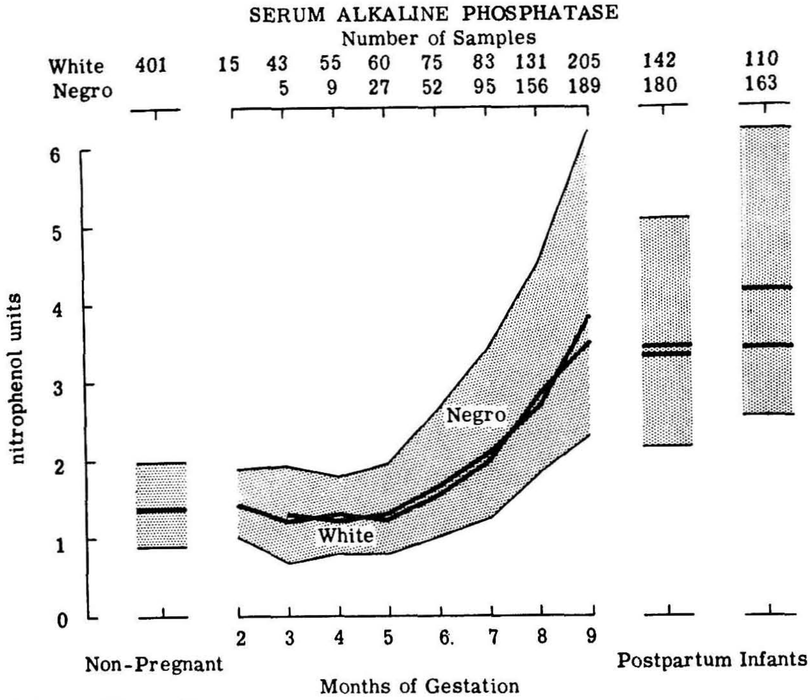

Fig. 3 The median serum alkaline phosphatase levels of white non-pregnant women, of Selected white and Negro women during gestation, after delivery, and of their respective nowborn term infants, portray the trend graphically. The 10th to 90th percentile range for the combined racial groups serves as a standard for normality.

ues for the white women were 0.7 gm to 1 gm higher than those for Negro women during the last 5 months of pregnancy. The postpartum medians and ranges were nearly identical for the two racial groups. The Selected white infants displayed higher hemoglobin levels than did the Negro infants and the median hemoglobin levels of the Selected infants were approximately 50% greater than the values for their respective mothers.

The serum of non-pregnant white women had higher concentrations of vitamin C than that of the Selected white women in the first trimester of pregnancy (fig. 2). A downward trend throughout pregnancy extended into the postpartum period, but throughout gestation the levels of the white women were much higher than those of the Negro

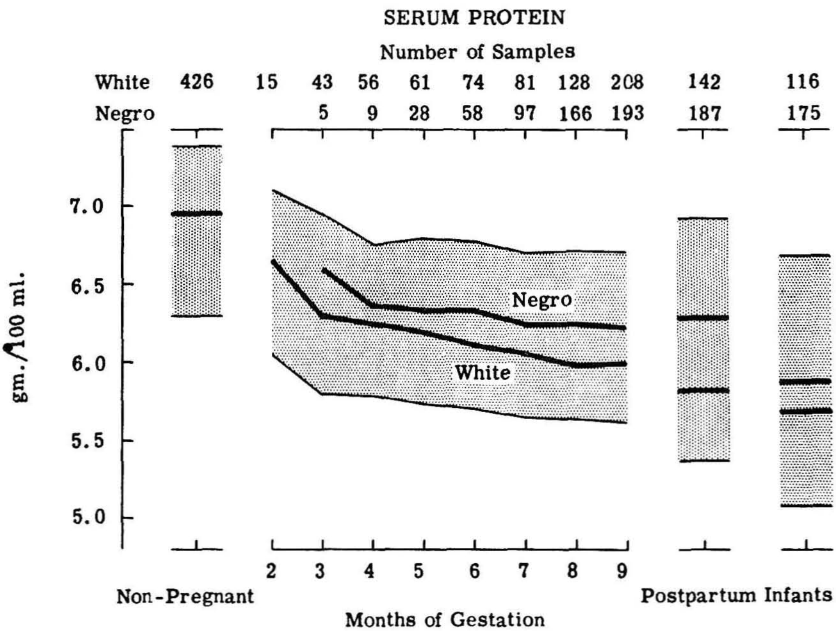

Fig. 4 The median serum protein levels of white non-pregnant women, of Selected white and Negro women during gestation, after delivery, and of their respective newborn term infants, portray the trend graphically. The 10th to 90th percentile range for the combined racial groups serves as a standard for normality.

women. The vitamin C levels of the Negro women, though much lower early in pregnancy, did not show as much decline before delivery. The median vitamin C concentrations in infant blood were almost alike for the two races but the range was higher for white infants. The pattern for alkaline phosphatase (fig. 3) is different from those for hemoglobin and the vitamins because its concentation in serum more directly parallels skeletal growth and development in the fetus and mineral storage in the maternal organism. The median for non-pregnant white women was 1.36 nitrophenol units; for Selected white pregnant women in the first trimester it was 1.27 units. The trend was definitely upward through the 9th month, decreasing early in the puerperium, for both the Selected white and Negro women. Throughout pregnancy and early puerperium, the serum phosphatase values for

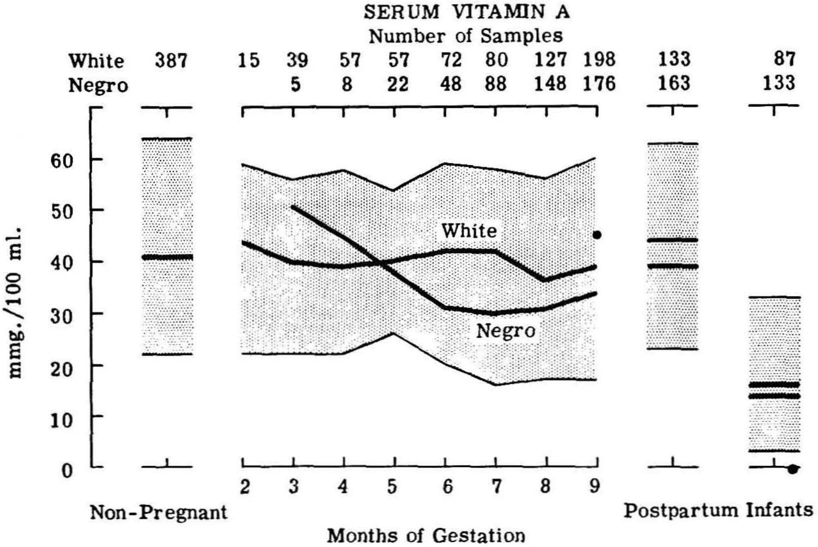

Fig. 5 The median serum vitamin A levels of white non-pregnant women, of Selected white and Negro women during gestation, after delivery, and of their respective newborn term infants, portray the trend graphically. The 10th to 90th percentile range for the combined racial groups serves as a standard for normality.

white and Negro women had approximately the same scatter within the 10th to 90th percentile range. The greatest difference between medians for the racial groups of mothers was 0.31 units at the 9th month. The difference was greater between the infants, the white being 0.72 units lower than the Negro infants, and the median levels of 3.42 for white and 4.14 units for Negro infants were greater than the medians for the maternal groups (2.94 and 2.98 units) in the third trimester of pregnancy.

The median serum protein level of the non-pregnant white women was higher than the medians for white or Negro women at any time during gestation. For women of both races the trend of serum protein concentration was downward throughout pregnancy (fig. 4). The median serum protein levels of the Selected white women were consistently

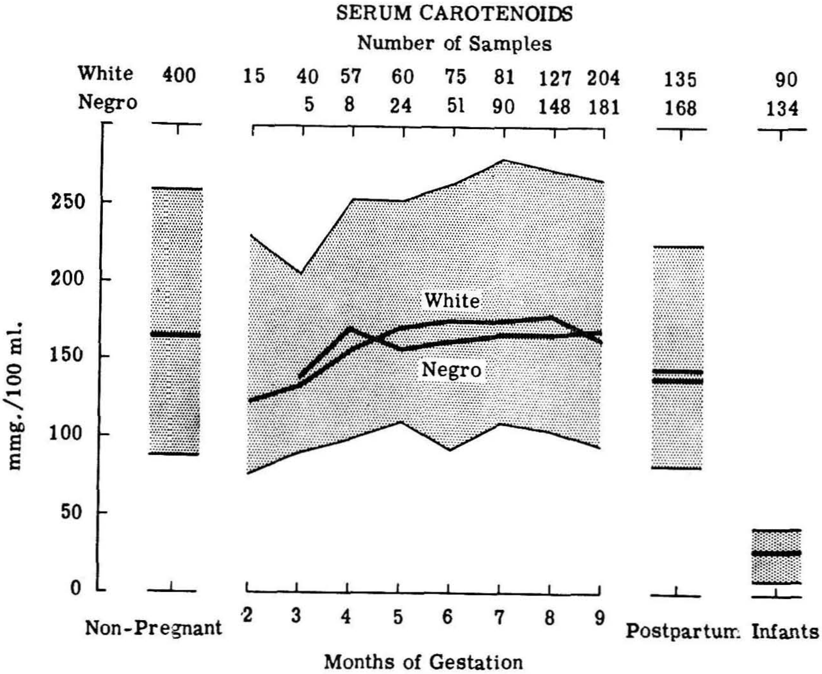

Fig. 6 The median serum carotenoid levels of white non-pregnant women, of Selected white and Negro women during gestation, after delivery, and of their respective newborn term infants, portray the trend graphically. The 10th to 90th percentile range for the combined racial groups serves as a standard for normality.

lower than those of the Selected Negro women, the median differences ranging from 0.11 to 0.46 gm/100 ml of serum. Median serum protein levels of the infants were lower than those of their respective mothers and both the median and the range for the Negroes exceeded that for the white race.

The median serum vitamin A concentrations of non-pregnant white women and Selected white patients in the first trimester of pregnancy were not different (fig. 5). The median values and the 10th to 90th percentile ranges were consistently higher for white than for Negro women during the last 5 months of gestation and postpartum. Too few samples for comparison were obtained from Negro patients during the third and 4th months. Although the difference was small between the medians for white and Negro infants, that of the Negroes was lower.

The median serum carotenoid level for non-pregnant white women was higher than that for the Selected white subjects in the first trimester of pregnancy (165 and 131 μg/100 ml, respectively). For both white and Negro subjects, however, upward trends in early pregnancy (fig. 6) were followed by leveling off after the 6th month and lowered values postpartum. The median serum carotenoid values for white women were 8 to 13 μg/100 ml higher from the 5th through the 8th months and 6 μg lower than those for Negro women in the 9th month and postpartum. The 10th to 90th percentile ranges were approximately equal, but the range for the white women was at a higher level. The levels for white and Negro infants were not different and were much lower than those of their mothers.

Viewing the physiological patterns which characterize women at various stages in the reproductive cycle, and their babies, the irregularities that occur in the third and 4th months of pregnancy may be ascribed to small numbers of Negro blood samples. The 10th to 90th percentile ranges of variability are greater for some blood components, possibly owing to the cumulative effect of factors, such as accuracy of chemical method, non-fasting blood samples and individual variability.

Beyond the influences of methodology, physiological factors are of even greater consequence. In early gestation blood volume change is initiated and the intensity of endogenous maternal physiological and nutritional orientation to the gravid state is at its peak. The maternal dietary intake must be shared between two organisms of different vitalities, the competition being dominated in early pregnancy by the enlivened fetal and placental tissues. The rapid placental growth in early gestation does not parallel that of the fetus, although a definite ratio exists between the weights throughout pregnancy (Wolfram, '41).

The placenta serves the fetus in both nutritive and protective roles. The differences in the average values of the various blood components of the mothers and their respective infants demonstrate the adjustments required to maintain homeostasis within the two bodies. For example, the placenta apparently conserves hemoglobin (fig. 1) and vitamin C (fig. 2) for fetal construction, function and reserves but is not impelled to provide concentrations of sera protein (fig. 4), carotenoids (fig. 6) and vitamin A (fig. 5) greater than those of the mothers.

Dietary intake must be relied upon to furnish the essential nutrients that the body cannot synthesize. Some of the evidence of racial differences in levels of blood components obtained in this investigation may be accounted for by less satisfactory dietary intake and prenatal care of the Selected Negro patients. The subtle alterations in physiological conditions are intermingled with those inconstant metabolic activities involving environment and the nutritive state and make difficult the interpretation of changes in blood composition during pregnancy with any degree of finality.

NUTRITIONAL STATUS

Clinical assessment

Clinical methods are essential in the assessment of nutritional status. They are in large measure subjective, and criteria may be altered from time to time and vary from one clinician to another. The general assessment by medical inspection usually is concerned with physical state of health, of which nutritional state is a component part. Symptoms, too, frequently are subjective and many early signs of disturbed health are not specific, making differential diagnosis of nutritional disease, even in advanced stages, exceedingly complex.

Medical histories, carefully taken, can contribute valuable information in the assessment of nutritional status providing accurate and established terminologies are recorded.

Maternal stature, pregravid weight, weight changes and physical health are considered indices of the past and present state of nutrition. The progressive gains in body weight during gestation are only a gross measurement of storage of nutrients because *en masse* growth is known to vary in chemical composition. Nevertheless, excessive weight gains or losses increase the susceptibility of the mother to disease and the health hazards of the infant. Indeed, Tompkins and Wiehl ('51) pointed out that patients who are underweight at the beginning of pregnancy, or who fail to gain acceptably during the first two trimesters, possess increased probability for premature labor, and excessive gains during the second and third trimesters establish the pattern for preeclampsia. In our study, the average weight gains for all groups of white and Negro mothers ranged from 23 to 25 pounds.

The birth weight of infants is considered an integral part of the clinical assessment of nutritional status. The median birth weight of the Selected white infants (3,307 gm) exceeded that of the Negro infants (3,089 gm) by approximately 200 gm. Infants weighing over 4,500 gm are alleged to constitute a definite obstetrical problem (Nathanson, '50). Anderson et al. ('43) and Brockway et al. ('50) believe that separate birth weight standards for white and Negro infants are desirable. In the study reported here, the percentage of prematures among the Negro infants would be much lower if the criterion were 2,300 instead of 2,500 gm. Taback ('51) found that when limits of 2,350 gm for nonwhite and 2,500 gm for white infants were used, the differential in incidence of prematurity between the races was eliminated. A recent study in Hawaii (Taff and Wilbar, '53), which included several racial groups generally smaller than Caucasians, indicated that 2,500 gm was an acceptable upper limit of immaturity; however, the mean gestation interval for Negro women is alleged to be somewhat shorter than that for the white race (Anderson et al., '43; Taback, '51).

In the present study, the relationships of median birth weights for white and Negro infants with the pregravid weights of the mothers, the maternal weight changes during pregnancy and the median birth weights of the infants were found to be slightly positive (Moyer et al., '54). These observations corroborate the findings of some investigators (Kerr, '43; Beilly and Kurland, '45) but not those of others (Sontag et al., '35; Klein, '46).

Infant birth weight was slightly related to maternal age but was not related to diet ratings nor to estimated protein intake. The median birth weight of infants of women who had "good" prenatal care was greater than for infants of women who had "poor" prenatal care: for white and Negro infants the difference was negligible and may have been due to chance. In all groups of term infants, average birth weights of liveborn, singleton males exceeded those of females.

Dietary assessment

Evaluation of the dietary intake of nutrients is an essential adjunct to any assessment of health and nutritional status but dietary intake alone does not measure nutritional status, for nutrition also involves digestion, absorption and utilization of foodstuffs. The median dietary rating for the Selected Group was 64% for the Negroes and 74% for the white women (table 4). Only among white subjects did 10% or more of the food records rate 90% or above. Among the Selected women, three times as many Negro as white patients gave records evaluated as inadequate in relation to the Recommended Dietary Allowances for pregnant women.

From the results of some investigations, the effects of prenatal diet have been thought to influence not only the course of pregnancy but also the health of the child at birth and several months thereafter (Ebbs et al., '41; Burke et al.,

TABLE 4

Ratings of food intake records — Selected Group

	WHITE WOMEN				NEGRO WOMEN		
	Group A	Group B	Group C	Total	Group A	Group B	Total
Records, number	55	12	146	216	224	38	266
Total food intake [1] median rating, %	67	83	77	74	64	64	64
Food Groups [2]							
I. Leafy, green, yellow vegetables							
high, %	44	33	25	30	29	29	29
low, %	54	50	45	48	63	50	61
II. Citrus, analogous foods							
high, %	51	66	70	64	54	32	51
low, %	35	17	14	20	37	50	39
III. Potatoes, other vegetables, fruits							
high, %	0	8	1	1	0	3	0
low, %	96	42	67	73	97	89	96
IV. Milk, milk products							
high, %	36	25	17	22	23	11	21
low, %	53	17	30	36	58	71	60
V. Meat, eggs, legumes							
high, %	4	0	10	8	6	13	6
low, %	56	25	27	34	48	40	47
VI. Bread, cereals							
high, %	71	83	38	49	70	37	65
low, %	11	0	12	11	7	13	8

[1] A qualitative dietary procedure tested for reliability was used to evaluate food intake records with respect to the Recommended Dietary Allowances. Records obtained during the first trimester of pregnancy were rated in relation to the allowances for adult women; intakes in the last trimesters in relation to the allowances for pregnancy. A combination of servings which supplied the recommendations was scored 100%.

[2] Food intakes which included a sufficient number of servings from a food group to meet the allowances were ranked "high" with respect to that food group; if the number of servings provided less than 60% of the allowances the ranking was "low."

'43b; Balfour, '44; Leverton and McMillan, '46; People's League of Health, '46; Tompkins, '48). Recently, Smith et al. ('53) reported that the weight and composition of fetal liver tissue reflects the maternal dietary intake during pregnancy. A positive correlation between average protein intake of mothers and the pediatric rating of their babies was found by Burke et al. ('43a) and was confirmed by records of weighed food intakes of pregnant women obtained by Dieckmann et al. ('51a, '51b). Conversely, in several investigations the diet of pregnant women was thought to have little or no correlation with laboratory and clinical findings (Williams and Fralin, '42; Dieckmann et al., '44; Sontag and Wines, '47).

Inferior nutrient intake and substandard prenatal care were more prevalent among Negroes than among white patients in the Selected Group. Maternal serum vitamin C levels of the white, but not of the Negro subjects in the Selected Group, showed a positive relationship to the total diet rating. The intake of high vitamin C foods by women of both races was positively associated to their serum vitamin C levels; the relationship extended to the serum of the newborn. Maternal serum carotenoid levels were positively correlated to intakes of leafy green and yellow vegetables. A positive relationship was found between maternal diet rating and serum vitamin A levels during the third trimester and postpartum. Women with high serum carotenoid levels also had high serum vitamin A concentrations.

Compounds in serum vary in their behavior: some, such as carotenoids and ascorbic acid, tend to reflect the immediate past intake; others, such as protein, remain at concentrations that are within the statistically normal range even though clinical malnutriture may be present. In these cases, a *single* estimation that falls within the statistical normal range gives little information (Sinclair, '48). Lund and Kimble ('43b), after studying 197 women in different stages of pregnancy, stated that optimal plasma values can be maintained by diet alone so long as the intake contains liberal amounts of vitamin C-rich foods. This is supported by the present investigation and those of numerous investigators who reported good correlations between calculated vitamin C content of maternal diets and corresponding vitamin C levels in maternal blood (Lund and Kimble, '43b; Moore et al., '47; Teel et al., '48). A food purchase study on city families (Stiebeling, '50) pointed out that foods such as fruits and non-starchy vegetables, milk and some milk products, and protein foods, were purchased in larger quantities by high-income families than by those in lower income brackets. Previously, we have observed that an adequate mixed diet increased the serum vitamin C levels of handicapped and undernourished children and stabilized them at a healthful level within 8 weeks without recourse to vitamin supplements (Cooperstock et al., '48). Fleming and Sanford ('38) found that the vitamin C content of the maternal blood could be tripled by an adequate citrus fruit intake, and further that offspring will be born with higher blood levels than are usually found when women show low blood vitamin C values.

The nutritive requirements of an impoverished individual may differ markedly from those of one who has enjoyed full health and has a nutritionally and physically stable body throughout life. With women, evidence of latent malnutrition may not appear until after they have conceived. If dietary intake is insufficient to meet adequately the augmented nutritive requirements of the mother and fetus, malnutrition becomes intensified and may cause physiological stress or disease in the mother, extend to the fetus *in utero* or be reflected later in the health of the child.

Marginal diets usually are associated with long-standing, unsatisfactory economic conditions and undesirable dietary habits. It is very likely that undernutrition or malnutrition of long duration exists in many women at conception, superimposing a need for nutritional conditioning or reconditioning of the maternal body. Multiple deficiencies, especially those which have extended over long periods of time, are difficult to overcome and may have serious consequences during pregnancy. Such conditions may account for the restricted or variable physiological responses found in this study among the Negro subjects and the women in low-income families.

Seriatim biochemical assessment

Physical state, nutriture and health are closely related and may be evaluated either directly or indirectly by a combination of clinical, dietary and biochemical observations (National Research Council, '43, '49). Scrimshaw ('50) stated: "In any situation, nutrition must be evaluated as one of several environmental factors. Under some circumstances, nutrition will be found to be the major factor and under others, a minor one. The exact influence of a given nutritional situation in an individual case will depend upon the sum of the environmental factors, including nutrition, acting upon the genetic make-up."

The results for the Selected subjects permit differentiation of chemophysiological changes from racial differences, presence of malnutrition and other factors. In addition, determinations of several components in a single sample of blood make broader interpretations possible.

Pregnancy increases the nutritive requirements for many individually indispensable food substances, and these substances must be provided in addition to the usual requisites for varying conditions of activity and environment. The nutritive stress created by conception presents many complex problems because one organism is living within another, the fetus totally dependent upon the maternal body for the proper environment within which to carry on its own more or less independent physiological processes. Satisfactory nutrition of the two organisms depends upon an adequate food supply for the mother, its digestion, absorption, transport in the maternal and fetal blood, diffusion into extra-cellular fluids and passage into cells, as well as removal of waste.

Outstanding progress has been made in the development of substitutes for mother's milk and some research has indicated more rapid weight gains by artificially fed infants than by those breast fed. These results and the fact that cow's milk has a concentration of protein greater than that of human milk have stimulated the belief by some that breast milk may not meet the requirements of infants, especially those born prematurely. However, though still incomplete, our knowledge encompasses some 250 chemical components of milk (Macy, Kelly and Sloan, '53) and nutrition research is continually providing evidence which emphasizes the importance of the relative distribution of many food components in a dietary as well as the level of intake.

The experiences in one epoch of the life cycle may be carried over into another and thereby modify biochemical individuality and alter metabolic requirements during succeeding stages of growth and maturity (Toverud et al., '50). For example, an infant girl who has severe rickets because of inadequate dietary may carry through childhood and womanhood the effects from infant malnutrition such as distorted pelvis or other parts of the skeletal system. Similarly, overstrain of the function of hematogenesis during pregnancy is shown by secondary anemia which, in mild form, is common and in some patients becomes serious. The blood requirement of the fetus, the blood loss during parturition, and other causes of this anemia represent the maternal metabolic overload.

Newborn infants from mothers with hypochromic anemia show a normal blood picture, but develop anemia during the first year of life. If iron is given to the mother during pregnancy, or to the infant, this anemia is prevented. Apparently, the fetus of an iron-deficient mother does not store enough to carry the child through infancy. Provision of ample supplies for the nutritive processes of the maternal and fetal bodies is a matter of great importance, since the requirement may include filling in the nutritive reserves that were depleted by previous undernutrition. Investigators who have studied the etiology and treatment of osteomalacia, beriberi and other deficiencies have demonstrated that in human beings, as in other animals, the young may start life with reduced nutritive reserves. Such an individual must carry a greater metabolic load than the body is physiologically capable of managing; consequently, a crisis arises unless measures are taken to replete the overtaxed and undernourished tissues. Years ago, the need for knowledge of the nutritional history was demonstrated in this laboratory during inquiries into building and maintaining reserves during pregnancy and lactation (Hummel et al., '37).

BIOCHEMICAL ASSESSMENT OF BLOODS

Hemoglobin

Protein is present in all living tissues and forms the matrix of the cells, the cytoplasm and the nucleus. The several blood proteins perform preeminent roles in growth, in metabolism and in maintaining the integrity of the body tissues and fluids. Observations of individual blood proteins served a basic purpose in studies of physiological changes characteristic of human reproduction (Macy and Mack, '52). In investigating the composition of erythrocytes, studies were made of the stroma portion of the red blood cell and of the hemoglobin portion which makes up so large a portion of the cell solid. Many types of hemoglobin long have been known, but inasmuch as the heme groups within the molecule appeared to be similar, investigation suggested that specificity of hemoglobins depends largely upon differences in amino acid composition and upon their arrangement in the globin portion of the molecule (Beach et al., '39; Pauling et al., '49).

Hemoglobin and other blood proteins are of primary significance in maintaining health, and dietary protein must be relied upon to furnish the essential amino acids of which blood proteins are composed. Concentrations of hemoglobin and total serum protein are among the most commonly used measures of nutritional status in population groups. Whether in the absence of blood volume change nutritional status with respect to hemoglobin (McLester and Darby, '52) or to protein (Youmans et al., '43; Milan and Anderson, '44; Scrimshaw et al., '51; Macy and Mack, '52) is directly reflected by blood levels of those constituents remains questionable, but studies have indicated that the hypoproteinemia observed in pregnancy and during the puerperium (Scrimshaw et al., '51) may be attributable to changes in blood volume, excessive loss of plasma, faulty nutrition and excessive loss or a defect in the synthesis of protein (Macarthur, '48).

A range of 10 to 12 gm hemoglobin/100 ml of blood is generally regarded as the lower limit compatible with health during the reproductive cycle. The commonly accepted standard of hemoglobin concentration for adult females is 14.2 ± 2 gm/100 ml (Wintrobe, '51). For clinical purposes, the normal range for women is 11 to 15 gm/100 ml (Sunderman and Boerner, '49). Dieckmann and Wegner ('34b) and Sturgis ('48) considered hemoglobin levels below 10 gm in pregnancy as diagnostic of anemia.

TABLE 5

Hemoglobin levels of white women in the first trimester of pregnancy

	NON-PREGNANT [1] WOMEN	PREGNANT WOMEN	
		Selected	Group C
Samples	524	59	138
Median, gm/100 ml	13.4	12.8	12.8
Below 10 gm/100 ml, %	0.2	0	0.7
Below 12 gm/100 ml, %	4	15	20

[1] For adult white males, the mean for 68 determinations was 15.5 gm.

Few blood samples were obtained from the pregnant women in Groups A and B during their first trimesters of pregnancy; however, more of the private patients sought medical care early in gestation. Hemoglobin levels of the white women in Group C and of the Selected white patients during the first trimester of pregnancy are compared to values for non-pregnant white women in table 5. Data for all groups of subjects and for their infants are summarized in table 6 and portrayed graphically in figure 7.

The average hemoglobin concentrations for the Selected white patients during the first and second trimesters were

TABLE 6

Maternal and infant hemoglobin levels

	WHITE SUBJECTS				NEGRO SUBJECTS			
	Mothers			Term infants [1] (1–9 days)	Mothers			Term infants [1] (1–9 days)
	Second trimester	Third trimester	Postpartum (1–8 days)		Second trimester	Third trimester	Postpartum (1–8 days)	
Selected								
Samples	195	420	140	119	90	411	190	182
Median, gm/100 ml	12.1	12.1	12.3	19.6	11.2	11.2	12.2	18.9
Below 10 gm/100 ml, %	1	2	1		16	13	7	
Below 12 gm/100 ml, %	47	47	41		72	73	45	
Group A (public clinic)								
Samples	22	198	76	72	198	857	324	284
Median, gm/100 ml	11.8	11.9	11.8	19.8	11.1	11.3	11.6	18.9
Below 10 gm/100 ml, %	0	10	13		16	16	16	
Below 12 gm/100 ml, %	64	52	55		80	73	59	
Group B (private clinic)								
Samples	21	53	35	29	96	214	121	102
Median, gm/100 ml	12.1	12.1	11.4	19.5	11.2	11.2	11.8	18.5
Below 10 gm/100 ml, %	0	4	17		14	12	16	
Below 12 gm/100 ml, %	43	47	63		81	78	55	
Group C (private)								
Samples	344	614	175	127				
Median, gm/100 ml	12.1	12.0	12.0	19.4				
Below 10 gm/100 ml, %	2	2	7					
Below 12 gm/100 ml, %	46	48	49					

[1] For premature infants, 5 samples from white and 31 samples from Negro infants in Group A showed median hemoglobin values of 19.8 and 19.0 gm, respectively; one sample from a Negro infant in Group B had a value of 21.5 gm; the median for 5 samples from infants in Group C was 22.2 gm.

12.8 and 12.1 gm/100 ml, respectively, compared to 13.4 gm for non-pregnant white women. Thus, the intensity of physiological activities owing to the gravid state was evidenced in the second trimester, the period when the placenta grows most rapidly and blood volume increases. Values for none of the Selected women in the first trimester and for only 1% of the group during the second trimester of pregnancy were

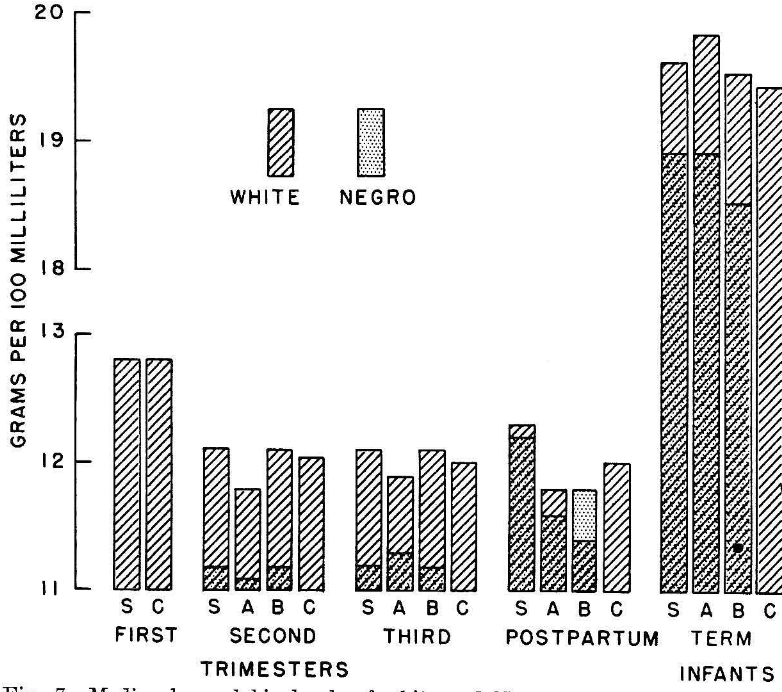

Fig. 7 Median hemoglobin levels of white and Negro women and their infants in Selected (S) Group and in Groups A, B and C.

below 10 gm/100 ml. For the non-pregnant women, 0.2% of the hemoglobin determinations were below 10 gm/100 ml. For the first and second trimesters, 15 and 47%, respectively, of the values for the Selected women were below 12 gm % but only 4% of the samples from non-pregnant women were in this category.

The median hemoglobin level of non-pregnant white women (13.4 gm/100 ml) was higher than the medians for all groups of white or Negro pregnant women. The same level was reported by Ohlson et al. ('44) as the mean for 16- to 30-year old college women. A similar average might not be found with another group of women because many factors other than gestational state may influence hemoglobin level. Indeed, low-grade anemia from iron deficiency frequently is present prior to pregnancy (National Research Council, '43).

The average hemoglobin concentrations for the white women in the Selected Group and in Groups B and C approximated 12 gm/100 ml during the second and third trimesters of pregnancy, and postpartum. Values for the white women in the public clinic Group A were slightly lower (table 6) and higher percentages were below 12 gm/100 ml. These observations agree with those of other investigators dealing with lower income groups (National Research Council, '43; Medical Research Council, '45).

All groups of Negro women had average hemoglobin values slightly higher than 11 gm/100 ml during the second and third trimesters of pregnancy, but all of the averages were below the lowest average for the white groups. The averages (table 6) disclosed no difference for socioeconomic levels of Negroes attending the public and private clinics, but racial difference was supported by the higher percentages of low hemoglobin levels for all Negro groups than in the corresponding white groups at the same stage of pregnancy.

Longitudinal study of hemoglobin data for 70 white and 30 Negro individuals in the Selected Group, who provided samples at intervals during pregnancy and postpartum, indicated no trend characteristic of progressive changes with the pregnant state. Both group averages and the seriatim data indicated a downward trend from the first to the third trimester for the Selected white women. No trend was evident from late pregnancy to the puerperium for either group averages or individuals.

Anderson et al. ('46), from Mexico City, reported that hemoglobin levels have a tendency to drop during pregnancy. The average values for hemoglobin for both white and Negro pregnant patients decreased in the third trimester as compared with the second (Moore et al., '47). Furthermore, more Negroes (17%) than white subjects (8%) had hemoglobin levels below 10 gm. Young et al. ('46) found a difference of 0.7 gm/100 ml in mean hemoglobin levels at 0 to 24 weeks and at 32 weeks to term.

The present investigation verifies a racial difference in hemoglobin levels in the populations in Detroit, first pointed out in an infant growth study conducted by this laboratory in 1938. Significant hemoglobin differences between healthy white and Negro infants were found when seriatim blood samples were taken monthly during the first year of life, the Negro blood being 0.5 to 1.0 gm hemoglobin/100 ml lower (Munday et al., '38). Two years later, Dill et al. ('40) reported similar findings for adult white and Negro males. Moore et al. ('47) for white and Negro pregnant patients, and two surveys (Milam and Muench, '46; Nutrition Branch and Program Branch, '49) found similar racial differences in hemoglobin levels. Anderson and Sanstead ('47) summarized current views of the racial difference between hemoglobin levels: "Probably some of this may be attributed to the poorer general health, and in some respects poorer nutrition, of the Negro, but one wonders whether it may not be partially a racial difference."

The racial difference in hemoglobin levels also was shown by the full-term infants. Differences in the average values for white and Negro Selected infants and for those in Groups A and B were as much as 1 gm hemoglobin/100 ml. Normally the fetus acquires a reserve store of iron from the maternal organism via the placenta, especially during the last trimester of pregnancy. The mean hemoglobin levels of white infants approximated 19.5 gm and of Negro infants almost 19.0 gm, values over 50% greater than the averages for their maternal groups during the third trimester and postpartum (fig. 7). These findings for the newborn are comparable to the observations of other investigators summarized by Smith ('51). Merritt and Davidson ('33) pointed out that racial factors, as well as birth weights, should be considered in the evaluation of infant hemoglobin data.

The extent to which hemoglobin will be formed for use in construction of new tissues, for maintaining and repairing newly-formed and more mature tissues, and of replacing the spent hemoglobin depends in large measure upon the availability in the body of the substances from which its component moieties may be constructed; on one hand, iron and organic components for porphyrin formation and on the other, essential amino acids for globulin formation. The number of organs and components in the body and diet that converge and perfect the synthesis, the metabolism, the distribution and destruction of hemoglobin, are legion. The mechanisms that control the distribution of essential amino acids for hemoglobin formation, for construction of new body tissues, or for other equally important functional purposes during abundant or restricted nutrient intake are little understood. In pregnancy, when the maternal dietary intake must be shared between two organisms of different vitality, the competition being dominated in large measure by the enlivened fetal and placental tissue construction and function, the problem is indeed more complicated since the very life and well-being of the new organism is determined by its success in obtaining regularly the amounts of nutrients required in the proper proportion for well-balanced physiological performance.

Serum total protein

The foregoing considerations with respect to hemoglobin apply equally to the other proteins in the blood. While the method applied in the present investigation estimates only the total concentration of protein present in the serum at a given time, the total is known to consist of several proteins each of differing composition and performing widely different physiological functions in the body. Average total serum protein levels of the white women in Group C and of the Selected white patients during the first trimester of pregnancy are compared to values for non-pregnant white women in table 7. Data for all groups of subjects and for their infants are summarized in table 8 and portrayed graphically in figure 8.

Metcoff et al. ('45) considered a serum protein level less than 6.0 gm % to be suggestive of hypoproteinemia; however, low concentration of protein in the blood serum may point to dietary protein deficiency only if disease or any other associated condition can be excluded. Blood volume changes may be a predominant factor in the apparent anemia and hypoproteinemia that occur (Toverud et al., '50; McLester and Darby, '52). Stress, due to delivery and surgical procedures with their accompanying anxiety, also influences total blood protein level and distribution of its component proteins (Margulis et al., '52).

TABLE 7

Serum protein levels of white women in the first trimester of pregnancy

	NON-PREGNANT [1] WOMEN	PREGNANT WOMEN	
		Selected	Group C
Samples	426	58	136
Median, gm/100 ml	6.95	6.35	6.37
Below 6 gm/100 ml, %	3	16	13

[1] For adult white males the mean for 40 determinations was 7.10 gm.

The average total serum protein concentration of the Selected patients tended to decrease with the progression of gestation; for three trimesters, the values for white women were 6.35, 6.18 and 6.01 gm/100 ml, respectively, and for the last two trimesters values for Negroes were 6.34 and 6.24 gm, respectively. Longitudinal data for seriatim blood samples from Selected white women substantiated the trend of the group averages showing slight but definite lowering of serum protein as pregnancy progressed. The trend for Negroes was indefinite. Neither cross-sectional nor longitudinal data (Moyer et al., '54) showed a definite trend in serum

TABLE 8

Maternal and infant total serum protein levels

	WHITE SUBJECTS				NEGRO SUBJECTS			
	Mothers			Term infants [1] (1–9 days)	Mothers			Term infants [1] (1–9 days)
	Second trimester	Third trimester	Postpartum (1–8 days)		Second trimester	Third trimester	Postpartum (1–8 days)	
Selected								
Samples	191	417	142	116	95	456	187	175
Median, gm/100 ml	6.18	6.01	5.83	5.69	6.34	6.24	6.29	5.87
Below 6 gm/100 ml, %	29	49	62		13	27	30	
Group A (public clinic)								
Samples	23	207	76	68	215	943	326	280
Median, gm/100 ml	6.47	6.14	6.04	5.78	6.38	6.26	6.20	5.86
Below 6 gm/100 ml, %	17	34	46		13	26	34	
Group B (private clinic)								
Samples	21	52	35	28	92	209	112	95
Median, gm/100 ml	6.22	6.10	6.26	6.07	6.29	6.23	6.09	5.88
Below 6 gm/100 ml, %	19	40	31		20	30	45	
Group C (private)								
Samples	344	594	173	126				
Median, gm/100 ml	6.16	5.95	5.71	5.67				
Below 6 gm/100 ml, %	33	55	70					

[1] For premature infants, 5 samples from white and 30 samples from Negro infants in Group A showed median total serum protein values of 5.80 and 5.25 gm, respectively; one sample from a Negro infant in Group B had a value of 5.80 gm; the median for 5 samples from infants in Group C was 5.40 gm.

protein concentration from the 9th month of pregnancy to the puerperium.

The Selected white subjects had lower average serum protein levels than comparable groups of Negro subjects in the last two trimesters of pregnancy, and postpartum. Average serum protein levels for white women in the public clinic Group A exceeded those for private patients in Group C

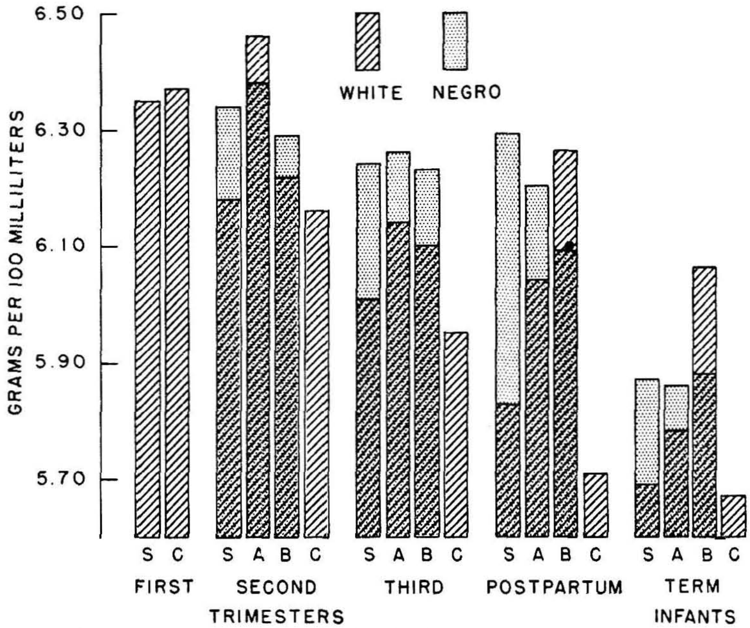

Fig. 8 Median total serum protein levels of white and Negro women and their infants in Selected (S) Group and in Groups A, B and C.

for each stage in pregnancy and postpartum. Furthermore, the percentage of samples from private patients with concentrations below 6 gm/100 ml were substantially higher than for the public clinic group. Similar observations were reported by Scrimshaw et al. ('51) for pregnant women in Rochester, New York; in every stage of gestation higher serum protein levels were found for clinic patients than for private patients. Results indicating lower serum protein levels during the puerperium than in early pregnancy are comparable to those in other reports (Plass and Bogert, '24; Mull and Bill, '45; Rinehart, '45; Hoch and Marrack, '48).

Assuming values below 6 gm serum protein/100 ml to be indicative of hypoproteinemia, then 17 to 33% of the white women and 13 to 20% of the Negro women in Groups A, B and C were so classified during the second trimester of pregnancy. During the third trimester, 34 to 55% of the white and 26 to 30% of the Negro women were in this category (table 8). Postpartum, 31 to 70% of the white and 34 to 45% of the Negro women had serum protein values below 6 gm/100 ml. As Albanese and Higgons ('53) pointed out, it is clear that concentrations of serum protein are not dependable criteria of the nutritional state in some individuals and there may be racial characteristics to be considered also. Racial differences in serum protein levels previously had been observed (Milam, '46; Moore et al., '47).

The average serum protein concentrations for the Selected white and Negro infants were 5.69 and 5.87 gm/100 ml, respectively, with smaller differences between averages for white and Negro infants in Groups A and B. These levels are consistent with the results of a recent summary by Smith ('51). The average serum protein levels for term infants in all groups were lower than the corresponding averages for maternal sera during the second or third trimester of pregnancy, or postpartum — results consistent with those of other investigators (Miller et al., '51; Overman et al., '51; Macy and Mack, '52). Physiologically, total serum protein has less significance than the quantities and proportions of the component proteins, for relative amounts of the constituent blood proteins vary during the reproductive cycle and in response to disease and conditions of stress in the mother. Nutritional status methods are not refined sufficiently to distinguish between current and latent needs. The intensity with which the maternal body accumulates active body tissue, the rapidity with which labile protein and mineral reserves are built up, and the extent of alterations taking place in hormonal excretions (Macy and Hunscher, '34; Hummel et al., '37; Toverud et al., '50; Macy and Mack, '52) may influence the levels of total serum protein.

Serum vitamin C

In considering "Scurvy in Retrospect" and reporting on the *Lind Bicentenary Conference,* Harris ('53) stated: "Little is yet known about the detailed physiology of vitamin C action, except that it is needed for the elaboration of the intercellular cementing substance, collagen, or in a more general way, for the functional activity of the formative cells in general. Chemically, the vitamin is concerned in the conversion in the animal organism of folic acid (pteroylglutamic acid) into folinic acid, and in the metabolism of tyrosine. Vitamin C itself has intense reducing activity, but it has not yet been shown that its characteristic antiscorbutic action can be attributed intrinsically to its redox properties. Among various new points brought out . . . was the suggestive fact . . . that ascorbic acid may also have a role to take in the metabolism of cholesterol."

Vitamin C is an important regulatory factor in normal cell function, tissue growth, maintenance and repair. It is neither stored nor synthesized in the body to any appreciable extent, hence must be furnished regularly in the diet from day to day to meet the current nutritional needs. Excesses are excreted in the urine. If the diet is short of vitamin C during pregnancy and the body tissues are not kept saturated with this nutrient, the growth impulses of a woman and her offspring *in utero* may be thwarted by impairment of physiologic function (Toverud et al., '50). Parturition entails some replacement of blood loss and repair of tissues and may also include operative procedures which tend to increase vitamin C needs for cellular activity involved in building new, and repairing and maintaining old tissues (Crandon et al., '40). Although the exact functions of vitamin C in the body are not fully understood, it does play an important part in all growth processes and is found in abundance in active and growing tissues.

The distribution of vitamin C in the body varies from one organ to another, depending upon the type and intensity of metabolic activity. The highly specialized and functionally active placental tissue contains a relatively high concentration of the vitamin, as do the adrenal glands (Pratt et al., '46a, '46b). The most active metabolism of vitamin C, however, occurs in the cells of the placental villi (Scipiades, '40). The placenta seems to serve as a governing device permitting only regulated amounts to pass from mother to fetus (Tonutti and Plate, '37). It has been pointed out that the loading of the Golgi apparatus with vitamin C, such as is found in the placenta, is characteristic of an organ through which

TABLE 9

Serum vitamin C levels of white women in the first trimester of pregnancy

	NON-PREGNANT [1] WOMEN	PREGNANT WOMEN	
		Selected	Group C
Samples	464	53	132
Median, mg/100 ml	1.47	1.34	1.33
Below 0.2 mg/100 ml, %	0	0	0
Below 0.6 mg/100 ml, %	3–10	9	8

[1] For adult white males the mean for 33 determinations was 0.92 mg.

the vitamin is "passing" in contrast to an organ in which it is "stored."

Values of 0.2 to 0.6 mg vitamin C/100 ml serum are generally regarded as the lowest compatible with health (Youmans, '41; Farmer, '44). Average serum vitamin C levels of the white women in Group C and of the Selected white patients during the first trimester of pregnancy are compared to values for non-pregnant white women in table 9. Differences between the averages are not significant. None of the samples had concentrations under 0.2 mg vitamin C/100 ml serum; however, approximately 8% of the women in each of the three groups showed less than 0.6 mg vitamin C/100 ml.

Average concentrations of serum vitamin C in the second and third trimesters of pregnancy, and postpartum, are re-

TABLE 10

Maternal and infant serum vitamin C levels

	WHITE SUBJECTS				NEGRO SUBJECTS			
	Mothers			Term infants [1] (1–9 days)	Mothers			Term infants [1] (1–9 days)
	Second trimester	Third trimester	Postpartum (1–8 days)		Second trimester	Third trimester	Postpartum (1–8 days)	
Selected								
Samples	188	404	138	110	91	428	181	166
Median, mg/100 ml	1.35	1.20	0.56	1.26	0.56	0.60	0.44	1.24
Below 0.2 mg/100 ml, %	0.5	1	10		6	6	14	
Below 0.6 mg/100 ml, %	7	16	53		56	50	66	
Group A (public clinic)								
Samples	22	194	74	68	205	891	318	270
Median, mg/100 ml	0.76	0.58	0.40	1.17	0.58	0.64	0.44	1.28
Below 0.2 mg/100 ml, %	9	9	12		8	6	12	
Below 0.6 mg/100 ml, %	18	52	68		53	47	68	
Group B (private clinic)								
Samples	17	47	31	20	85	191	107	82
Median, mg/100 ml	0.75	0.79	0.49	1.30	0.49	0.60	0.38	1.36
Below 0.2 mg/100 ml, %	12	4	10		12	9	23	
Below 0.6 mg/100 ml, %	41	32	68		61	50	73	
Group C (private)								
Samples	328	585	172	120				
Median, mg/100 ml	1.40	1.32	0.56	1.27				
Below 0.2 mg/100 ml, %	0	0	6					
Below 0.6 mg/100 ml, %	6	5	54					

[1] For premature infants, three samples from white and 26 samples from Negro infants in Group A showed median serum vitamin C values of 0.35 and 1.27 mg, respectively; the median for 5 samples from infants in Group C was 1.55 mg.

corded for all groups of white and Negro women, and for their infants, in table 10 and are presented graphically in figure 9. Median serum vitamin C levels for Selected white patients during the three trimesters of pregnancy were 1.34, 1.35 and 1.20 mg/100 ml, respectively. Postpartum, the median was 0.56 mg. Concentrations were much lower for the

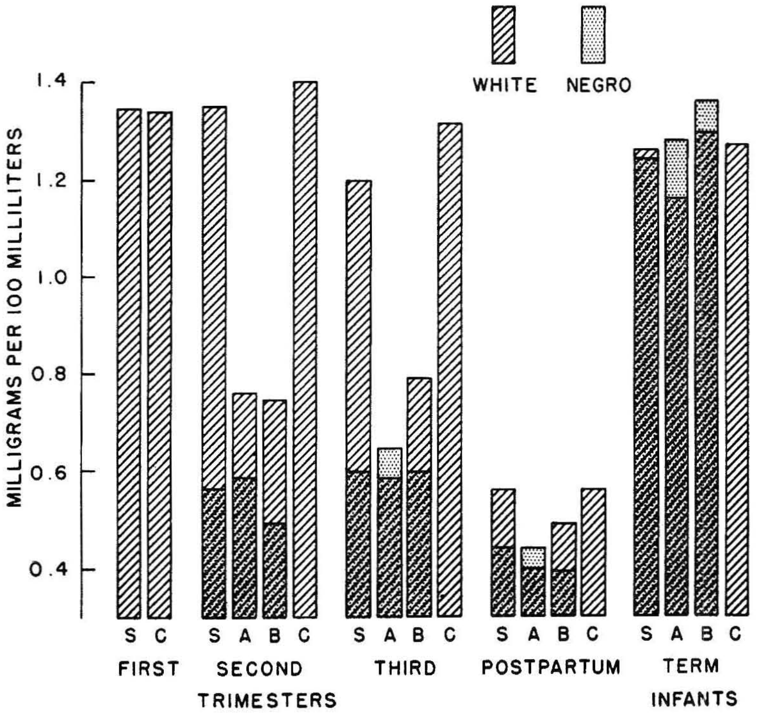

Fig. 9 Median serum vitamin C levels of white and Negro women and their infants in Selected (S) Group and in Groups A, B and C.

Selected Negroes, the averages being 0.56, 0.60 and 0.44 mg vitamin C/100 ml in the last two trimesters and postpartum, respectively. In the second trimester, the average serum vitamin C level of Selected white women was 8% lower than that of the non-pregnant white women; postpartum, the level was 62% lower but the value, 0.56 mg, was comparable to the highest median found for Selected Negro women, 0.60 mg, in the third trimester of pregnancy. Longitudinal data showed for women of both races decreases from the first to third trimesters of pregnancy.

Assuming that serum vitamin C levels below 0.2 mg/100 ml indicate a deficient nutritive state, approximately 0.5 to 1.0% of the white and 6% of the Negro women in the Selected Group during the second and third trimesters of pregnancy, and 10 and 14% postpartum, respectively, were in this category. Considering 0.6 mg the minimum compatible with optimum health, during the two trimesters 7 and 16% and 56 and 50% of the white and Negro Selected women, respectively, were in this class; the postpartum averages were 53 and 66%, respectively.

The average concentrations of serum vitamin C of the white private patients in Group C during the last two trimesters of pregnancy were approximately double those of the white women in public clinic Group A. The medians for white women in private clinic Group B were higher than those for Group A in the third trimester and postpartum. Average postpartum values for Group C exceeded those for both clinic groups.

None of the white private patients during pregnancy, and only 6% postpartum, had vitamin C levels below 0.2 mg/100 ml, whereas of the white women in Groups A and B, 4 and 12% during pregnancy and 10 and 12% postpartum fell within this category. During the second and third trimesters of pregnancy, 6 and 5% of the women in Group C had less than 0.6 mg vitamin C/100 ml. Postpartum for white women in Groups A, B and C, 68, 68 and 54%, respectively, had values below 0.6 mg.

Some investigators have reported no significant changes in blood ascorbic acid levels as pregnancy progresses (Camara and Concepcion, '40; Young et al., '46; Moore et al., '47; Hoch and Marrack, '48), whereas others report a slight downward trend in successive trimesters (Anderson et al., '46; Darby et al., '48), with a decrease after delivery (Lund and Kimble, '43b; Darby et al., '48; Teel et al., '48). No doubt the disparity of results is due to failure of experimental methods and procedures to differentiate individual physiological variability, and differences owing to growth needs of the placenta, fetus and mother, blood volume changes, physiological readjustments and marginal dietary intakes. The lower concentrations postpartum may reflect decreased food intake and increased vitamin C demands for wound healing following delivery; for milk production; for endocrine readjustment and repletion for glandular activity as well as for blood volume readjustment.

Low serum vitamin C values do not indicate to what extent tissue reserves have been depleted and concentrations below those considered consistent with good health in an individual may not represent a state of vitamin C deficiency unless the low levels are found repeatedly (Farmer, '44), especially during the different physiological phases of the reproductive cycle (Hamil et al., '47; Munks et al., '47). Serum vitamin C concentrations of mothers consuming excellent diets containing 51 to 254 mg vitamin C daily and observed on 10 successive days following delivery, showed a wide range of normal, individual physiological differences (Munks et al., '47). Because of the wide individual variability with respect to serum vitamin C, interpretations based upon the seriatim blood studies of individual women as they progress through the reproductive cycle take on greater significance than group averages in nutritional status studies. A previous study emphasized (Munks et al., '47): "Further research is needed to clarify the influences exerted by the many factors involved in the vitamin C metabolism of pregnant and nursing women. Among these are the possibility of fetal synthesis of the vitamin, physiological adjustment of the maternal body from conditions of pregnancy to those of lactation, including possible reorganization of the glands of internal secretion, the level of requirement for the vitamins, as opposed to maximum level of storage (saturation), and differences in the requirements before pregnancy, during gestation, and the lactation period."

Serum vitamin C levels for the white and Negro Selected infants averaged 1.26 and 1.24 mg/100 ml serum, respectively. Twenty-six samples from Negro premature infants in Group A had comparable levels at birth. Both white and Negro term infants in all groups had vitamin C concentrations ranging from 1.17 to 1.36 mg/100 ml serum and for all groups, the average levels were much higher than those of the respective groups of mothers postpartum. This finding compares favorably with previous observations from this laboratory (Hamil et al., '47) and with those of other investigators (Ingalls et al., '38; Mindlin, '40). Average serum vitamin C concentrations for infants are two to 4 times those of the mothers' serum and give credence to the theory that the placenta exerts selective control over vitamin C passage and may act as a barrier to reentrance of ascorbic acid to the maternal circulation. Lund and Kimble ('43b) expressed the belief that "selective retention" would account for the difference between the maternal and fetal values throughout all ranges, as well as for the dependence of the fetus on the mother for vitamin C.

A consequential factor to be considered involves growth rates and the vitamin C requirements of the placenta and fetus. Rapid placental growth in early gestation, no doubt, augments the maternal vitamin C requirement which may be reflected in maternal serum vitamin C levels. Also, it has been reported that the younger the fetus, the higher the vitamin C content of its tissues (Giroud et al., '36). Little is known about the factors that control the changing composition of the placenta and its storage capacity. According to Zsigmond and Scipiades ('42), the vitamin C content of the placenta increases during the course of pregnancy and then decreases near its termination. Without doubt endocrine changes exert some influence upon maternal blood levels of vitamin C, just as the ascorbic content of the adrenal gland is high in pregnancy.

Attention is now being given to various forms of stress and the manner in which the body adapts itself to them (Selye, '51; Margulis et al., '52; Gastineau, '53; Mitchell, '53). The activity of the hormones produced during stress is to some extent influenced by diet and the nutritive state of the individual. Vitamin C and proteins especially are involved in the metabolic mechanism of the adaptation syndrome. Nutritional stress accompanies the process of growth and physiological accommodation of the body to the gravid state. If nutritive needs are not met by the diet, undernutrition or malnutrition may result in the mother, and the residual effects alter her future health and that of the infant. Body tissue reserves may be diminished prior to pregnancy by poor diet, illness, excessive menstrual blood loss and closely-spaced pregnancies. Consequently, if a woman is undernourished during the prematernal epoch of life and at the time of conception, her maternal nutritive demands are augmented, over and beyond the usual demands, for purposes of nutritional conditioning or reconditioning her body (Hummel et al., '37; Toverud et al., '50).

It is generally recognized that fetal needs take priority over maternal needs for vitamin C, and that the fetus may build up a substantial reserve of this vitamin at the expense of the mother (Snelling and Jackson, '39; Javert and Stander, '43; Lund and Kimble, '43b; Teel et al., '48). Since several studies have demonstrated that the concentration of the vitamin in maternal blood is associated with level of intake, the presumption is that the fetal level also is influenced. Smith et al. ('53) supported the importance of adequate vitamin C nutriture for the prospective mother by finding a significant statistical relationship between the amount of ascorbic acid in the fetal liver and the amount of the vitamin in the maternal diet.

Serum vitamin A and carotenoids

Vitamin A and its precursors, the carotenoids, are essential for growth and the preservation of health. They have special roles in the formation of epithelial cells and the maintenance of their integrity, in the shaping and moulding of bone (Mellanby, '47), in the formation of teeth and in the visual cycle (Wolbach and Bessey, '42). Vitamin A is a necessary dietary component for sustaining health and function during reproduction. In mammals, vitamin A deficiency may cause irregularities in the oestrus cycle, and during pregnancy may produce fetal abnormalities (Toverud et al., '50). Vitamin A and carotenoids participate in many physiological functions, some of which are not clearly defined, particularly in relation to endocrine activity and to metabolism.

The body has a capacity for storing vitamin A, particularly in the liver. For this reason the effects of restricted intake may not readily become apparent in adult human beings (Moore, '37; Medical Research Council, '49), but in babies and children avitaminosis may develop more quickly and have more severe consequences (Toverud et al., '50). If increased nutritive demands for vitamin A are not adequately met by diet during gestation, the maternal body will be deprived of stores essential for supporting health and building up a reserve for the exigencies of labor, delivery, puerperium and lactation. Under severely restricted conditions, the fetus may be unable to grow, develop and function to capacity *in utero*. Deprivations in prenatal life may deter effective growth, function and health in succeeding periods in the life cycle.

Vitamin A and carotenoid blood levels have been used as one of the indices of vitamin A nutriture. Their concentrations in the blood depend upon intake, absorption, storage, mobilization from stores to blood, transfer to the tissues, destruction and elimination (Moore and Sharman, '51). Whereas preformed vitamin A does not occur as such in the plant kingdom, most leafy vegetables are rich in beta-carotene and other pigments which may or may not be physiologically active. Because of the interdependence of vitamin A and carotenoids in metabolic and physiological activities, parallel low blood values would tend to intensify a deficient nutritional state. In addition to differences in intake of vitamin

A and carotenoids, changes in blood concentrations have been attributed to age, sex, race, season, economic status and infections (Wolbach and Bessey, '42).

Ranges of 30 to 70 µg vitamin A and 100 to 300 µg carotene/100 ml serum are generally considered compatible with health. Most investigators consider 20 µg vitamin A/100 ml serum to be the lower limit of normalcy (Bessey and Lowry, '47;

TABLE 11

Serum vitamin A levels of white women in the first trimester of pregnancy

	NON-PREGNANT [1] WOMEN	PREGNANT WOMEN	
		Selected	Group C
Samples	387	54	130
Median, µg/100 ml	41	41	38
Below 20 µg/100 ml, %	8	6	6
Below 30 µg/100 ml, %	19	26	29

[1] For adult white males the mean for 32 determinations was 50 µg.

TABLE 12

Serum carotenoid levels of white women in the first trimester of pregnancy

	NON-PREGNANT [1] WOMEN	PREGNANT WOMEN	
		Selected	Group C
Samples	400	55	133
Median, µg/100 ml	165	131	140
Below 60 µg/100 ml, %	3	0	0
Below 100 µg/100 ml, %	15	22	14

[1] For adult white males the mean for 33 determinations was 124 µg.

Jolliffe, '49), and although not known definitely, less than 60 µg of carotene/100 ml is judged to be incompatible with health and well-being (Murrill et al., '41). The average vitamin A concentrations for white non-pregnant women and for the white Selected and private patients (Group C) were 41, 41 and 38 µg/100 ml serum, respectively, during the first trimester (table 11): serum carotenoid values were 165, 131 and 140 µg, respectively (table 12). Assuming 20 µg of vitamin A and 60 µg carotenoids as the lower limits harmonious

TABLE 13

Maternal and infant serum vitamin A levels

	WHITE SUBJECTS				NEGRO SUBJECTS			
	Mothers			Term infants [1] (1–9 days)	Mothers			Term infants [1] (1–9 days)
	Second trimester	Third trimester	Postpartum (1–8 days)		Second trimester	Third trimester	Postpartum (1–8 days)	
Selected								
Samples	186	405	133	87	78	412	163	133
Median, μg/100 ml	41	39	44	16	34	32	39	14
Below 20 μg/100 ml, %	4	8	7		13	19	7	
Below 30 μg/100 ml, %	21	26	16		38	44	23	
Group A (public clinic)								
Samples	19	184	71	56	191	862	315	237
Median, μg/100 ml	36	31	40	15	31	31	35	14
Below 20 μg/100 ml, %	21	20	14		17	20	13	
Below 30 μg/100 ml, %	47	47	31		46	48	33	
Group B (private clinic)								
Samples	13	43	21	15	69	175	87	51
Median, μg/100 ml	42	36	33	14	37	37	32	12
Below 20 μg/100 ml, %	8	9	14		7	10	13	
Below 30 μg/100 ml, %	31	21	38		32	32	47	
Group C (private)								
Samples	335	592	171	96				
Median, μg/100 ml	40	39	45	14				
Below 20 μg/100 ml, %	4	7	5					
Below 30 μg/100 ml, %	22	25	16					

[1] For premature infants three samples from white and 23 samples from Negro infants in Group A showed median serum vitamin A values of 8 and 11 μg, respectively; the median for 4 samples from infants in Group C was 5 μg.

TABLE 14

Maternal and infant serum carotenoid levels

	WHITE SUBJECTS				NEGRO SUBJECTS			
	Mothers				Mothers			
	Second trimester	Third trimester	Postpartum (1–8 days)	Term infants [1] (1–9 days)	Second trimester	Third trimester	Postpartum (1–8 days)	Term infants [1] (1–9 days)
Selected								
Samples	192	412	135	90	83	419	168	134
Median, μg/100 ml	170	170	138	28	162	167	144	28
Below 60 μg/100 ml, %	0.5	1	3		4	0.5	2	
Below 100 μg/100 ml, %	7	8	23		17	9	14	
Group A (public clinic)								
Samples	22	190	72	61	194	885	320	246
Median, μg/100 ml	140	134	124	25	153	154	134	27
Below 60 μg/100 ml, %	9	3	4		2	1	3	
Below 100 μg/100 ml, %	27	20	29		15	12	23	
Group B (private clinic)								
Samples	13	46	23	17	75	180	99	59
Median, μg/100 ml	130	174	123	28	164	176	140	28
Below 60 μg/100 ml, %	0	0	9		0	0	2	
Below 100 μg/100 ml, %	15	6	13		11	6	20	
Group C (private)								
Samples	339	596	173	100				
Median, μg/100 ml	175	183	152	30				
Below 60 μg/100 ml, %	0	0.2	1					
Below 100 μg/100 ml, %	5	3	11					

[1] For premature infants, 4 samples from white and 24 samples from Negro infants in Group A showed median serum carotenoids values of 20 and 28 μg, respectively; the median for 4 samples from infants in Group C was 20 μg.

with health, 8% of the samples from the non-pregnant, but not more than 6% of the samples obtained from the white pregnant women during the first trimester, were below the *minimum* levels.

Tables 13 and 14 present average serum vitamin A and carotenoid levels for all groups of white and Negro women during the second and third trimesters of pregnancy, and postpartum, and for their infants. The data are presented

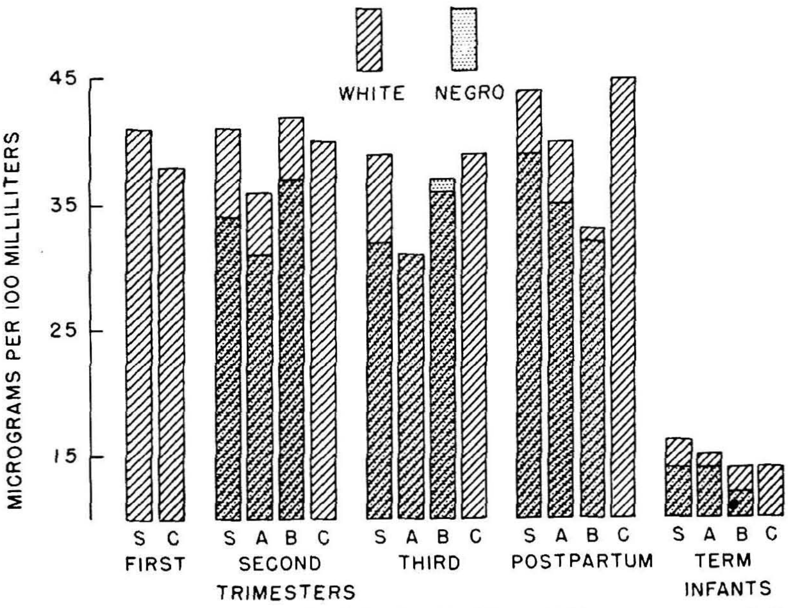

Fig. 10 Median serum vitamin A levels of white and Negro women and their infants in Selected (S) Group and in Groups A, B and C.

graphically in figures 10 and 11. The concentrations for white and Negro women in the Selected Group were comparable for the second and third trimesters, with slightly lower levels for the Negroes. Higher vitamin A values were found for both groups postpartum. The increase from late pregnancy to the puerperium however, was not verified by longitudinal data (Moyer et al., '54), emphasizing the importance of obtaining consecutive blood samples from the same individuals as they experience progressive physiological changes.

The women in Groups A, B and C similarly showed lacks of trend for serum vitamin A concentration during the reproductive cycle. Inconsistencies in results observed in this and other investigations (Bodansky et al., '43; Lund and Kimble, '43a; Anderson et al., '46; Darby et al., '48) with respect to serum vitamin A levels as gestation advanced and a return to non-pregnant levels following delivery (Abt et al., '42; Byrn and Eastman, '43; Lund and Kimble, '43a; Darby et al., '48; Hoch and Marrack, '48) are probably ac-

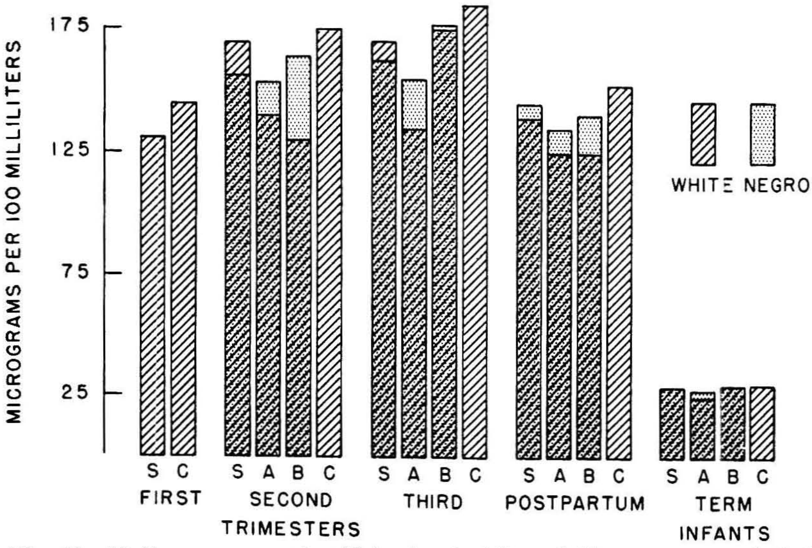

Fig. 11 Median serum carotenoid levels of white and Negro women and their infants in Selected (S) Group and in Groups A, B and C.

counted for by lack of precision in methods, in their application to the nutritive and socioeconomic characteristics of the patients, in differences in blood volume changes and in other factors influencing pregnancy.

Using 20 and 30 μg vitamin A/100 ml serum as criteria for the lower limits of satisfactory vitamin A nutriture, approximately one-fifth and one-half of the samples from the indigent Group A, respectively, were below the minima, whereas in the higher economic Groups B and C, 10% or less and 21 and 32%, respectively, were below the minima.

Dietary intake evaluations (table 2) corroborate the serum vitamin A findings. The white women in the higher economic groups (B and C) had more adequate diets and therefore, a lower percentage of diets ranked in the below 60% category. In contrast, the white women in the indigent class Group A consumed dietaries in large measure probably unsafe for health, and 42% appeared in the below 60% rating. The Negro groups likewise had 39 to 43% of their dietary intakes ranked as unsatisfactory. The intakes of leafy, green and yellow vegetables were similar for all groups and races, with a tendency toward higher percentages of the dietaries ranking below 60% for the white and Negro women in Group A and Negro women in Group B. Table 4 presents the ratings of food intake records for the women selected from Groups A, B and C. It is apparent that group differences among the Selected white women were similar to those noted for all of the women in the groups. The same similarity was found for the Negro Selected women from Groups A and B and for all of the women in the groups. What may be of greater consequence from the standpoint of health is the fact that the white women in the low income Group A and all of the Negro groups had 50% and more of their diets ranked low in milk and milk products.

The average serum carotenoid levels for the white and Negro women in the Selected Group were comparable for the second and third trimesters, with slightly lower averages for the Negroes (table 14). The mean for the first trimester samples from Selected white women given earlier (131 μg) was somewhat lower than the averages of 170 and 170 μg/100 ml recorded for this group during the last two trimesters of pregnancy. Averages for women of both races in the Selected Group were lower during the first 8 days postpartum (table 14). The general observations of average group values agree in principle with those of other investigators who found that carotenoid levels rose as pregnancy progressed

(Bodansky et al., '43; Anderson et al., '46; Darby et al., '48) and average concentrations fell after delivery (Darby et al., '48; Hoch and Marrack, '48).

In the present study, statistical evaluation of the data indicated no definite trend throughout pregnancy according to group averages; however, longitudinal data for individuals showed a tendency toward an increase. The decrease from late pregnancy to early puerperium indicated by group averages was verified by the longitudinal data, emphasizing the usefulness of the two types of data in evaluating the reliability of trends associated with change in physiological activity.

The averages for Groups C and B, but not Group A, corresponded in trend to those indicated by longitudinal data for the Selected white and Negro women, with higher values in the third than in the second trimester. Lower average levels postpartum were found for all groups. Group averages for white private patients (Group C) during the second and third trimesters were considerably higher than those for white public clinic patients (Group A). Similarly, group averages for Negro women served by the private clinic (Group B) exceeded those of Negroes seen in the public clinic (Group A).

Small percentages of the groups of women (zero to 9%) in this investigation had levels of serum carotenoids below 60 µg. During pregnancy, 12 to 27% of the white and Negro women in Group A had less than 100 µg carotenoids/100 ml but only 3 to 15% of the women in the higher socioeconomic Groups B and C had levels below 100 µg. On the whole, most of the women in the present investigation had the nutritional advantage of fair serum carotenoid concentrations.

The serum vitamin A concentrations for Selected white and Negro infants were less than one-half the average concentrations found for their mothers during the third trimester and postpartum. The average value for Selected white term infants, 16 μg vitamin A/100 ml serum, was slightly higher than the 14 μg average for the Selected Negroes. Similar differences between racial groups were observed in Groups A and B.

The premature infants in Groups A and C appeared to be less satisfactorily fortified with vitamin A, as judged by the blood levels, than the full-term infants. The Selected full-term infants showed a significant sex difference in vitamin A levels — females being higher than males. This substantiates the findings of Szymanski and Longwell ('51) and suggests possible association of vitamin A with the estrogenic hormone even in the sexually immature infant.

The average serum carotenoid concentrations for the white and Negro Selected infants were 28 and 28 μg/100 ml serum, respectively, and were approximately one-fifth the concentrations of the maternal values postpartum (table 14). The serum carotenoid levels of premature infants were lower than those of full-term infants. As with vitamin A, sex differences were found for infants in the Selected Group, females being higher than males.

Malnutrition is frequently associated with low serum vitamin A, especially in infants and children (de Haas and Meulemans, '38; May et al., '40; Lewis et al., '41; Cooperstock et al., '48). It may take considerable time on a deficient vitamin A diet before healthy adult males can be depleted to the point of altering the serum vitamin A levels (Medical Research Council, '49); however, the fact is that this study of women under the nutritional stress and gestational demand of the reproductive cycle and other similar investigations (Toverud et al., '50) reveal lowered vitamin A and carotenoid blood levels in low-income groups. This emphasizes the need for exact knowledge about the effect that deprivations of these and other nutrient factors may have on subsequent health of mothers and babies.

Serum alkaline phosphatase

Alkaline phosphatase enzymes are widely distributed in the organs and tissues of the body, occurring in higher concentrations in bone and ossifying cartilage. Serum alkaline phosphatase activity is related to calcium and vitamin D nutriture and was observed to increase in rickets and other bone disorders, such as osteomalacia and osteitis (Kay, '30, '32). In addition to bone disease, elevated phosphatase activity also may be associated with liver damage and metabolic disturbances (Moog, '46; Wolman and Evans, '49). Because the alkaline phosphatase enzymes participate so actively in growth, sexual maturation, metabolism and health,

TABLE 15

Serum alkaline phosphatase levels of white women in the first trimester of pregnancy

	NON-PREGNANT [1] WOMEN	PREGNANT WOMEN	
		Selected	Group C
Samples	401	58	140
Median, nitrophenol units [2]	1.36	1.27	1.26

[1] For adult white males the mean for 33 determinations was 1.54 nitrophenol units.

[2] One unit is the amount of phosphatase activity per liter of serum required to liberate 1 millimole of nitrophenol per hour from sodium paranitrophenyl phosphate under the specific conditions of the test.

blood concentration of alkaline phosphatase has been used as a standard for judging vitamin D deficiency in nutritional status studies of population groups (Youmans et al., '44; Adamson et al., '45; Bessey and Lowry, '47; Harrison et al., '48). Beck and Clark ('50) presented plasma alkaline phosphatase levels for pregnancy and Clark and Beck ('50) from birth to 27 years of age. They stated that "the plasma alkaline phosphatase activity seems to be closely related to growth rate as indicated by height measurements and to be derived from osteoid tissue."

The average alkaline phosphatase concentration of non-pregnant white women (table 15) was 1.36 nitrophenol units —

a level which differs little from the averages of 1.27 and 1.26 nitrophenol units for white women in the Selected Group and in Group C, respectively, during the first trimester of pregnancy. Table 16 presents the average serum alkaline phosphatase values for the 4 groups of mothers during the second and third trimesters of pregnancy, and postpartum and of their infants (fig. 12). During the second trimester the average levels for the Selected white and Negro women were

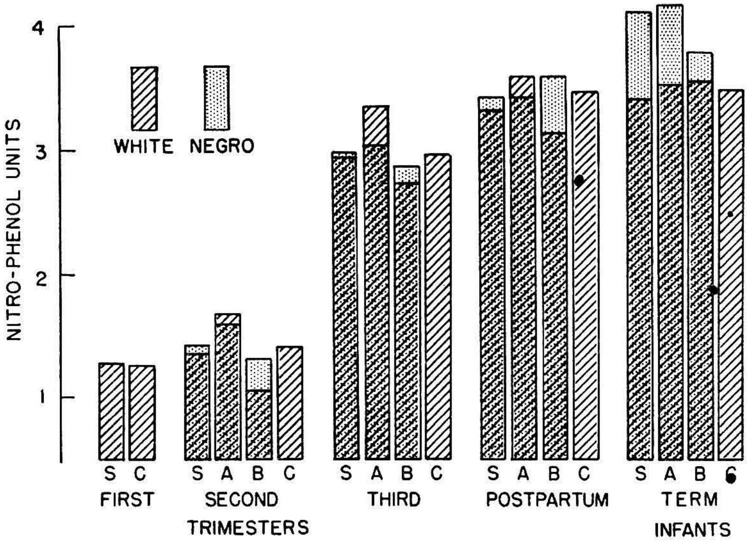

Fig. 12 Median serum alkaline phosphatase levels of white and Negro women and their infants in Selected (S) Group and in Groups A, B and C.

1.36 and 1.42 units, respectively. During the third trimester, average values were approximately doubled (2.94 and 2.98 units, respectively), and the increase extended into the postpartum period (3.33 and 3.43 units, respectively). Similar average concentrations of the enzyme and increasing trends during the second and third trimesters of pregnancy and postpartum, were found for white and Negro women in all groups.

The data demonstrate that physiological changes in alkaline phosphatase concentrations occur with regularity during

TABLE 16

Maternal and infant serum alkaline phosphatase levels

	WHITE SUBJECTS				NEGRO SUBJECTS			
	Mothers			Term infants [1] (1–9 days)	Mothers			Term infants [1] (1–9 days)
	Second trimester	Third trimester	Postpartum (1–8 days)		Second trimester	Third trimester	Postpartum (1–8 days)	
Selected								
Samples	190	419	142	110	88	440	180	163
Median, nitrophenol units [2]	1.36	2.94	3.33	3.42	1.42	2.98	3.43	4.14
Group A (public clinic)								
Samples	23	203	77	69	210	920	323	280
Median, nitrophenol units	1.68	3.36	3.61	3.54	1.59	3.04	3.43	4.18
Group B (private clinic)								
Samples	18	50	34	23	90	200	110	84
Median, nitrophenol units	1.06	2.73	3.14	3.56	1.32	2.86	3.60	3.80
Group C (private)								
Samples	336	599	173	122				
Median, nitrophenol units	1.41	2.96	3.48	3.48				

[1] For premature infants, 5 samples from white and 29 samples from Negro infants in Group A showed median serum alkaline phosphatase values of 3.25 and 3.75 nitrophenol units, respectively; the median for 5 samples from infants in Group C was 6.75 nitrophenol units.

[2] One unit is the amount of phosphatase activity per liter of serum required to liberate 1 millimole of nitrophenol per hour from sodium paranitrophenyl phosphatase under the specific conditions of the test.

the reproductive cycle and the magnitude of change corresponds in large measure to anatomical growth and development, accomplished by enlarged physiological activity. Although group averages for serum alkaline phosphatase indicated a definite trend upward through pregnancy and early puerperium, longitudinal data for seriatim blood samples from individual women substantiated the consistent increase throughout pregnancy, but not in the puerperium. The values for individuals showed a decrease in serum alkaline phosphatase for white and Negro women after the 9th month. While this decrease was slight in comparison with the increase for the 8th and 9th months, according to group averages, the seriatim data demonstrated that it was definite for individuals (Moyer et al., '54). The group averages for Selected subjects on the basis of month of gestation (table 3) also demonstrated the change from the 9th month to the puerperium indicated by the longitudinal data.

The results obtained in this investigation are in accord with those of Beck and Clark ('50) and Speert et al. ('50) who found little change in alkaline phosphatase levels during pregnancy until a rise occurred in the third trimester. This rise coincided with the metabolic processes associated with ossification of the developing fetus which reaches its height during the last three months of pregnancy (Hummel et al., '37; Kelly et al., '51). The enlarged demands of the fetus during the last three months of intrauterine life are paralleled by augmented storage of minerals and nitrogen (Macy and Hunscher, '34), to meet the requirements for physiological growth.

The individual pattern of changing structure may be altered from time to time by prevailing nutritional state, diet and health. The extent of physiological differences that occur during the normal states of reproduction, and genetic differences must be determined before it is possible to evaluate nutritional state with certainty.

Of the Selected women, 39% of the Negro and 13% of the white had total dietary intakes which, according to present knowledge of requirements for pregnancy would be unsafe for robust health. Further, substandard total dietary intakes were the rule for all Negro groups (A and B) and the low-income white group (A), and included low consumption of milk and milk products, meat and eggs and vitamin C-rich foods — all foods bearing essential nutrients for bone and protoplasmic growth and function. The greatest amount of fetal bone formation takes place in the last trimester and the amount of minerals stored by the mother is dependent upon her nutritive state (Hummel et al., '37). Increased serum alkaline phosphatase activity corroborates the increased demands for minerals by the mother and fetus during late gestation.

Only among white women in Group C and those in the Selected Group did 10% or more of the food records rate 90% or above (table 2). Moore et al. ('47) found that diets of 4% of the white and none of the Negro pregnant women studied met or exceeded the recommended allowances for the latter half of pregnancy. Burke et al. ('43a) reported similar findings for pregnant patients; only 14% of the women consumed diets which could be considered "excellent" or "good" in food intake. Tompkins ('53) stressed the importance of supervision and instruction of the obstetric patient in her essential nutrient needs. Reports of food intake studies of pregnant women in Holland (Hartog et al., '53), and in Australia (Woodhill, '52) also stressed the need for education on nutrition during pregnancy.

In general, more food intake records of Negro than of white women rated less than 60% although the percentage for the white women in the public clinic Group A approximated the percentage for the Negro groups. Ebbs et al. ('42) and other investigators believe that many women in low-income groups receive inadequate diets. Jeans et al. ('52), from a study of dietary habits of low-income groups, stated that faulty eating habits, as well as economic status, are major factors influencing the food intake in pregnancy.

The serum alkaline phosphatase levels for white and Negro women in the Selected Group indicated that white individuals had lower values than corresponding enzyme levels for Negroes. The same relationship was found for women in Group B, but a reversal of trend is evident for Group A. These findings tend to substantiate those of Scrimshaw et al. ('49) who reported that the enzyme level appeared to be lower in the white American than in groups with greater skin pigmentation when dealing with women rated clinically as "normal."

The average serum alkaline phosphatase values for the Selected white and Negro infants were 3.42 and 4.14 nitrophenol units, respectively (table 16). The average enzyme levels for the Negro infants in Groups A and B also exceeded the averages for the white infants in those groups. The average serum alkaline phosphatase levels for term infants in all groups did not differ substantially from the early postpartum values for their mothers. The average enzyme level (3.75 nitrophenol units) of 29 samples from Negro premature infants in Group A is somewhat lower than the average of 4.18 units observed for the Negro term infants. There was no consistent sex difference.

RELATIONSHIPS OF COMPONENTS IN MATERNAL AND INFANT BLOOD FOR SELECTED SUBJECTS

It is essential to differentiate certain specific physiological, structural and functional changes before an evaluation can be made of those having to do with a depleted nutritional state, malnutrition or disease. In addition, by employing simultaneous determination of several nutrients and components on a single sample of blood, as well as other diversified methods for determining developmental and functional changes which take place in sequence within the individual and among various subjects, broader interpretations, with larger implications of nutrition and health, are possible. The Selected subjects permit a study of the significant factors which may alter the usual interrelationships between

TABLE 17

Relationships for Selected subjects

		MOTHERS			INFANTS	
		Second trimester	Third trimester	Post-partum	Male	Female
Pregravid maternal weight *versus* infant birth weight					+	+
Weight gain[1] in pregnancy *versus* infant birth weight					+	+
Prenatal care *versus*						
serum vitamin C		+	+	+	+	+
serum alkaline phosphatase	— white	—	—	—	—	—
	— Negro	—	—	+	—	—
serum carotenoids		0	+	+	0	0
Diet rating *versus*						
serum vitamin C	— white	+	+	+		
	— Negro	0	0	0		
serum vitamin A		0	+	+		
Dietary vitamin C intake *versus* serum vitamin C		+	+	+	+	+
Green, yellow vegetable intake *versus* serum carotenoids		+	+	+	0	0
Number of pregnancies *versus*						
serum protein		0	0	+		
serum vitamin C	— white	0	—	0		
	— Negro	—	—	0		
serum alkaline phosphatase		—	—	—		
Hemoglobin *versus*						
serum protein	— white	0	0	0	++	0
	— Negro	++	++	+++	++	++
serum vitamin C	— white	++	+++	++	0	0
	— Negro	0	0	0	0	0
serum vitamin A	— white	0	+++	0	0	0
	— Negro	0	++	0	0	0
serum carotenoids	— white	0	++	+++	0	+++
	— Negro	0	0	0	0	0
Serum vitamin C *versus* serum carotenoids	— white	+++	+++	++	0	0
	— Negro	+++	+++	+++	0	++
Serum vitamin A *versus* serum carotenoids	— white	+++	+++	+++	0	0
	— Negro	+++	+++	+++	++	0
Mothers *versus* infants						
hemoglobin	— white				0	0
	— Negro				+++	++
serum protein	— white				+++	++
	— Negro				0	0
vitamins C	— white				++	+++
	— Negro				+++	+++
serum alkaline phosphatase	— white				++	++
	— Negro				++	0
serum vitamin A	— white				0	+++
	— Negro				0	++
serum carotenoids	— white				+++	+++
	— Negro				+++	++

"0" indicates no statistically significant relationship; "+" indicates positive relationship judged by average values; "++" indicates significant positive relationship at the .05 level; "+++" at the .003 level; "—" signs indicate negative relationships judged by the same standards. White and Negro subjects were studied separately but values are reported separately when they differ.

[1] Weight change in pregnancy was not calculated unless a weight was taken within two weeks of delivery.

maternal and infant bloods, and consequential changes in the concentration of blood components due to physiological and environmental factors, including maternal weight change and dietary intake, respectively.

A statistical evaluation of the relationships of maternal and infant blood values was determined by means of correlation coefficients and presented in detail in a separate publication (Moyer et al., '54). Only the significant relationships are included in table 17.

Maternal blood components

Maternal hemoglobin for the Selected Negro patients was positively associated with total serum protein during the last two trimesters, and postpartum, but a relationship was not found for the white subjects. Maternal hemoglobin data for the white women were positively related to serum vitamin C in the final trimesters and postpartum, but the Negro women showed no relationship. Maternal hemoglobin levels were not consistently related to maternal levels of serum alkaline phosphatase, vitamin A or carotenoids. Comparison of averages revealed no relationship between maternal hemoglobin and number of pregnancies, weight change, prenatal care, age of primigravidas, diet rating, dietary protein intake, Rh factor, or season (Moyer et al., '54).

Statistically significant relationships were not found between maternal serum protein levels during the last two trimesters and postpartum, and sera vitamin C, alkaline phosphatase, vitamin A and carotenoids. For the same intervals in gestation, maternal serum protein concentrations did not show a consistent relationship to number of pregnancies, weight change, prenatal care, age of primigravidas, diet rating, dietary protein intake, or season. The average postpartum serum level of primigravidas was slightly lower than that of multigravidas. Correlation coefficients for maternal serum vitamin C levels of white and Negro subjects during the last two trimesters of pregnancy and postpartum *versus* maternal blood levels of hemoglobin, sera protein, alkaline phosphatase, vitamin A and carotenoids indicated no consistent relationship except for serum carotenoids. Maternal serum vitamin C and carotenoid levels were positively related at all stages of the reproductive cycle investigated. The maternal serum vitamin C during pregnancy and postpartum showed significant positive relationships to maternal hemoglobin levels for white women, but not for Negroes — a finding which may be related to the inferior diets of the Negroes.

Averages for serum vitamin C levels of the subjects were studied in relation to number of pregnancies, weight change, age of primigravidas, prenatal care, season, diet rating and intake of vitamin C foods. Positive relationships were found with prenatal care and high intake of vitamin C foods. For the white, but not for the Negro women, maternal vitamin C levels were positively associated with the over-all diet rating.

In a relationship study of maternal serum vitamin A levels *versus* maternal hemoglobin, sera protein, vitamin C, alkaline phosphatase and carotenoids, only the serum carotenoids showed a significant positive correlation during the second and third trimesters and postpartum for both races. No association or inconsistent relationship was found between the maternal serum vitamin A level and number of pregnancies, gestational weight change, prenatal care, age of primigravidas, season, diet rating and intake of leafy, green and yellow vegetables.

Statistical evaluation of maternal serum alkaline phosphatase levels for women during the second and third trimesters, and postpartum, demonstrated a lack of association with hemoglobin, sera protein, vitamin C, vitamin A and carotenoid levels. Judged by average values for the same intervals in the reproductive cycle, the enzyme levels indicated negative relationship to number of previous pregnancies for both white and Negro women. The enzyme activity was consistently higher throughout pregnancy and early postpartum for primigravidas than for multigravidas (one to 5) who, in turn, had higher values than the grandmultigravidas (6 and over) except for the third trimester for white women. These findings are not in complete accord with a previous report (Beck and Clark, '50) that multiparas, as compared to primiparas, showed a tendency toward higher plasma alkaline phosphatase values during the 10th lunar month.

Serum alkaline phosphatase levels of the Selected women showed no association to weight change during pregnancy and no consistent relationship to age of primigravidas. The enzyme level was not related to the rating of the dietary intake during pregnancy, nor to season of the year.

The current study did not reveal a significant difference between the serum alkaline phosphatase levels during the 9th month or the last two weeks of pregnancy of the mothers bearing males and those bearing females. Meranze et al. ('37) report a similar lack of relationship; however, Beck and Clark ('50) found a highly significant difference in enzyme levels during the 10th lunar month for women bearing male and those bearing female infants.

In the current study, three white and 12 Negro women bore liveborn twins. In a comparison of the third trimester, serum alkaline phosphatase levels of these women with the medians observed for the white and Negro women, respectively, the majority (9 *versus* three) having third trimester samples had higher levels than the medians; however, all values were within the range established by the Selected mothers, the highest values being 7.7 nitrophenol units. Similar tendencies have been noted (Meranze et al., '37; Ebbs and Scott, '40), but Young et al. ('46) failed to confirm this observation for twin pregnancies.

Nutritive requirements during pregnancy depend upon the extent to which nutritional conditioning and reconditioning are necessary. This is borne out using serum alkaline phosphatase as an index for the assessment of the nutritional status. The data demonstrate that the women in the low-income Group A had higher average concentrations during the second and third trimesters than were found at comparable intervals for the higher economic Groups B and C. There was also a tendency for white subjects to have lower levels of enzyme activity than the indigent white women. In a comparison of the serum alkaline phosphatase levels of Negro patients, those in Group A exceeded those in Group B and tended to be higher than the average value found for the Negro subjects.

The lower nutritional status of the Negro mothers in general when compared to corresponding white mothers is probably correct as judged by nutrient intake, prenatal care and serum alkaline phosphatase with which this report is concerned, and is verified further by analogous observations of hemoglobin and serum protein, of serum vitamin A and carotenoids, and of serum vitamin C levels of the same women at each stage of pregnancy observed. Twice as many of the diets of the white women in Group A classified as incompatible with health in comparison with corresponding diets of individuals in the Selected white and higher socio-economic Groups B and C. From 39 to 43% of all diet records of Negroes, including the Selected Group, had substandard ratings and were comparable to the white subjects in the low-income Group A (42%).

Infant blood components

In an interrelationship study of the blood levels in the Selected Group of infants (table 17), the hemoglobin levels of white males, of Negro males and of Negro females showed positive relationships to the serum protein levels. Other relationships for infant serum protein levels were not found.

Infant serum vitamin C levels were not related to concentrations of other blood components but mothers' postpartum serum levels of the vitamin were positively associated with levels of the newborn.

Neither serum vitamin A nor carotenoid concentrations for the Selected infants were related to levels of hemoglobin, sera protein, vitamin C, alkaline phosphatase in the blood of the infants. However, infant serum carotenoid concentrations were positively related to maternal serum carotenoid levels postpartum. Thus, if the mother is well fortified with vitamin A or its precursors, she is more apt to provide her infant with higher stores to draw upon during prenatal life. The methods and procedures applied in this survey are not sufficiently refined to determine the extent to which differences observed in infant blood constituents are associated with nutrient intake and vitamin A nutriture of their respective mothers, or to racial characteristics.

The premature infant appears to be less satisfactorily fortified with vitamin A, judging by blood levels, than is the full-term infant. The Selected full-term infants showed a significant sex difference in vitamin A levels, females being higher than males, which substantiates the findings of Szymanski and Longwell ('51) indicating a possible association of vitamin A with the estrogenic hormone, even in the sexually immature infant.

In infant blood, serum alkaline phosphatase levels were not related, or were inconsistently related, to other infant blood components. The diverse and unlike concentrations of blood components associated with newborn infants and their respective mothers bear witness to the intricate controlling physiological mechanisms and safeguards that are brought into operation during childbearing which some investigators (Lund and Kimble, '43b) have termed "selective retention" of the placenta in the case of vitamin C.

Maternal — infant relationships

The data accumulated allow a study of the significant factors which may change the usual interrelationships between respective maternal and infant blood. Such information takes on greater significance when it is realized that the very life and well-being of the fetus is determined by its ability to obtain regularly the nutrients required, and in the right proportion, directly from the maternal blood and therefore, indirectly from the maternal diet for well-balanced physiological performance. Insofar as the mother is concerned, her ability to provide adequately for her own augmented metabolic needs during the reproductive cycle, as well as for the fetal and placental needs, may be a determining factor in her health in later life. The placenta serves the fetus as a nutritive, protective and excretory organ.

The relationships of maternal and infant blood values were determined for the Selected Group by correlation coefficients (Moyer et al., '54). Hemoglobin levels of Negro infants were positively correlated with maternal postpartum levels. No association was found between levels of serum protein in infant blood and maternal prenatal care, dietary protein intake or Rh factor. The serum protein concentrations of only white mothers were related to levels in the blood of their infants. When groups are inconsistent, a real difference between races and sexes is questionable — a conclusion which agrees with opinions of others (Kagan, '42; Trevorrow et al., '42; Milam, '46; Medical Research Council, '49). A significant positive relationship was found between serum vitamin C in white and Negro infants and their respective maternal vitamin C levels. Infant serum vitamin C levels also were positively related to maternal prenatal care and to the maternal intake of vitamin C foods.

The markedly lower serum vitamin A and carotenoid concentrations of the newborn than those of their respective mothers are in contrast to results obtained in this and earlier investigations of hemoglobin (Munday et al., '38) and serum vitamin C (Hamil et al., '47) made in this laboratory, in which both components in infant blood were two or more times the average values of their respective mothers' blood during the last trimester of pregnancy. The explanation of these seeming contradictions in physiological performance must be sought beyond blood volume changes that do occur in pregnancy and in young infants. The placenta apparently selects and controls, if maternal dietary intakes are adequate, the amounts of nutrients that pass from the mother's blood to that of her infant and fortifies it with plenty of nutrients to satisfy its changing growth and functional needs, and for a reasonably satisfactory storage. For the Selected Group, the enzyme level of the infants showed positive relationship to the maternal postpartum level for the white and Negro male and for the white female, but not for the Negro female. The negative relationship between maternal prenatal care and maternal serum alkaline phosphatase levels extended to the infants; that is, infants of cooperative mothers who had good prenatal care tended to have lower enzyme levels than infants of mothers who had poor ratings.

SUMMARY AND CONCLUSIONS

This investigation is concerned with 1,064 pregnant patients (378 white and 686 Negro) who were chosen for study from three socioeconomic groups; namely, a public prenatal clinic for low-income and indigent populations (Group A); a private prenatal clinic for families with moderate means (Group B) and a group of private patients, characterized as middle-class with a few wealthy individuals (Group C). It contributes to the scope of knowledge of the mean and range normality standards of physiological and chemical variations of women during childbearing, and some of the factors that may augment or decrease them. It presents, for the first time, average and range normality standards of 6 blood components determined on single samples of blood collected successively following conception, and demonstrates a specific physiological course of uncomplicated pregnancy and parturition of 427 mothers and their respective, full-term newborn infants. The blood components determined were hemoglobin, sera total protein, vitamin C, vitamin A, carotenoids and alkaline phosphatase. These constituents represent various developmental and functional processes and participate in several body systems.

Three types of control subjects were used in the investigation. The individual physiological variability of 427 Selected pregnant patients and the analytical procedures were checked by comparable seriatim blood data collected concurrently on 48 non-pregnant white women and 24 white men of similar ages. Observations on these three groups extend knowledge of individual physiological variability, of seasonal and environmental influences, of racial and sex differences, of time following conception when changes and adjustments become evident biochemically and other influencing factors.

The reliability of the normality standards of blood concentration levels at equivalent stages in the reproductive cycle was enhanced by the elimination of all women and their infants with recognizable complications and of excluding spurious blood data falling outside the upper and lower 10% limits, and including only the 10th to 90th percentile values of the Selected Group in the formulation of the standard physiological curves of gestation. The average and range normality standards have served as a basis for investigating, characterizing and evaluating deviations in nutritional status, clinical symptoms, dietary intakes; racial, socioeconomic and other influences.

By the use of objective biochemical assessments of concentrations of blood components representing various metabolic processes of several body systems, it is demonstrated that there is a specific reproducible course of each blood component during pregnancy of women, and after delivery. The indications are that the normality blood standard may be altered by several associated factors, such as socioeconomic status, race, prenatal care and nutritional status.

The placenta, with its component proteins, carbohydrates, fat, enzymes, vitamins, hormones and minerals, varies its chemical composition during gestation in accordance with the demands made upon it by the growing fetus. It serves the fetus in nutritive, protective and excretory roles. The median infant blood concentrations are higher in hemoglobin and vitamin C, but lower in total serum protein, vitamin A and carotenoids, than those of their respective mothers, whereas alkaline phosphatase concentrations are similar for mother and infant. The placenta appears to conserve hemoglobin for fetal construction, function and reserves, whereas it plays a protective role in the case of vitamin C, vitamin A and carotenoids by limiting what the fetus receives by restricting egression from maternal blood to the fetal organism. The greatest of influences beyond the current needs of the fetus and adnexa, and of growth and storage in the maternal body (including enlargement of the uterus and breasts and reserve liver stores in anticipation of the birth of the child, parturition and lactation) and adequacy of the dietary intake, is repleting nutritive stores that may previously have existed, due to undernutrition or malnutrition resulting from dietary habits, submarginal diets, injury or disease.

Unfortunately there is so little knowledge available on how and when nutritive reserves can best be attained by human beings which will enable the preservation of the health of the mother while she is building for nutritional stability in the new generation and during succeeding epochs of her own life. If a cue may be taken from experimental investigations on animals, metabolic studies of undernourished pregnant women and the effect of rubella during the first trimester of human pregnancy, the timing factor with respect to enforcement of untoward deficiencies and infection may be crucial to the life and health of the developing embryo. For instance, in animal investigations, deficiencies of vitamin A, riboflavin, choline, folic acid and other essential nutrients drastically enforced at the time of conception in some species, or within a brief period immediately following, or an attack of rubella within the first trimester of human pregnancy, may lead to malformations of multiple nature, restricted growth, impaired nutritional stability, and therefore, the health of the fetus. Prematernal, as well as prenatal, preparation would seem essential to the protection of the health of the new generation. It is of greatest importance to entend and apply fundamental scientific research to the human mother during childbearing, to develop more precise methods of observing, recording and evaluating the results.

Dietary intake is an essential part of health and nutritional status assessment. A simple qualitative dietary intake evaluation was tested for reliability against analyzed mixed diets and was used for classifying individual pregnant women into broad groups with differentiating dietary intake characteristics and for relative comparisons with respect to blood concentration, socioeconomic status, race and prenatal care. The trends observed indicate lower nutritional status of the Negro mothers in general when compared with corresponding values for the white race, and are verified by the more objective blood concentration levels for several components at each trimester of pregnancy, after delivery, and of the mothers' newborn infants. Biochemical assessments of the Negro mothers were supported by a higher percentage of marginal dietary ratings, a higher percentage of "poor" prenatal care and generally lower socioeconomic status. Clinical, biochemical and dietary intake assessments, therefore, agree in indicating that lower income, inferior dietary intake and patient-choice of substandard prenatal care are reflected in objective biochemical blood concentration levels considered to be in the direction of concentrations incompatible with healthful living.

Twice as many of the diets of the white patients in Group A were classified as incompatible with health when compared with white individuals in the Selected and higher socioeconomic Groups B and C, inasmuch as the nutrient intake was less than 60% of the Recommended Dietary Allowances. While it is known that the Recommended Dietary Allowances of the National Research Council represent not merely minimum requirements of average individuals, but levels enough higher to cover substantially all individual variations in the requirements of normal people, it is evident that dietary intakes carrying less than 60% of the essential nutrients might be inadequate for many women under the nutritive stress of pregnancy.

All of the Negroes, including those in the Selected Group, had substandard dietary ratings comparable to the low-income whites in Group A. While it is important to point out that white and Negro pregnant women in the low-income Group A shared equally with Negroes in the private clinic Group B in the disadvantages arising from inferior diets, it is of equal importance that marginal diets are usually not of short duration but arise from long-standing unsatisfactory economic conditions or undesirable dietary habits. The biochemical findings in the case of some blood components would indicate that undernutrition is likewise of long duration, probably existing at the time of conception. Should this be the case, there is superimposed upon the usual augmented needs of reproduction, additional nutritive demands for purposes of nutritional conditioning or reconditioning of the maternal body.

Health authorities are challenged to determine whether racial differences observed between white and Negro subjects are truly racial or whether improved nutritional status of the Negroes of this country will tend to lessen or nullify the differentials observed between the two races. Multiple deficiencies due to inadequate or unbalanced diets of long duration are reflected in inferior health and are difficult to replete, especially in adolescence and young adulthood, and may have more serious consequences upon the outcome of pregnancy if malnutrition exists at conception or during the first trimester of pregnancy when organ differentiation is taking place in the fetus. These may account for some of the restricted and variable physiological responses in the Negro race and low-income white groups. Methods of assessing nutritional status are not sufficiently refined to distinguish between current and latent nutritive needs. The increasing number of teen-age girls who are assuming the responsibilities of motherhood today poses a real challenge to parents, doctors and health authorities to see that nutritive needs are met in full measure during each epoch of life, that the forthcoming generations may be healthy in mind and body.

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ADDENDUM

Since this manuscript was submitted, several papers have appeared from "The Vanderbilt Cooperative Study of Maternal and Infant Nutrition": I. Background. II. Methods. III. Description of the sample and data. (J. Nutrition, *51:* 539, 1953.) IV. Dietary, laboratory and physical findings in 2,129 delivered pregnancies. (J. Nutrition, *51:* 565, 1953.) V. Description and outcome of obstetric sample. (Am. J. Obstet. Gynecol., *67:* 491, 1954.) VI. Relationship of obstetric performance to nutrition. (Am. J. Obstet. Gynecol., *67:* 501, 1954.)