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THE INFLUENCE OF PRENATAL NUTRITION UPON THE DEPOSITION OF IRON IN THE LIVERS OF FETAL RATS AND ITS INFLUENCE IN ENABLING THESE ANIMALS TO BUILD HEMOGLOBIN AND ERYTHROCYTES

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The story of studies concerned with the metabolism of iron constitutes one of the most interesting chapters in the history of medicine. On February 6, 1935, a new mile-stone in achievement was set up when Dr. William B. Castle received the John Phillips Memorial Prize in recognition of his remarkable contributions to this field of medicine. These investigations have a fitting prologue in the classical contributions of Zaleski, von Bunge and his pupil Abderhalden. As early as 1886 Zaleski (1) had published figures giving the iron content of the livers of dogs.

Age of Dog	Iron in dried Liver. Mgs. per cent	
New-born	390.7	
Adult	89.1)	
	77.9)	average 70
	42.9)	

Von Bunge, in 1889 (2,3), pointed out on the basis of these figures that in the liver of the new-born animal there is from five to nine times as much iron as there is in similar tissues of the adult. In the same year Lapicque (4) demonstrated a progressive loss in liver iron in young rabbits during the lactation period.

Age in days	Iron in dried Liver. Mgs. per cent
8	500
11	100
21	70

Four years later (1893) von Bunge (5) published his findings on the iron content of the embryos of both rabbits and guinea pigs.

Guinea Pigs		Rabbits	
Embryo wt.	Mgms. iron c.c. body wt.	Embryo wt.	Mgms. iron c.c. body wt.
16.6	4.6	7.8	6.4
32.3	4.4	15.3	8.5
45.6	5.6	38.5	9.0
64.3	5.3		
94.4	5.0		
101.8 *	6.0	59.5	18.2
**	4.4		3.2

*(New-born wt.)
**(At three weeks of age)

These results show very clearly the progressive depletion of liver iron throughout the lactation period and that the initial stores of iron are directly proportional to the length of the nursing period. Von Bunge pointed out that in view of the extremely low iron value of milk, this represented a wise provision on the part of Nature in guaranteeing an adequate source of iron during the time the animal is restricted to this kind of food. He says, "Rabbits are blind at birth, have very little hair, are awkward in their movements, and have to remain in warm nests for two weeks. Guinea-pigs are born with eyes open, and thick warm furs; they run about within a few hours and seek their own nourishment".

Abderhalden (6), in 1899, produced nutritional anemia in animals by limiting the diet to milk for a considerable period after the expiration of the usual time of nursing. He showed also that the addition of inorganic iron to the milk did not result in an increase in the hemoglobin, although it seemed to exert a favorable effect upon the growth of the animal. While many believed that this was sufficient

basis for the assumption that inorganic iron cannot participate in hemoglobin synthesis, Abderhalden himself thought otherwise. He said, "The mere fact that the addition of iron to nutriment poor in iron does not have any distinct influence upon the formation of hemoglobin in no ways speaks against the participation of inorganic iron in the synthesis of hemoglobin in the case of normal nutrition, but it indicates that other building material is wanting as well as the iron".

Hugounenq (7), a contemporary of Abderhalden's, demonstrated that in the human fetus at least two-thirds of the iron reserve is laid down during the last three months of fetal life.

Age of fetus in months	Total iron content in mgs.
5.5	126
6.0	119
At term	383) average 402
	421)

Subsequently these facts received further confirmation by such investigators as Mayer (8) and by Langstein and Edelstein (9). The "iron depot theory" rests upon the work of the period just covered.

Very little else pertinent to the subject of this thesis was forthcoming until 1920 when Whipple and Robscheit-Robbins (10) began the publication of a series of papers dealing with the ability of the animal organism to regenerate blood under controlled conditions. These investigators were able to show that of all the foods used to supplement the special bread diet, liver possessed the greatest ability

to provide the essentials for hemoglobin production (11). Stimulated by the significance of this announcement, Minot and Murphy (12) began a series of investigations which culminated in the discovery of such a value for liver in pernicious anemia that it has meant the continuance of life for untold numbers of individuals suffering from this disease. These investigators established the fact that the inclusion of liver in the diet of patients suffering from pernicious anemia provoked a remarkable response in blood production. It was not long until Cohn and his collaborators (13) had prepared a very potent extract from liver.

The clinical observation that pernicious anemia is nearly always associated with a marked decrease in, or a total absence of hydrochloric acid served to focus attention on the possible role that the stomach might play in the genesis of that substance found in the liver which had been demonstrated to possess such remarkable therapeutic powers in blood regeneration. It was in the further elucidation of this problem that Castle (14) and his co-workers in Boston and Sturgis and his associates (15) in Ann Arbor were able to contribute information which led to the recognition accorded Dr. Castle, mention of which has already been made. These investigators have been able to show that the stomach mucosa is capable of producing a substance of enzymatic nature (intrinsic factor) which, by acting upon something present in the food (extrinsic factor)--possibly vitamin G, produces a hematinic principle which is absorbed from the intestine and deposited in the liver. It is also found in the kidney but this probably

represents accumulations of circulating hematinic material which have been prevented by the kidney from escaping into the urine.

Clinicians observed that liver or liver extract was not only beneficial in pernicious anemia but that it also exerted curative power in certain other related anemias such as Sprue. Nevertheless, in spite of its extreme potency in these anemias it remained entirely without effect in those anemias dependent upon a primary cause such as hemorrhage. Whipple's observation that liver represented an extremely rich source of material for hemoglobin production following hemorrhage and Minot's demonstration that it possessed equal potency in pernicious anemia introduced an apparent contradiction. This contradiction was clarified in some degree by the findings of Steenbock, Hart and their associates (16) when they proved that the presence of copper in the animal organism was essential for the utilization of iron in the manufacture of hemoglobin. This made it apparent that Whipple owed his results, in part at least, to the iron and copper content of the liver while Minot's results were due to something else in the liver exclusive of iron and copper. Whipple (16, 17) was able to show that iron alone increased hemoglobin production over the amount provided by the basal diet. Furthermore iron plus copper was even more efficient in this respect and a further summation of effect was noted when liver or kidney was added. It appears from this work that liver possesses a principle entirely separate from copper or iron or the pernicious anemia factor that is effective in secondary anemias.

Perhaps the chief outgrowth of these findings in respect to blood production is the tendency to regard anemia, for example pernicious anemia, as a "conditioned" anemia, that is, conditioned by the lack of intrinsic factor. Other anemias may be conditioned by the lack of extrinsic factor; by the lack of iron or hydrochloric acid; by failure of adequate absorption from the intestine; by destruction of essential materials in the intestine; by failure of adequate storage in the liver, et cetera. Furthermore iron no longer plays an isolated role in the production or cure of anemias for copper, vitamins, amino-acids, certain unknown substances in normal gastric juice and in liver are known to play an active part also (18, 19). Pathological changes in the stomach, intestine, liver and bone marrow may still further complicate the picture.

Iron plays a triple role in the body. Its importance in hemoglobin synthesis for the transport of oxygen is well recognized. It is known also to be an essential part of the nucleus where it plays an important part in cell division (growth). More recently, however, has come to be recognized another important function of iron, namely the part it plays in intra-cellular oxidations. Keilin, Warburg and Parsons and Hickmans have ably presented this aspect of its activity (20, 21, 22).

From the preceding, the inference may be drawn that the alleviation of an anemic condition by the administration of materials containing iron is not necessarily proportional to the iron content

of those materials. This can not be otherwise as long as other elements are necessary also. Moreover it has been shown that when various food materials are added to an anemia producing diet in quantities so adjusted that their iron contents are the same, the benefit derived is not necessarily the same (23, 24). The explanation of this is based on the fact that iron exists in most food materials in two forms, inorganic and organic. The organic iron, for the most part, occurs as hematin compounds. It is the hematin iron that is not available to the body for hemoglobin synthesis although the presence of copper slightly increases its utilization. For this reason the availability of the iron found in food materials for hemoglobin formation depends upon the relative amounts of organic (hematin) iron and of inorganic iron. The Wisconsin investigators have shown that the available iron is directly proportional to that portion of the food-iron which reacts with Hill's dipyridyl reagent (25). Thus 47 per cent of the iron present in yeast is available for hemoglobin fabrication. Approximately 50 per cent of the iron found in wheat and oats and other cereals and cereal preparations is available for the same purpose. Hematin-iron is utilized only to a small extent and that only when proper amounts of copper are present.

The hypochromic and chlorotic types of anemia are considered clinically as indices of iron deficiency. The problem investigated in the researches to be reported in this paper dealt primarily with

the dietary influence upon the stores of iron in the maternal liver; to what extent this latter influenced the iron endowment of the fetal livers and to what degree both were reflected in the individual blood streams as exemplified by erythrocyte counts and hemoglobin estimations. The iron depot theory explains very well why normal young can survive with little evidence of injury a prolonged period of iron depletion. It does not, however, account for the marked anemia developing in others when subjected to the same post-natal conditions. Leichtenstern (26) was the first to record the high hemoglobin content of the blood of newborns and its rapid decrease during the early days of life. Since that time numerous observers have recorded red cell counts and hemoglobin estimations in the newborn extending over the first two years of life or more.

It would not serve the purpose of this paper to record these numerous observations except to note in passing some general deductions that may be drawn from them. In the first place all observers agree that the number of red cells and the quantity of hemoglobin show a decrease throughout the lactation period. Parsons (27) and Greengard (28) agree with Mackay (29) that the hemoglobin curve shows two drops, - one beginning at birth and showing a sharp drop from its high point to a level of about half this value by the third month of life, - the other beginning about the sixth month of life and falling steadily until after mixed feeding has been started. The second drop seems to be associated with an exhaustion

of the iron reserves of the infant. The first drop is not so well understood. For a full discussion of this the reader is referred to Mackay's original article. Secondly, there are significant variations in the amount of hemoglobin at birth as well as at the end of the first year of life. Mackay (30) cites Aschenheim as claiming that the normal lower limit for new-born infants is 55 per cent; Finkelstein as holding the value at 65 per cent; Holt at 75 per cent and Hutchinson and Williamson at 100 per cent. Mackay's own figures ran 20 to 25 per cent below Williamson's values and Greengard's values also were distinctly lower. Strauss (31) stated that infants born to anemic mothers had on an average 116 per cent hemoglobin while those born to normal mothers had 123 per cent. While he did not believe that the difference in these two values was statistically significant nevertheless they are well over any of the values stated above. Mackay found individual values running as high as 179 per cent but she places the average normal value at 145.7 per cent. No doubt some of the above variation can be accounted for on the basis of different technics for hemoglobin estimation. Nevertheless initial levels ranging from 55 to 179 per cent need more than this to explain them. Mackay's figures for hemoglobin values at the end of the first year are as follows: for infants whose feedings have been supplemented with iron, 86 per cent; for breast fed children 73.9 and for bottle fed babies 69.1 per cent. Strauss, in the work referred to above, showed that while the initial hemoglobin value may be the same it is not necessarily so at the end of the first year. For example, at the end of the first year 6 infants born of

normal mothers had a hemoglobin level of 67 per cent while the average hemoglobin of 6 infants born of anemic mothers was 46 per cent. The results of these two workers alone are sufficient to show a "zoning" effect, that is, hemoglobin values centering about points whose values are 46, 67, 69, 74 and 86 per cent. The explanation of the value for hemoglobin at the end of the first year is similar to that explaining the second drop in the hemoglobin curve noted above, namely, - that it is due to available iron reserves and to variations in the available iron content of the diet ingested during this period. The explanation of the variations in the initial hemoglobin values will be discussed later in connection with another subject.

The divergent instead of parallel curves noted above in the cases cited by Strauss introduces the third point to be mentioned, namely, - there is a variation in the rate of hemoglobin decline. In further confirmation of this point Greengard, in comparing his figures with those obtained by Williamson, states that the hemoglobin at birth is not only lower than Williamson's cases but that it also drops off much more rapidly and to a much lower point, the minimum being reached in 8 weeks instead of 12 to 16 weeks.

The decline in hemoglobin values from birth to the end of the lactation period; the variations in the initial and terminal hemoglobin values during this time and the marked differences in rate and extent of hemoglobin losses place added importance on the

zoning effect noted above. Children born with a low initial level, with low iron reserves and maintained on a diet low in iron will represent one extreme while infants born with high hemoglobin values, with large iron reserves and given iron supplements in their food will represent the other extreme. Between the two extremes will lie an intermediate group. All young will fall into one of these groups. Since it is not possible to determine the extent of the iron reserves but only of the hemoglobin values, the treatment must of necessity be prophylactic. The question naturally arises, What is the penalty for being a member of the lowest group? Mackay (32) states that the morbidity rate for the anemic group of infants is twice that of the non-anemic group. The anemia itself appears to reduce resistence to infection--especially respiratory infections. Adequate amounts of iron also provide for a distinctly better rate of growth. Jukes (33) found that, for the chick at least, the anemic state was one of the major conditions associated with the mortality of embryos. An adequate iron reserve undoubtedly permits the individual to withstand more successfully the onsets on health and the various periodic and increased hazards of life. At some time during the nursing period, members of the lower group will succumb either to respiratory infections induced in large degree by the increasing anemia or to some more obscure condition still dependent upon the developing anemia for its existence. To how low a level the hemoglobin may drop and still permit continued existence depends upon the success attending other

compensatory mechanisms. In this connection the writer would like to mention a type of experience he has had in working with young rats born of mothers on anemia producing diets. As the number of red cells and the amount of hemoglobin declined to very low levels the number of unexpected fatalities increased. Upon going into the laboratory in the morning, especially after a cold night, entire litters of animals would be found dead. They would be found lying in natural positions. Careful autopsies revealed nothing that could be assigned as the cause of death. Parsons and Hickmans (22) recite similar experiences. Barbour (34) states that life is not possible when the body temperature drops below 26° C. It is conceivable that when one or more of those substances within the body concerned with the oxidative mechanism reach a certain low level heat production cannot balance heat loss. Iron is an important one of these materials. The individual may be said to literally freeze to death. The actual temperature at which death occurs will depend upon the degree of anemia - the worse the anemia the higher the lethal temperature.

The maintenance of life and the perpetuation of the species has made necessary the production of a most flexible compensatory mechanism. This is especially true of the oxidative mechanism (heat and energy production). Mackay has shown that when iron therapy is instituted during the second post-natal month, the infant's blood

responds by showing a higher hemoglobin level. It rises until it attains 86 per cent or what she terms the "normal" level. Contrast this level, said to be normal for the infant at this age, with that of the expectant mother who is said to be anemic if her hemoglobin drops below 80 per cent (35) or, according to Moore (36), 79 per cent or 70 per cent according to First and Goldstein (37). Evidently what is normal for one is abnormal for the other. What is undoubtedly meant by "normal" level is that amount which represents a physiologic balance between the oxygen demands of the tissues and the ability of the blood to obtain sufficient oxygen from the environment and transport it to the tissue cells. Improvement in the blood condition following any anti-anemic therapy will progress only to that point where a physiological balancing occurs. Continuation of the therapy beyond this point serves only to build up certain reserves and to replace the losses which are constantly taking place as a result of various metabolic activities. Improvement in the anemic condition need not have for its index a rise in the number of red cells or in the amount of hemoglobin although this is frequently the case. It might just as well be the restoration to normal of reserves of iron and other necessary materials; of an increase in muscle hemoglobin or of an improvement in the type of circulating red cell. Which type of improvement occurs will depend upon the primary defect. As far as the number of red cells and the quantity of hemoglobin are concerned, the levels at any one time represents a compromise between the desirability of having enough oxygen and the disadvantage of

having blood too viscous. However, in a chronic oxygen deficiency the adaptation ultimately employed is associated with a concentration of hemoglobin in the blood with maintenance of the usual circulatory rate, blood reaction and gaseous exchange in the lungs. This assumes, of course, that the heart is capable of exerting enough power to maintain a circulation. In case of a defective heart, the body would rather suffer from anoxemia than cease to live at all (38).

As intimated above the body has several ways of adapting itself to an oxygen shortage. (a) The hemoglobin may be filled with oxygen at a higher pressure than obtains in the alveolar air. This is due to actual secretory powers on the part of the pulmonary epithelium or the endothelial cells of the pulmonary capillaries (38). (b) The blood may make a more rapid circuit. Richards and Strauss (39) have shown that the cardiac output of anemic patients with a hemoglobin of 20 per cent was 14 liters per minute; with a hemoglobin of 26 per cent the cardiac output was 10.5 liters per minute and with a hemoglobin of 30 per cent it was 8 liters per minute. Above 40 per cent the cardiac output drops very rapidly from 5 to 6 liters per minute to normal values lying between 4 and 5 liters. As long as the hemoglobin remained above 50 per cent the cardiac output remained within normal limits. (c) In anemia the normal oxygen capacity of the blood (18.5 to 20 volumes per cent) may drop to as low as 5.4 volumes per cent. This creates a lower oxygen tension in the tissues. Under such circumstances the oxygen may be made more available to the tissues by changing the reaction of the blood - increasing the tissue pH; in-

creasing the concentration of hemoglobin in the blood by splenic contraction or by making more red blood corpuscles. This latter response will be conditioned by the availability of necessary building material. (d) An increase in percentage of utilization of oxygen by the tissues which is especially noticeable at oxygen capacities between 10 and 6 volumes per cent. Muscle hemoglobin may play an important role in this adjustment (38, 39, 40). (e) The production of a different type of hemoglobin possessing a greater affinity for oxygen at lower tensions (41, 42, 43). The oxygen content of the blood reaches its lowest limit of availability when the hemoglobin is less than 80 per cent saturated (48 mm. pressure).

One of the above adaptations is well explified by the demonstration that muscle hemoglobin can be made to increase by increasing the activity of the experimental animal (44). Blood hemoglobin also increases in an effort to compensate for decreased oxygen tensions in the atmosphere. Boycott (38) states, "We have round about five million red cells per cmm. of blood and an amount of hemoglobin in each 100 c.c. which will combine with 18.5 c.c. of oxygen, giving the whole erythron an oxygen-carrying power of about 600 c.c. because we happen to breathe air at about 760 mm. pressure containing 21 per cent oxygen. 100 per cent on the scale of the Haldane hemoglobinometer ceases to be the "normal" value directly we vary the conditions and alter the pressure of oxygen in our atmosphere: people living at 5,764 feet in Johannesburg have a "normal" nearer 110 per cent; the natives spending their whole lives

at 14,000 feet in the Andes an average normal of 145 per cent. The blood of these people actually carries at least as much and sometimes more oxygen than that of ordinary persons at sea-level, so that in this respect compensation is exact and complete.***** Normal people use about 30 per cent of the oxygen in the arterial blood, and severe anemias 80 per cent, while in a case of splenomegalic polycythemia, with 170 per cent. of hemoglobin, only 17 per cent. had disappeared by the time the blood got back into the large veins".

Another interesting fact concerning the remarkable adaptability of the blood in supplying oxygen to the tissues according to the demands being made and the nature of the supply is to be found in the data relative to the red cell counts and hemoglobin values of the blood of infants immediately before and after birth. Lichtenstein (44) states that "the hemoglobin values of premature babies during the first two weeks are practically the same as those found among full-term new-born children". Mackay (29) found the average percentage figure for hemoglobin level at birth of healthy infants to be approximately 146 and that this decreased to about 74 per cent by the middle of the second month with a subsequent rise to 86 per cent. Presumably the high figure at birth represents close to the maximum attained before birth. According to the work of Goldbloom and Gottlieb (45, 46) and of Eastman (47) the jaundice of the new-born is a physiological condition which is the result of a change from an environment requiring the presence of polycythemia for the maintenance of oxygenation to one in which no such extraordinary measures

are necessary. The lowering of the hemoglobin from 146 to 74 and 86 represents an adaptation to a new environment.

The extraordinary if not desperate efforts of the organism to provide a blood stream adequate in oxygen transport may be seen in the marked variation in hemoglobin in the new-born. Instances have already been cited of hemoglobin values as high as 179 per cent and as low as 55 per cent being considered within normal limits. In the preceding paragraph it was shown that fetal polycythemia is a normal compensatory mechanism. If 146 per cent represents a normal average what can account for values as high as 179? Gottlieb and Kearns (48) have shown that the severity of post-natal icterus is directly proportional to the degree of polycythemia and that both are indirectly proportional to the normality of the placenta. They showed that in the involved placentae numerous villi had become partly or completely hyalinized thus affording evidence of advanced senility in the vascular tree. Such changes appear to lead to an accentuation of the normal compensatory polycythemia. So far as the writer knows, no cause has been assigned to these placental changes. In experimental laboratories it has been known for some time that deprivation of vitamin E will cause certain placental changes and developmental defects to occur which makes it impossible for the fetus to develop to term. Resorption occurs and sterility follows unless this vitamin is restored. Urner (49) has studied the pathological changes occurring in the placentae of animals on a total vitamin E deficiency. Up to the eighth or ninth days no abnormalities were noted. On the tenth day a change of color was noted and by the

twelfth day no normal implantations remained. The changes were characterized by mesodermal deficiencies and failure in the establishment of a normal contact between maternal and fetal blood. In view of these changes and those described by Gottlieb and Kearns it would be highly desirable to know the sequence of events occurring in a partial deficiency of vitamin E. Can the condition described by Urner be tapered down to match that of Gottlieb and Kearns by adding increasing quantities of vitamin E?

The significance of the variations in the upper extreme brings to the fore a possible importance that should also be attached to differences in the lower limit. If an extreme polycythemia represents a compensation for a placental defect then it also means the safe passage of an intra-uterine crisis. The continued existence of the fetus will depend, in such emergencies, upon the available stores of blood building materials and the ability of the hematopoietic tissues to use them. In case of too early exhaustion of the available reserves the fetus will be doomed or only allowed to continue its existence on the chance of a less severe emergency developing. In any event, the lower limit represents a more desperate situation than that represented by the higher values. The essential blood building materials may have been provided in such limited quantities that the requirements of the hematopoietic tissues were barely met in providing a medium for oxygen transport sufficient to meet the minimal requirements of the fetus. The development of any emergency demanding a better oxygen transport immediately condemns that fetus to death. It thus appears that neither extreme

should be considered normal except in the sense that it represents an adaptation without which the fetus would have perished.

The large amount of circulating hemoglobin in the infant's blood before birth and for some two months after birth, representing a fairly easily or desperately attained compensation, does not necessarily indicate a loss of these materials to the body. Rumage, Sheldon and Sheldon (50) determined the iron content of the livers of 111 children coming to autopsy. These children ranged in age from 1 week to 10 years. They also determined the iron content of the livers of 14 fetuses varying in age from that equivalent to 5 cms. in length to 30 weeks. When the milligrams of iron per 100 grams of liver (dry weight) are plotted against age it will be seen that the fetal store of iron is brought about, as the authors state, by an increase in the <u>percentage</u> (saturation) during the first six months, and by the growth in size of the liver (total iron) during the last three months. The percentage remains almost stationary during this latter period. The rise in liver iron (saturation) during the first two months after birth is undoubtedly due to the storage of iron set free by post-natal blood destruction while the steady dro during the remainder of the first year is caused by the demands made on the iron reserve for the formation of hemoglobin and the growth of the body. The authors remark that these figures must be viewed with suspicion since the material was derived from diseased and not from healthy bodies. While this may have some bearing on actual values it will probably not influence to any considerable extent the trends shown.

Nevertheless it remains highly desirable that data regarding the mineral content of tissues from healthy bodies be obtained. Gladstone (51) has reported on the iron content from livers from 100 cases that came to autopsy. In his conclusions he states "Largest amounts of iron are found in the liver from one to ten weeks after birth, and these are believed to depend upon post-natal intra-vascular destruction of blood". Sheldon and Ramage (52) in a spectrographic examination of the meconium from 24 newborn infants, showed that iron was present in such small quantities that it was barely discernable. The highest quantity determined was only 180 mgms. per cent while most of the cases with identifiable amounts contained but 20 mgs. per cent. Liver itself contained on an average 250 mgs. per cent. The fetal gall bladder and the fetal bile contain iron in considerable amounts. This indicates that a large proportion, if not all of the iron excreted by the fetus occurs by way of the bile. This finds its way into the intestine where it contributes materially to the formation of meconium. The fact that meconium in most cases is extremely low in iron is indicative that this element is reabsorbed and carried back to the tissues for further use. The fetal liver and tissues in general are thus seen to possess an unusual avidity for iron. However, due to the extreme variations in liver iron and to the fact that the mother's diet is often deficient in this mineral, it seems just as reasonable to believe that this represents an attempt on the part of the fetus to conserve its iron. It is

also true that both factors may be at work.

It is permissible to think of the human body as being composed functionally of a group of balanced reactions. There is no doubt but that from the mechanical standpoint at least the various functional units of the body must bear a definite and constant ratio to each other in order to perform the most efficient service. It is also true that the functional units of the human mechanism show a much greater elasticity in adapting themselves to inequalities of other parts than holds for any inanimate device. Nevertheless points are frequently reached where the incapacity of one unit so effects the working of the mechanism as a whole that even with a maximum of compensatory effort there occurs a break in functional capacity and the organism soon whips itself to death. The oxidative processes within the body upon which the heat and energy requirements depend demand that a definite balance be maintained between heat lost and work performed on the one hand and food and oxygen intake on the other. Hence it is not unlikely that the quantity of food required by the individual - when heat production and activity is reduced to a minimum - should bear a definite ratio to the surface area of the body--that is, the most constant factor with which heat loss can be correlated. Furthermore, it is probable that there exists a constant ratio between the cross-sectional area of the aorta and body surface; between the alveolar surface of the lungs, the absorptive surface of the small intestine, the number of glomeruli in the kidney, the number of red cells and the quantity of hemoglobin and the body surface. When a condition

of constant heat loss and energy expenditure has been attained it is reasonable to assume that the amount of latent heat and energy (food) and oxygen being consumed also has approached constancy. With such considerations as these in mind, it at once becomes apparent that the establishment of "basal" or "standard" conditions is essential for the determination of various physiological constants. Furthermore variations in the oxygen tension of the atmosphere or in the mechanism for its transport to the tissues or in the nature and quantity of food supplied the body will provoke an adjustment within the body whereby either the transporting mechanism becomes more efficient or the metabolic processes are reduced or both occur.

The tendency of the normal organism is to maintain these various physiological processes at a constant level. Since, however, variations in environment occur it is necessary, in order for the organism to withstand successfully these changes, for adjustments to be made. Furthermore, abnormal conditions within the organism itself may make an adjustment necessary. If the desirable end result is physiological constancy, then a diminution of one factor demands a compensatory increase in another. Superimposed upon these are the changes in level of activity and heat production brought about by environmental variations. It will be seen that the arbitrary establishment of "normal" values will either demand frequent re-adjustment to variations in "standard" conditions or limitation of their applicability to those individuals who are capable of meeting the "standard" or "basal" conditions. In either

instance the so-called "normal" value as it is usually employed loses much of its significance.

Thus in the red cell counts and hemoglobin levels of the blood of new-born infants, a question arises as to the significance of values ranging all the way from 55 to 179 per cent. Justification has already been given for fetal polycythemia. It is the normal reaction to lower oxygen tensions when sufficient blood building material is available. An accentuation of anoxemia (or anoxia) due to placental pathology is cause for still further production of hemoglobin providing there is sufficient building material. There is reason, therefore, for believing that unusually high values should not be considered normal in sensu strictu but rather as a successful salvaging, due to a plentiful supply of blood structural elements, of a life that otherwise would have been lost. Moreover the values at the lower limit, in view of what has already been said, probably represent equally as strenuous an attempt at compensation. The critical factor in this instance being a low reserve of iron and perhaps of other essential materials for hemoglobin synthesis. As has been noted previously the post-natal decline in hemoglobin proceeds at a faster rate and to a lower level in these cases than in those having higher values. Both the low initial reserve of building material and the diluting effect of growth serve to reduce the hemoglobin.

The observation has been made many times by competent observers that no matter how anemic the mother, the infant is born with a quantity of red cells and hemoglobin within normal

limits (53, 54, 51). Strauss says that "the fetus is able to draw upon the mother for all the blood-forming materials necessary for its own immediate requirements, irrespective of the condition of the maternal blood". It would seem, therefore, that the lowest levels recorded within what is considered normal limits represents an irreducible minimum below which the continuance of life is not possible. If the infant is to be born alive and live, it is reasonable to assume that, in the face of a low reserve of blood building materials, the organism is presenting a bold front to the situation by utilising every resource available for adequate oxygen transport. The fact that infants can be born alive with hemoglobin values ranging from 55 to 116 per cent and arrive at the end of the lactation period with values of 46 per cent must mean, if it means anything at all, that this level of hemoglobin and the attendant reserve of building material is close to the lowest possible level. Lower levels presumably will dispose either to pre-natal or post-natal death as has already been discussed. The recognition of this condition explains the unusual rarity of extreme anemia in the new-born. Bonar (55) states that severe anemia in the new-born is remarkably uncommon. Happ (56) cites 3 instances of extreme anemia in very young babies. It is probably true that nature has established a dead-line in the matter of hemoglobin level. If the supplies of those materials essential for hemoglobin synthesis are not sufficient to meet the demands of the fetus it dies in utero. If they are adequate to the

point where the irreducible minimum can barely be met then the baby will be born alive only to die at some time during the first year - that period when there is a steady decline in hemoglobin. Hemoglobin levels above this minimum and reserves sufficient to meet the demands of growth and increased activity decree continued life. It is erroneous to consider low initial hemoglobin values "normal" in the sense that they also indicate "normal" iron reserves. No direct information upon this point is available. If the contention of this thesis is upheld, such values should be considered as indicative of an exhaustion of iron reserves and present the possibility that many of these infants could be saved by proper pre-natal and post-natal care. Owing to the lack of sufficient data, the treatment, of necessity, must be more prophylactic than curative.

Whatever the compensatory mechanism may be in toto it is obvious that there must be adequate sources of iron and other building materials for the synthesis of sufficient hemoglobin to meet the various exigencies of intra-uterine life. Crises in the life of the mother during the period of gestation such as pneumonia, influenza and pulmonary tuberculosis which tend to reduce the area of gaseous inter-change in the lungs, may tend to make a poor condition in respect to the fetus very much worse. Without entering into a detailed discussion of the various factors which enter into the production and maintenance of fetal apnea, it does not seem unlikely that crises may arise in the mother's organism due to disease processes or in

the fetus due to deficient reserves whereby inadequate gaseous exchange results. This may lead, in turn, to the initiation of respiration with the result that the fetus will aspirate amniotic fluid and die of strangulation. To what extent such considerations enter into the determination of the duration of the period elapsing before the initiation of the first breath is quite difficult to say. It is interesting to note in this connection the high frequency of bronchial pneumonia as a cause of death in the new born. Gladstone (51) noted aspirated amniotic fluid in 16 per cent of his series of premature and very young infants and pneumonia in 50 per cent of the infants under one year of age coming to autopsy.

The mechanism of compensation involving higher levels of hemoglobin maintenance also offers interesting possibilities. To what extent will the organism go in furnishing hemoglobin providing there exists a demand for better oxygen transport and the necessary materials are available? Mackay states that the treatment of the mother with iron 6 weeks before delivery had no effect on the hemoglobin level of the offspring. It is doubtful whether or not the hemoglobin level can be taken as an index of iron reserves. If it is true that the hemoglobin level is no more than that necessary for adequate oxygen transport, it is difficult to understand why extra iron supplies should find their way into the circulating hemoglobin rather than assist in building reserves. As McCay (57) states in discussing recovery from anemia, it "may often be merely apparent because the blood picture may indicate a recovery while the reserves remain

exhausted". In an anemic state the first available iron will go to replenish the circulating hemoglobin--further supplies to the creation of a reserve. Mackay succeeded in showing, however, that the institution of iron therapy in infants 2 to 3 months old was effective in raising the hemoglobin to a level of 86 per cent (58). This represented the best result obtainable. The reason, as has already been pointed out, is that such a level represents a physiological balance at this time of life. Individual differences of response to iron therapy would, after the hemoglobin had reached a stationary level, be more susceptible of demonstration by liver iron estimations, if this were possible.

It would seem apparent from the preceding discussion that, having given a constant physiological state, the amount of hemoglobin in the blood can not be increased by increasing in the diet those materials from which hemoglobin is made. These dietary improvements effect the infant either directly or indirectly depending upon whether they are made before or after birth. Although the evidence seems to favor the view that blood hemoglobin cannot be increased normally above a certain level by improving the diet, there is reason to believe that in many instances it is highly desirable to raise the amount of iron in the depots to a maximum level. Here again one finds a marked variation. Ramage, Sheldon and Sheldon (60) noted an iron content of infants' livers ranging from 374 to 48 mgs. per cent. From 7 years of age onwards the iron seemed to run at the

fairly uniform level of 88 mgs. per cent. The uniform level of 88 mgs. per cent cannot be considered as representing a maximum value for at least two reasons. In the first place the tissue was provided by diseased individuals and in the second place the diseased condition probably made impossible a dietary rich in iron or a metabolism completely efficient in its utilization. Polson (58) was able to show that the liver iron of a rabbit could be raised from the normal level of 36 mgs. per cent (dry weight) to as high as 7,670 mgs. per cent by administering iron over a period of 44 months. The average iron content of the livers of rabbits that received iron from 37 to 46 months was 5,190 mgs. per cent. These values are higher than those obtained from two human cases of haemochromotosis where the liver iron was found to be 2,950 and 3,420 mgs. per cent. It seems likely from this data, meager though it may be, that the liver is capable of storing more iron than investigations so far have been able to show it to contain. A corollary to this is that the benefits to be derived from larger iron reserves should be assured by more adequate intakes of iron.

The upper limits of iron deposition in the liver seems to be under a control analagous to that exercised in regulating glycogen deposit. Under normal conditions a certain upper limit cannot be exceeded. Surpassing the upper limit by the manipulation of one factor or a combination of them does not constitute

proof that this is a normal mechanism. The change in the body reserves from minimal to optimal by the addition of one egg or of one glass of milk to the diet accounts undoubtedly for the improvements in growth and resistance to disease that have been noted in this type of experiment. Such experiments constitute further evidence of the undesirability of minimal reserves and of the fact that the average dietary is deficient in certain essential elements among which iron should be included.

To what extent a physiological balance can be forcibly upset with impunity is difficult to say. An example in point is the marked polycythemia that may be invoked by the use of cobalt. Orten, Underhill, Mugrage and Lewis (60) have been able to produce the following changes in rats blood by the use of cobalt supplemented with manganese.

	c.c. blood per 100 gms. body weight	c.c. cells per 100 gms. body weight	c.c. plasma per 100 gms. body weight
Normal rats	6.36	2.95	3.45
Cobalt + manganese rats	8.34	6.02	2.33
Per cent increase or decrease	31	104	32

An increase in erythrocytes to 12 million or more; of hemoglobin to 25 grams per cent and of cell volume to as high as 87 per cent represents a tremendous increase in viscosity of the blood. The ability of the heart to handle this additional load bespeaks a most remarkable adaptation of this organ.

So much has been said and written in regard to the development of anemia during pregnancy and the various factors that contribute to it that it will be needless to repeat them here (35, 37, 56, 61, 58, 62, 63, 31). There are several points, however, that need mentioning. In the first place the anemia that frequently develops during pregnancy should not be looked upon as being due to blood dilution. It is a more serious matter than this. Three types of anemia have been described as occurring at this time: the pernicious type, the severe hemolytic type and the so-called physiologic type. It is the latter type that bears the most important relationship to the subject material of this paper although, at times, the other two types may play a role. Since iron as such exists in very small quantities in the serum it is essential that the chorionic epithelium, by hemolytic processes, break down the maternal red cells in order to free the blood elements for purposes of transport across the placental barrier. It is therefore obvious that if the maternal depots are well stocked with materials necessary for blood regeneration, an anemia will not develop. A true reduction of total hemoglobin in the maternal body is found only in association with a dietary deficiency or altered gastro-intestinal function. The physiologic type of anemia in pregnancy is due either to a lack in the diet of specific substances necessary for blood formation or to an abnormality of the gastro-intestinal tract preventing the proper utilization of such

such specific substances or to a combination of these two factors in the presence of an increased demand to supply the fetal blood requirements. Examination of such mothers fails to reveal any abnormalities other than those attributable to hypochromic anemia and gastric secretory defects.

Over 50 per cent of the physiologic anemias of pregnancy show a decrease in HCl. Pregnancy definitely effects gastric function by reducing the amount of acid produced which in turn predisposes to poor iron absorption and an impaired production of the anti-anemic principle. That iron absorption is not completely prevented is attested by the fact that large doses are effective in restoring the hemoglobin to normal levels. The significance of this lies in the need of a better realization of the necessity of a greater iron intake at such times. There is frequently associated with a reduced HCl production a curtailment in the secretion of the intrinsic factor. Both these conditions usually revert to normalcy upon the termination of pregnancy.

No information is as yet available to explain why pregnancy causes a reduction in the formation of HCl and possibly of intrinsic factor. That these complications exist makes it clear that not only should the iron intake be increased but also that good sources of vitamin G and anti-anemic principle be made available. Undoubtedly many other factors may also, at times, be essential such as copper, vitamin C, vitamin B, certain essential amino acids,

thryoxin, et cetera. These are, however, more or less irrelevant to the subject of this paper and will therefore receive no further mention.

Although all the elements essential for maternal maintenance and fetal development be present in the expectant mother's diet and care be taken to offset the deficiencies of gastric digestion, the fetus will still be dependant for its requirements upon placental transmissibility. In the rat and the human the maternal and fetal bloods come into most intimate contact since they possess the same type of placenta--haemochorial. The cow and the goat have the syndesmochorial type and the pig the epitheliochorial. With some substances the placenta acts as a barrier shutting off transport completely; with others it is only partially effective and with others yet it acts as a pump to actually build up levels in the fetal tissues that are higher than those existing in the mother's.

	Material	Fetal Blood	Mother's Blood	Reference
Group 1	(Insulin	barred	present	64, 65
	(Parathyroid extract	barred	present	66, 65
	(Adrenalin	barred	present	65
	(Pituitrin	barred	present	65
	(Fats	barred	present	67
Group 2	(Vitamin A	low	high	68
	(Vitamin B	low	high	69,70,71,72
	(Vitamin D	low	high	73
	(Chlorine	low	high	74,75
	(Total Protein	low	high	76,74
	(Fibrin	low	high	76
Group 3	(Urea	Present (diffusible)	present	77
	(Creatine	present diffusible	present	77
	(Creatinine	present diffusible	present	77
	(Magnesium	present diffusible	present	77
	(Uric acid	present diffusible	present	77
	(Antibodies	present diffusible	present	67

	Material	Fetal Blood	Mother's Blood	Reference
Group 4	(Sugar	high	low	67,75
	(Iron	high	low	78
	(Amino Acids	high	low	76,67,77,75
	(Albumin	high	low	76
	(Calcium	high	low	76,74,79,80,77,75,65
	(Inorganic Phosphorus	high	low	76,79,77,75
	(Potassium	high	low	74
	(Copper	high	low	78

It will be seen from the above tabulation that the substances listed in Group 1 are completely barred from entry into the fetal circulation. If the fat soluble vitamins are dependent upon fat as a vehicle for their transport to the fetus, it can readily be understood why the presence of these substances in fetal tissues is quite low. On the other hand a lower threshold value for these materials by the mammary gland will permit of a compensatory enrichment of the colostrum and milk thus adding to the importance of these foods in early life. The placental barrier does not completely prevent the passage of the substances listed in Group 2 while those materials forming Group 3 are found in nearly equal concentrations on both sides of the barrier. The greatest interest attaches to those elements found in Group 4 for they occur in fetal blood or tissues in higher concentrations than those found in the maternal organism. Does the placenta exert a secretory activity sufficient to build up this differential? The fact that it has been shown that the placenta has an oxygen consumption about the same as organs such as the colon (81) would seem to indicate as much. The site of this activity appears to be the chorionic epithelium (80,77).

Two theories have been proposed to explain how the various nutrient substances pass through the placental barrier (67). One is the Vitalistic Theory which claims that the wall of the chorionic villus takes an active part in placental interchange. The other is the Mechanistic Theory in which the wall of the villus is pictured as a passive, semi-permeable membrane conforming to the laws of osmosis anddiffusion. It will be seen that the controversy in this respect is no different from that concerning intestinal absorption, urine formation or the activity of the alveolar epithelium in external respiration (82). The probability is that when sufficient evidence is at hand, the phenomena referred to above will be satisfactorily explained on a purely physico-chemical basis. The result will be that the Vitalistic theory will give way to the Mechanistic.

As may be gathered from the preceding pages, very much has been accomplished relative to those conditions effecting blood formation in the mother herself and in her baby after it has been born. On the contrary, however, there is a marked paucity of data relative to the development of blood in the fetus and the rate at which it acquires those substances necessary for blood generation. So far as the writer knows Nicholas and Urner are the only investigators who have made observations on the red cells and hemoglobin of fetuses. Nicholas (83) determined the rate at which hemoglobin makes its appearance in fetal blood. He determined the age of the fetus from the crown-rump length. Since the size of the fetus

varies with the size of the litter (84) and the nutritional regimen of the mother, this method would seem to be open to criticism. He found hemoglobin to be present before the 14th day but was unable to get blood easily until the 16th day. His determinations were made by Newcomer's method and the percentage hemoglobin was based on Williamson's normal value for the human of 16.92 gms. per 100 c.c. blood being equal to 100 per cent. The following table gives his results:

Fetal age in days	Number of fetuses	Hemoglobin per cent
12-13	11	30
14	14	32
15	16	37
16	7	55
17	22	56
18	10	45
20	6	44
21	20	54
Newborn	7	65

These figures show two maxima: one at 17 days and the other at birth. Urner (49) observed the presence of red cells as early as the 10th day. He made no counts.

Boecker (85) determined the amount of iron in the livers and spleens of premature infants and found that the two tissues ran parallel. He noted a decrease in iron from the 6th month up to birth which was followed by a rise. Inoue (86) also determined the iron content of fetal livers and spleens. He observed the presence of iron as early as the second gravid month. From this time on the iron increased up to the fourth month. From the fourth to the sixth month a decrease occurred which in turn was followed by a rise which reached a maximum by the ninth month. Similar results were obtained

for the spleen. Ramage, Sheldon and Sheldon (50) found that the livers of 8 infants 30 weeks of age or under averaged 210 mgs. per cent of iron while 6 full-term infants averaged 250 mgs. per cent. The total amount of iron in the former group averaged 10.8 mgs. while the latter group possessed an average of 73.3 mgs. It will be noted that from the 30th to the 40th week there was an increase in iron concentration of only 20 per cent while, due to the growth of the liver during this period, there was an increase in total iron of nearly 60 per cent. Gladstone (51) determined the iron content of livers from fetuses ranging in length from 14 to 61 cms. A recalculation of his data on the basis that liver is 80 per cent moisture, gives the following results:

Length of fetus in cms.	Mgs. Iron per cent (dry weight)	Total Iron
10-20	83.0	.83
20-30	130.0	5.62
30-40	147.0	12.50
40-50	186.0	40.98
50-60	151.75	40.28
60---	200.0	114.00

These figures show that the concentration of iron in fetal livers reaches its peak several weeks before birth and then declines. There is evidence of an early post-natal rise due to hemosiderosis caused by blood destruction during this period. The remarkable rise in total iron at the 40-50 cms. period and the accompanying slight increase in iron concentration indicates that iron deposit did not keep pace with liver growth.

The foregoing data on liver iron cannot be taken at full value for the reason that they were derived from pathological tissues. Furthermore, due to variations in rate of liver growth full appraisal of iron metabolism on the basis of iron concentration alone will lead to erroneous conclusions. Whipple (87) has shown that there are variations in liver iron concentration due to senile as well as pathological changes. He has shown also that the total iron varies not only because of changes in liver size due to disease processes but also because of differences in concentration. There are, then, two points to be considered in studies on liver iron metabolism, namely the total amount of iron and its concentration in the liver. The concentration of iron will be determined by the factors engaged in establishing the extremes of liver saturation and the total amount will be governed by this also and, in addition, the size of the liver.

Whipple's data recalculated on the basis of dry weight

Tissue	Mgs. Iron per cent
Normal liver	58 to 61
Secondary anemia	35
Cirrhosis	45
Hepatitis	50
Leukemia	65
Carcinoma of liver	75
Pernicious anemia	125
Aplastic anemia	350

The highest single result was 810 mgs. per cent, - the lowest, 8.5 mgs. per cent. The former level represented a case of pernicious

anemia where unusual storage had occurred in the liver because of a failure in outlet. The latter instance represents a case of hepatitis and functional incapacity which indicates an inability of the liver, when suffering from this type of dysfunction, to store iron. Whipple has shown that normal dogs suffering from a severe anemia due to bleeding will have their liver iron reduced to "an irreducible minimum" of 4 to 5 mgs. per cent (20 to 25 mgs. per cent dry weight).

Iron exists in the liver in at least two forms. One in which it lies within the cell protoplasm and is not subject to iron stains and the other which is subject to staining. Gladstone (51) stained liver sections with an acidified solution of potassium ferrocyanide and, upon microscopic examination, classified them as normal or abnormal by the number of blue granules observed. Normal tissues gave no blue granules or very few. At the same time, chemical assay of the same tissues gave iron values as high as 43.8 mgs. per cent. An examination of Whipple's data (87) will show that there is no obvious correlation between the quantity of stainable pigment and the amount of liver iron. One liver may show as high as 134 mgs. iron per cent (dry weight) with no stainable pigment while another may have stainable pigment with only 120 mgs. per cent iron. It is probable, nevertheless, that the liver possesses an upper limit beyond which it is not possible to store iron in non-stainable compounds as well as a lower limit below which the liver will refuse further iron delivery to the blood stream. Hemochromotosis and hemosiderosis represent conditions, possibly, where iron in excess

has been introduced into the body and held in the liver in a manner different from that representing normal storage. It may be that the quantity of iron introduced is of no greater importance than the rate of its administration. Polson has shown that this does not necessarily interfere with hepatic function. Both types of iron are available for hemoglobin synthesis, the one in part and the other in toto. The acquisition of stainable iron is not peculiar to the liver - it is more a characteristic of the reticulo-endothelial system. In this sense, accumulation of liver iron should be limited to that portion which is not stainable and which is, as Whipple states, due to dietary factors.

There is still much to be learned with respect to blood formation and destruction. Mackay (29), in concluding her discussion of the probable causes of the fall in hemoglobin between the first week of life and the third month, said, "It is evident that further information about the drop in hemoglobin level in the first three months of life is requires". Strauss (31) in summarizing the views relative to hepatic storage of iron states, "when parents are deprived of iron********** there is reason to believe that new-born infants or animals will lack this store of iron, so that when they are placed on a diet deficient in iron, anemia will develop. Until quantitative chemical studies can be made of the livers of suitable infants, this explanation must remain in the realm of hypothesis". It was with the hope that the studies to be reported in this paper would contribute to a better understanding of some of the situations outlined above that this investigation was undertaken.

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A few years ago in studying the effect of various diets and of various supplements to the same diet on the reproductive ability of the albino rat, it was noticed that many of the young developed polyneuritis during the nursing period. This was quite surprising in view of the fact that the mothers' diet contained 2 per cent yeast, an amount known to be sufficient to protect them from signs of vitamin B deficiency. In the work that was done on this subject at that time evidence was adduced to show that the polyneuritis represented a true beri beri and that it could be prevented by increasing the vitamin B of the mothers' diet by from 300 to 400 per cent (69). Subsequently this work was confirmed by other investigators (70, 71). It was noted also that many of these young animals showed a severe anemia. The addition of more yeast to the diet of the mother prevented the development of beri beri and, in allowing the animals to live longer, drew attention more strongly to the blood condition. As already mentioned, upon going into the laboratory in the morning it was a frequent experience to find individuals or entire litters dead. Careful autopsies gave no clue as to the cause of death. The marked pallor of the animals made it appear that death might in some way be related to the anemic condition. In 1925 Hart, Steenbock, Elvehjem and Waddell began the publication of a series of papers (88) in which they reported improvement in anemias of dietary origin by including in the diet an alcoholic extract of cabbage. In a preliminary experiment a

few mature females were placed on Diet #3 and as many more on the same diet plus 1 per cent cabbage extract. As soon as litters were born the young were sacrificed in order to obtain the hemoglobin concentration of the blood. The average hemoblogin of 22 young from mothers receiving Diet #3 alone was 72.2 per cent; for 22 young from mothers receiving the same food but with cabbage extract in addition, the hemoglobin per cent was 88. These results were so significant that a larger series was decided upon. Since cabbage extract may have improved the condition of the animals by making more vitamin E available, it was deemed advisable to have another series of animals on the experimental diet reinforced with wheat germ oil. In all five different diets were to be used. This report is concerned with the first three.

Diet #1 or the Stock diet was made up as follows: cracked yellow corn, 72; linseed oil meal, 11; casein (Harris), 5; ground alfalfa, 4; sodium chloride, .5; calcium carbonate, .5; yeast, 7 and skimmed milk ad lib. The remaining four diets were composed of the constituents outlined in the following tabulation.

Food material	Diet #2	Diet #3	Diet #4	Diet #5
Casein (Harris)	18	18	18	18
Salt mixture*	4	4	4	4
Crisco	2	2	2	2
Cod Liver oil (Mead's)	3	3	3	3
Dextrine (bleached)	70	65	64	63
Sodium bicarbonate	1	0	0	0
Yeast (Harris)	2	8	8	8
Wheat germ oil	0	0	1	0
Alc. Ext. Cabbage	0	0	0	1

* The salt mixture had the following composition:

Sodium chloride	118.8
Magnesium sulphate	123.0
Sodium phosphate (dibasic)	179.0

Potassium phosphate (dibasic)	348.0
Calcium phosphate (dibasic)	349.0
Calcium lactate	77.0
Ferric citrate	29.5
Potassium iodide	.8

Groups of four animals each were kept in average sized galvanized iron cages. The food and water cups were cleaned and filled daily. The cages were cleaned twice a week and supplied with small amounts of excelsior. When the desired number of healthy, freshly weaned females were available they were placed on the above three diets until they were sexually matured. At this time daily vaginal smears were made to determine the estral rhythm. When they were found to be in the proper stage vigorous males were placed with them and the day of insemination noted. The males were then removed but the vaginal examinations continued until the occurrence of the placental leak. The ages of the fetuses were determined in reference to the day of insemination. The placental leak was considered merely as confirmatory of pregnancy. Usually five females were selected for each day of pregnancy beginning with the 14th day after insemination.

When the proper day had arrived for sacrificing an animal it was removed from the cage and placed under light ether anesthesia. The tip of the tail was then clipped and sufficient blood obtained for a red cell count and for a hemoglobin estimation. The abdomen was then opened and the uterus exposed. Fetuses were numbered according to the cornu occupied and the position relative to the cervix. The cornu on the right of the operator was designated as the right cornu. As a matter of fact, in respect to the rat, it was the left

cornu. This should not be overlooked when consulting the tables at the end of the paper otherwise some confusion might arise. If there were three fetuses in the right cornu and four in the left, they would be numbered R1, R2, R3, L1, L2, L3 and L4. If the second one on the right, for example, had died and was being resorbed the word "resorbed" was written in the record thus: R2 resorbed. L1 and R1 would occupy the vaginal ends of the uterine horns and L4 and R3 the ovarian ends. One fetus was removed at a time usually by peeling off the placenta although sometimes the cord was cut. Standard red cell and hemoglobin pipettes were filled with blood obtained from the severed carotids and jugulars. The fetus was then bled to death and the liver removed and placed in alcohol. No effort was made to number the livers therefore the data obtained from them can not be associated with the blood findings of the fetuses from whence they come. When all the fetuses had been removed in this manner, the mother was killed by bleeding to death. Her liver was then removed and placed in alcohol. In order to reduce the time of the anesthetic, a large series of red cell and hemoglobin pipettes were set up. Each red cell pipette, as it was filled with blood, was thoroughly shaken to bring about equal dispersion of the red cells in the diluent and set aside. The hemoglobin pipette was emptied, as soon as filled, into the appropriate tube containing hydrochloric acid. When all the fetuses and the mother had been cared for in this manner the bodies were discarded and the cell counts and hemoglobin estimations performed. The livers were changed to fresh alcohol a few days later then removed, dried in an incubator, carefully weighed and powdered.

For the determination of red cells, the improved, double-ruled Neubauer hemocytometer was used. The hemoglobin was determined by the Sahli method using the permanent standard developed by Haskins and Osgood (89). Usually it was necessary, when working with fetuses 14, 15 and 16 days old, to pool the blood of two or three in order to get enough to fill the pipettes. At such times the fetuses were placed in a small watch glass so that the blood might collect in the center.

For the determination of liver iron, Kennedy's method (90) was followed in all respects except in the preparation of the standard solution. For this the method of Dupray (91) was used. In general the procedure was as follows:

All livers were kept for at least 24 hours in alcohol. They were then removed and rolled thin on a smooth plate in order to break up the tissue. The macerated mass was placed in a Syracuse watch glass and dried in an incubator at 75° C. for 24 hours. The larger livers were removed at the end of this time, ground to a finer consistency and replaced for another 6 hours. At the end of this time all tissue was removed and carefully weighed. After thoroughly powdering it was considered ready for the chemical procedure. As the method followed with adult livers and livers over 100 mgs. in weight differed somewhat from that employed with livers weighing less than this, the methods will be described separately.

Two hundred mgs. of the powdered adult liver substance were carefully weighed out and placed in a distillation flask. To this was added 5 c.c. of iron-free sulphuric acid and 2 c.c. of 60

per cent perchloric acid. A fume sucker was attached to the arm of the flask and the contents boiled with gentle heat until the material was colorless. The contents of the flask were then cooled and poured, with three rinsings of distilled water, into a 50 c.c. graduated cylinder fitted with a ground glass stopper. The material, after diluting to 50 c.c., was set aside to cool.

Two 50 c.c. glass stoppered, graduated cylinders were set out and marked A and B. Into A 10 c.c. of the dilute standard solution were placed and to B were added 10 c.c. of the liver solution prepared as described above. To both A and B were added 10 c.c. of amyl alcohol and 5 c.c. of 20 per cent sulphocyanate. Both cylinders were shaken vigorously for one to two minutes and set aside in order to allow the alcoholic extract to settle out. Both colored portions were removed, placed in colorimeter cups and compared.

If all the dried, powdered fetal livers of one litter weighed more than 100 mgs. and less than 200 mgs. an amount equivalent to 100 mgs. was carefully weighed out and placed in the distillation flask along with 2.5 c.c. of sulphuric acid and 1 c.c. of perchloric acid. One c.c. of the standard iron solution was used for making up the standard for color comparison. If the collective weight of fetal livers was less than 100 mgs. the amount was carefully determined and .1 c.c. of the standard iron solution was taken for every 10 mgs. of liver used. The smaller amounts of liver were digested with 1 c.c. of iron-free sulphuric acid and 0.5 c.c of perchloric acid. The solutions in graduates A and B were made up to about 20 c.c. with distilled water.

The animals on Diets #1, #2 and #3 are referred to as Series I, II and III respectively. Determinations of fetal liver iron were performed in most cases on the pooled livers of all the fetuses of one litter. There is only one exception to this and that relates to the females in the third series. In this group separate iron determinations were performed on the livers of individual fetuses from two mothers for each day. This was done to provide evidence on the point of individual variation. In all instances the values tabulated represent individual averages.

The number of animals used is indicated in the following tables.

DIET # 1. FIRST SERIES.

DAY OF GESTATION	FETAL DEATHS	NO. OF FETUSES	NO. OF MOTHERS
14	3	43	5
15	0	46	5
16	2	43	5
17	0	44	5
18	0	51	6
19	0	45	5
20	1	37	6
21	0	29	5
Total	6	338	42

Percent fetal deaths------ 1.77
Average size of litter --- 8.1

DIET # 2. SECOND SERIES.

DAY OF GESTATION	FETAL DEATHS	NO. OF FETUSES	NO. OF MOTHERS
14	1	38	5
15	4	36	5
16	5	30	5
17	10	25	5
18	2	36	5
19	3	27	5
20	0	39	5
21	1	41	5
Total	26	272	40

Percent fetal deaths - - - - 9.5
Average size of litter - - - 6.8

DIET # 3. THIRD SERIES.

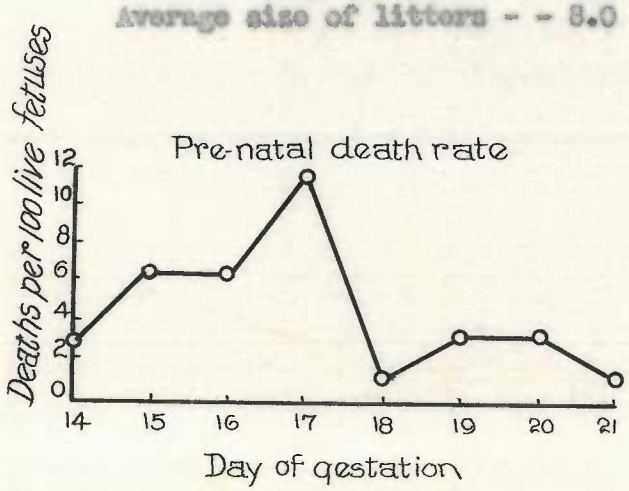
DAY OF GESTATION	FETAL DEATHS	NO. OF FETUSES	NO. OF MOTHERS
14	0	48	5
15	4	43	5
16	1	49	5
17	3	45	5
18	0	39	5
19	0	40	5
20	2	44	5
21	1	40	5
22	0	47	5
Total	11	393	45

Percent fetal deaths - - - 2.8
Average size of litters — 8.7

SUMMARY

DAY OF GESTATION	FETAL DEATHS	NO. OF FETUSES	NO. OF MOTHERS
14	4	129	15
15	8	125	15
16	8	122	15
17	13	112	15
18	2	126	16
19	3	112	15
20	3	120	16
21	2	110	15
22	0	47	5
Total	43	1003	127

Percent fetal deaths - - - 4.2
Average size of litters - - 8.0

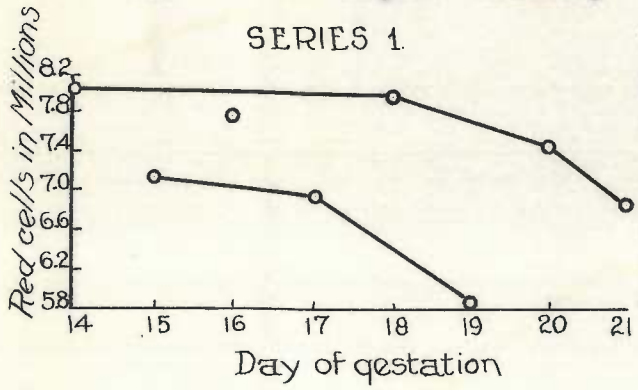


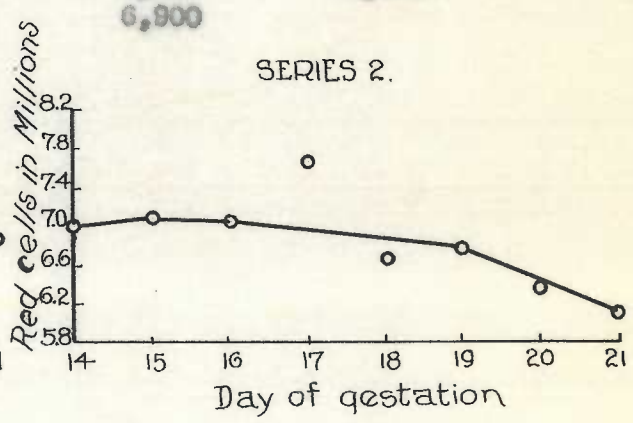
RESULTS

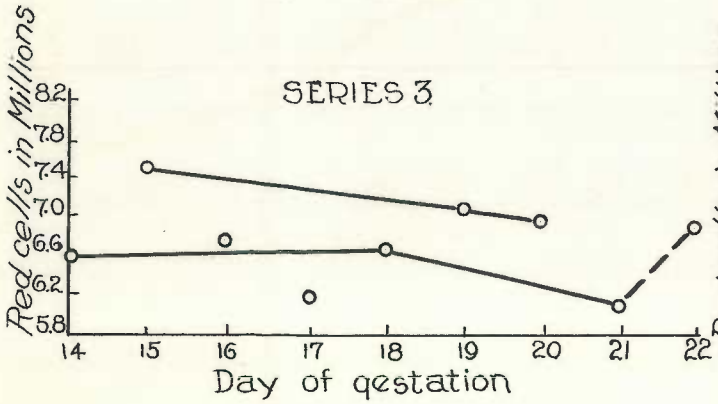
In tabulating the results, the averages for each day have been given. The animals on Diet # 1 (Stock food) have been designated as Series I ; those on Diet # 2 (Basal Diet plus 2 percent yeast) as Series II and those on Diet # 3 (Basal Diet plus 8 percent yeast) as Series III. For detailed data the reader is referred to the tables at the end of the paper.

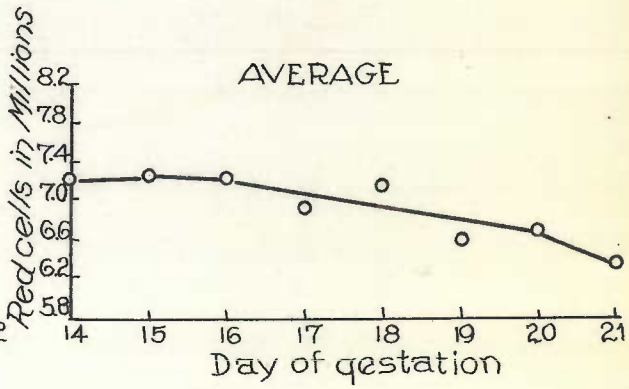
MOTHERS' ERYTHROCYTES

DAY	SERIES I	SERIES II	SERIES III	AVERAGE
14	8,139	7,018	6,600	7,252
15	7,204	7,112	7,500	7,272
16	7,827	7,072	6,800	7,233
17	6,960	7,693	6,200	6,951
18	8,085	6,669	6,700	7,148
19	5,858	6,824	7,100	6,594
20	7,461	6,428	7,000	6,963
21	6,895	6,142	6,100	6,379
22	Day of	delivery	6,900	



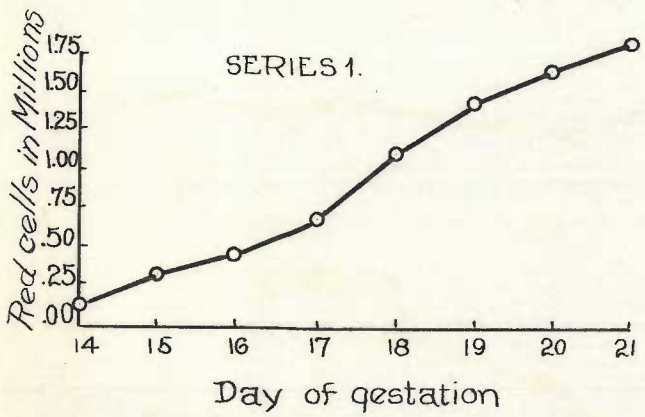


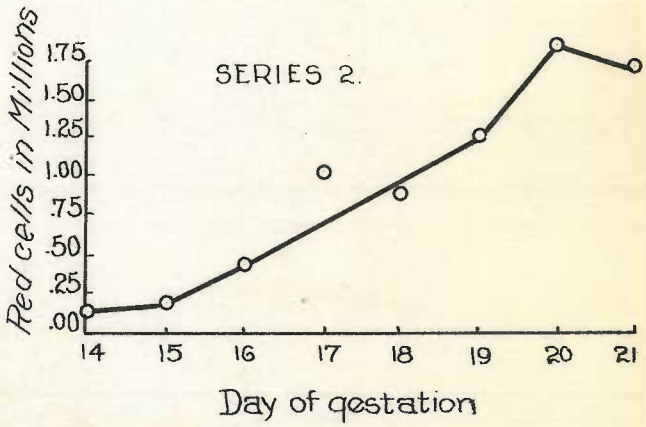


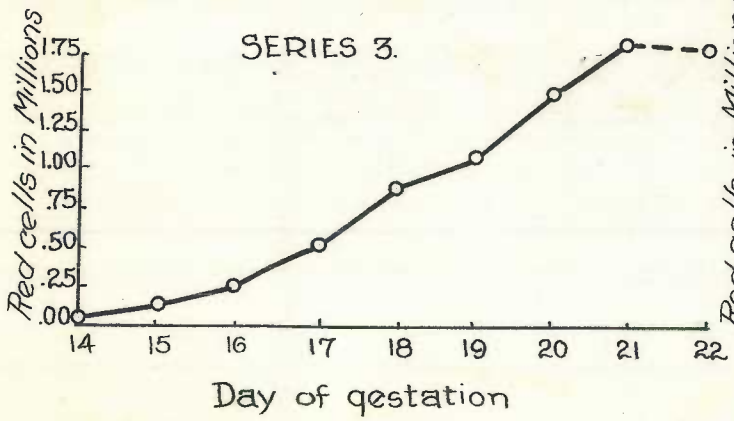


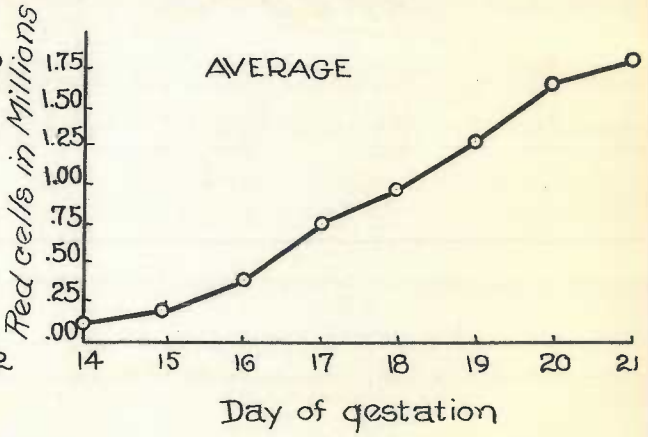
FETUSES' ERYTHROCYTES

DAY	SERIES I	SERIES II	SERIES III	AVERAGE
14	.144	.120	.098	.121
15	.324	.199	.140	.221
16	.476	.464	.274	.405
17	.703	1.027	.557	.762
18	1.131	.922	.930	.994
19	1.443	1.262	1.217	1.307
20	1.654	1.874	1.518	1.682
21	1.819	1.748	1.840	1.802
22	Day of birth		1.809	



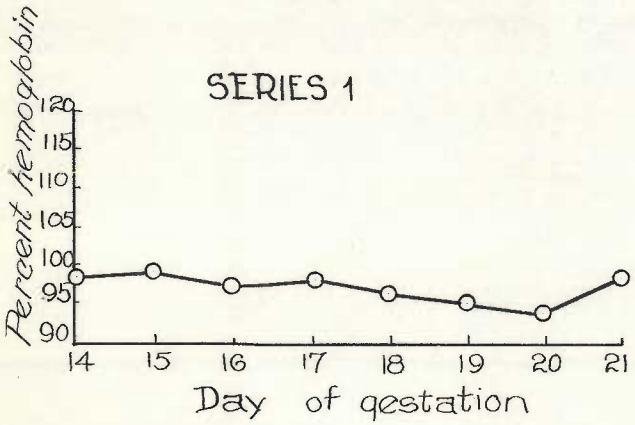


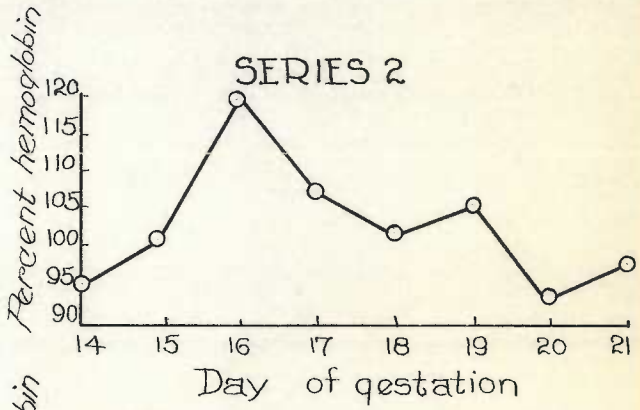


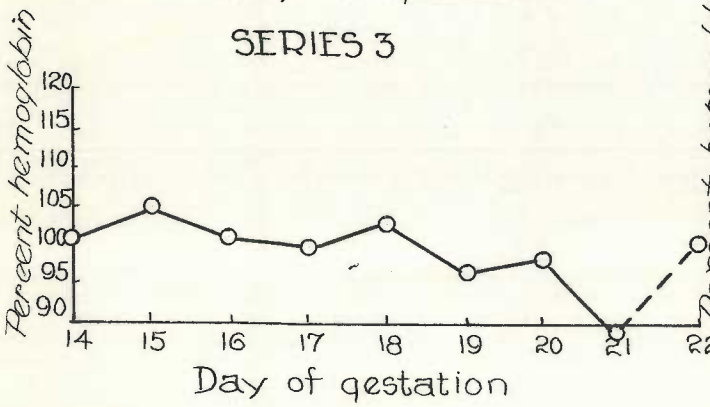


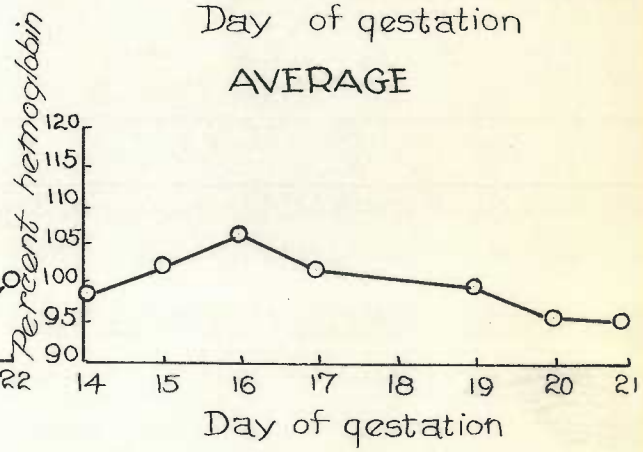
MOTHERS' HEMOGLOBIN

DAY	DIET # 1	DIET # 2	DIET # 3	AVERAGE
14	98.6	95.8	101.0	98.5
15	99.0	101.2	105.0	101.7
16	97.6	119.6	101.0	106.1
17	98.0	107.6	100.0	101.9
18	96.1	102.2	103.0	100.4
19	95.4	105.2	97.2	99.3
20	94.3	93.2	98.8	95.4
21	98.7	98.2	89.0	95.3
22	Day of delivery		101.0	



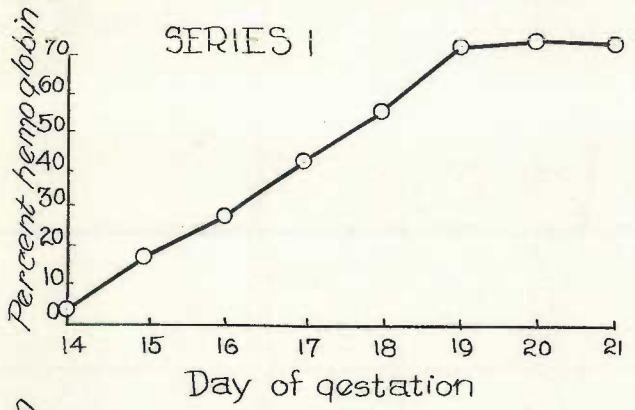


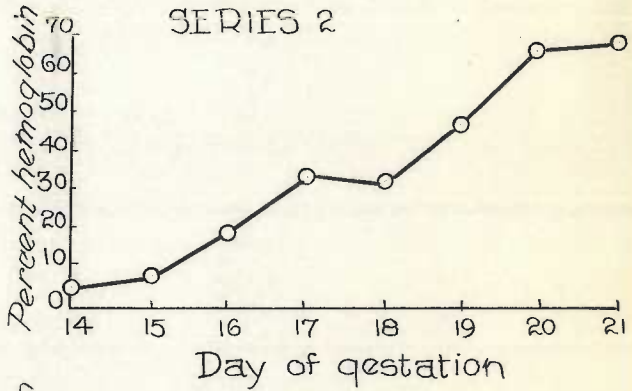


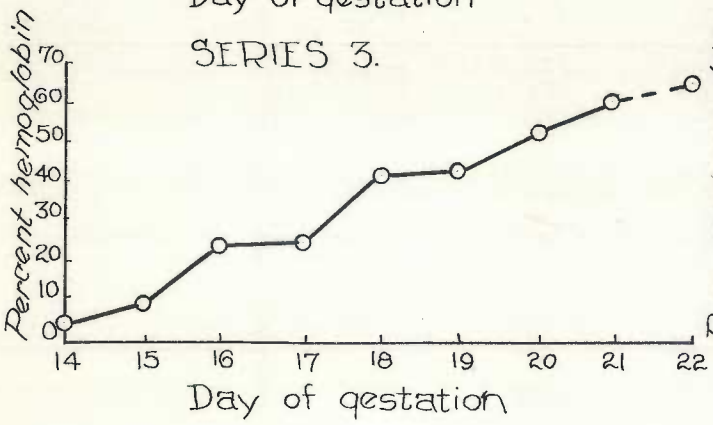


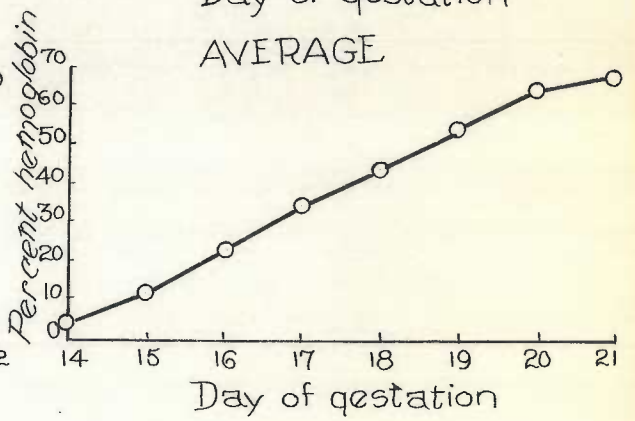
FETUSES' HEMOGLOBIN

DAY	DIET # 1	DIET # 2	DIET # 3	AVERAGE
14	4.3	5.3	4.7	4.8
15	18.0	8.5	9.5	12.0
16	28.8	19.5	25.9	24.7
17	43.0	34.2	26.2	34.5
18	55.5	31.7	41.8	43.0
19	72.4	47.2	44.1	54.6
20	72.6	66.5	53.6	64.2
21	72.4	68.2	60.8	67.1
22	Day of birth		67.2	



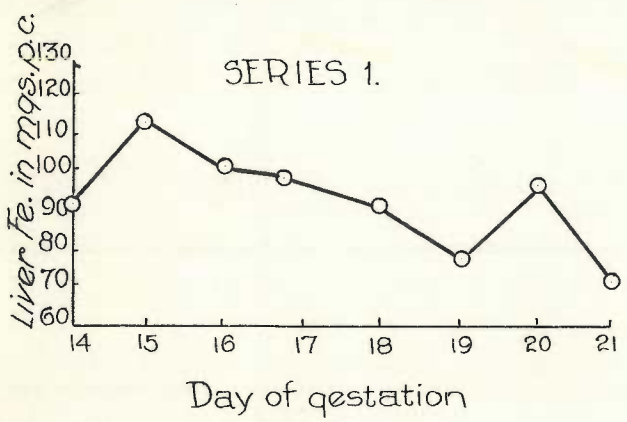


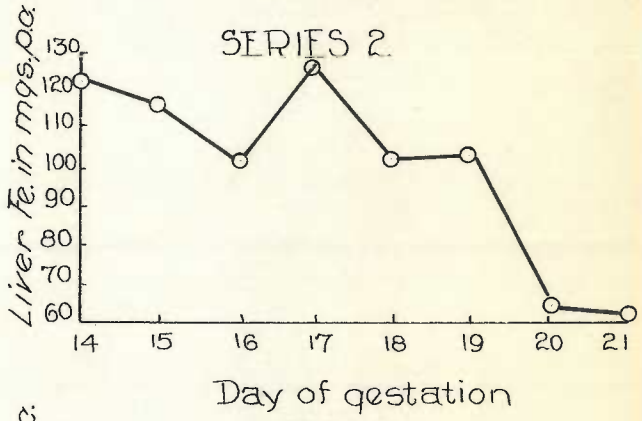


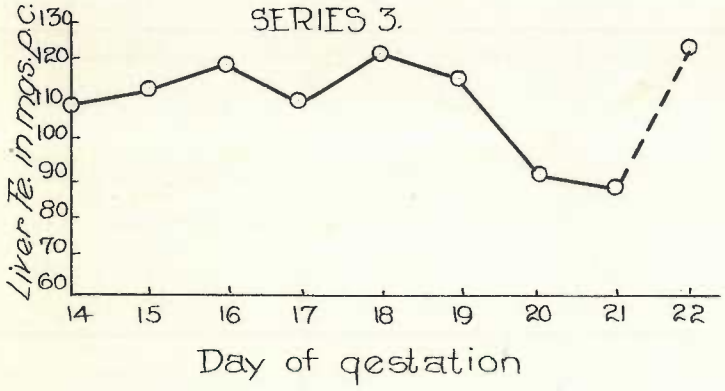


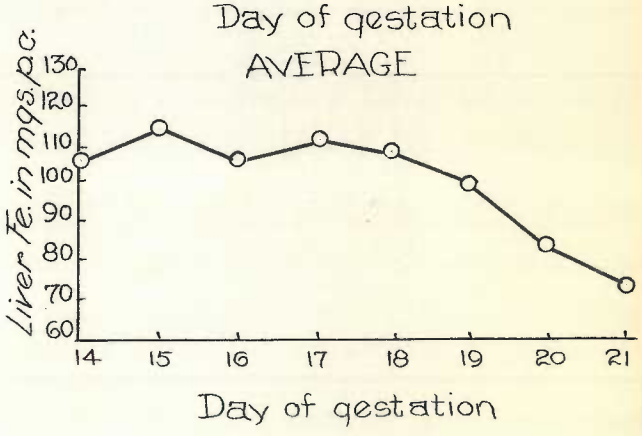
MOTHERS' LIVER IRON IN MGS. PERCENT (Dry weight)

DAY	DIET # 1	DIET # 2	DIET # 3	AVERAGE
14	91.9	123.9	110.0	108.6
15	114.5	117.5	113.0	115.0
16	102.7	103.1	120.0	108.6
17	99.2	128.5	110.0	112.5
18	92.5	104.3	122.6	109.8
19	78.7	104.8	117.3	100.3
20	97.3	64.0	90.8	84.0
21	71.1	63.4	98.0	74.2
22	Day of delivery		124.0	



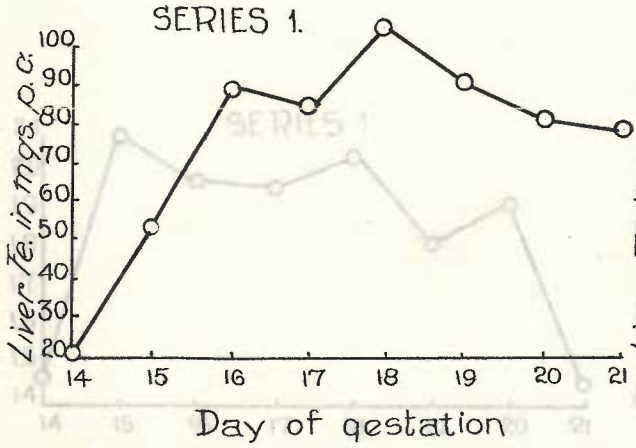


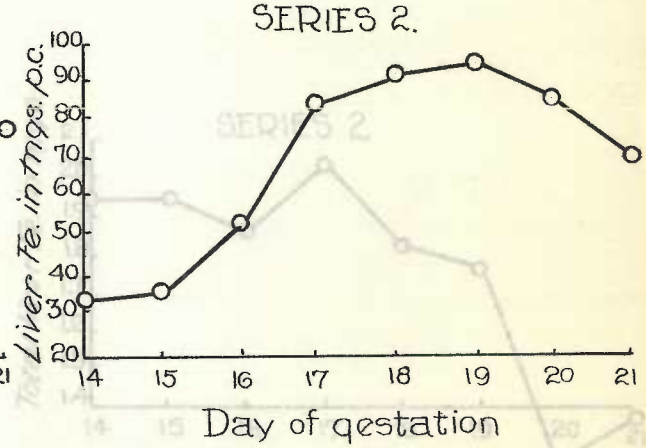


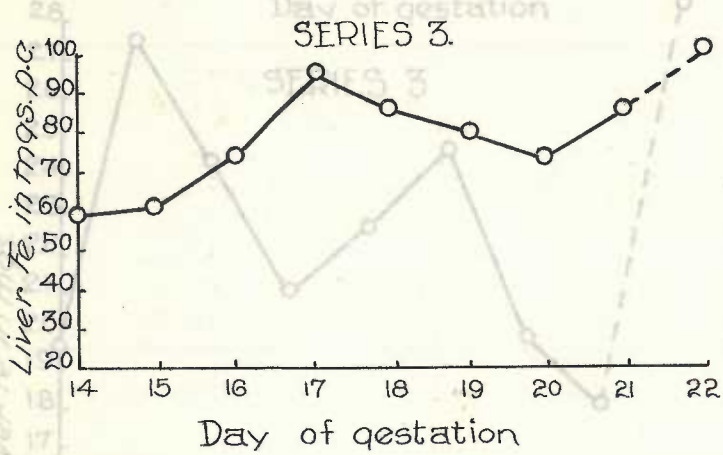


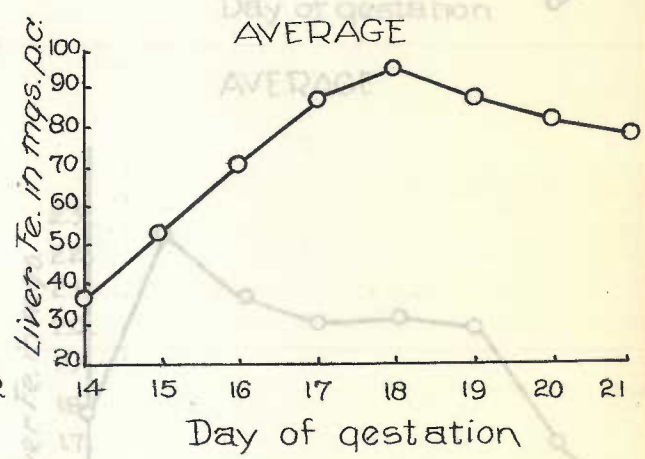
FETUSES' LIVER IRON IN MGS. PERCENT (Dry weight)

DAY	DIET # 1	DIET # 2	DIET # 3	AVERAGE
14	21.3	33.9	60.0	38.4
15	53.1	37.4	62.0	54.2
16	68.7	53.7	74.6	72.3
17	85.3	85.3	97.4	89.3
18	104.5	91.7	88.8	95.0
19	90.8	94.6	81.0	88.8
20	81.5	86.6	76.5	81.5
21	79.4	72.1	88.4	79.9
22	Day of birth		102.2	



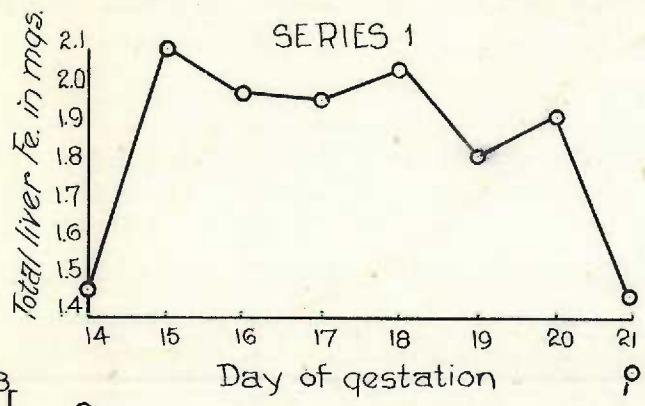


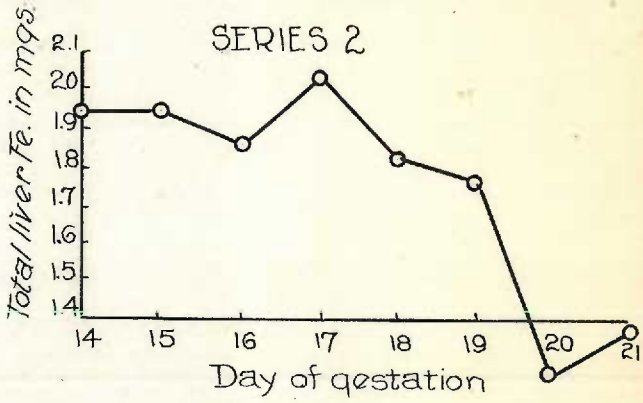


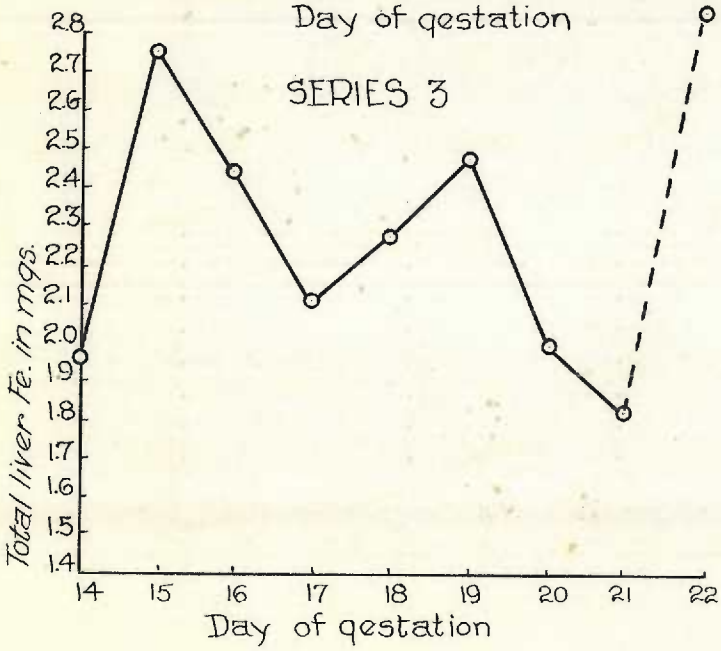


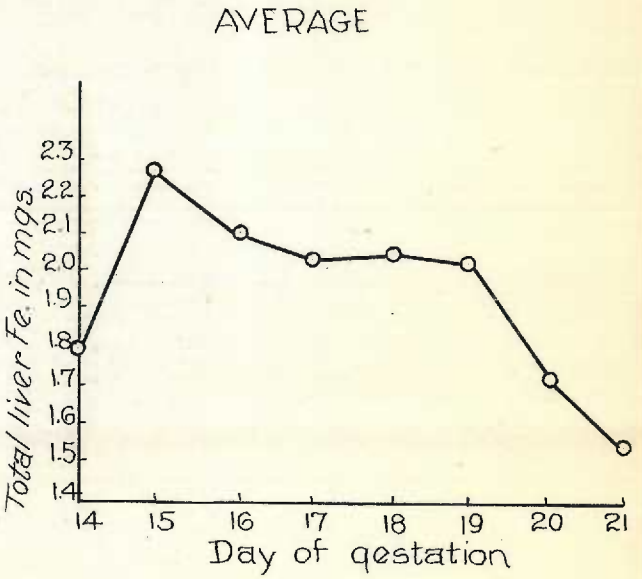
MOTHERS' TOTAL LIVER IRON IN MGS. (Dry weight)

DAY	DIET #1	DIET # 2	DIET # 3	AVERAGE
14	1.478	1.955	1.975	1.803
15	2.101	1.961	2.770	2.274
16	1.990	1.873	2.437	2.100
17	1.985	2.029	2.096	2.037
18	2.058	1.817	2.280	2.052
19	1.816	1.798	2.483	2.027
20	1.922	1.284	1.996	1.734
21	1.448	1.382	1.824	1.551
22	Day of delivery		2.857	



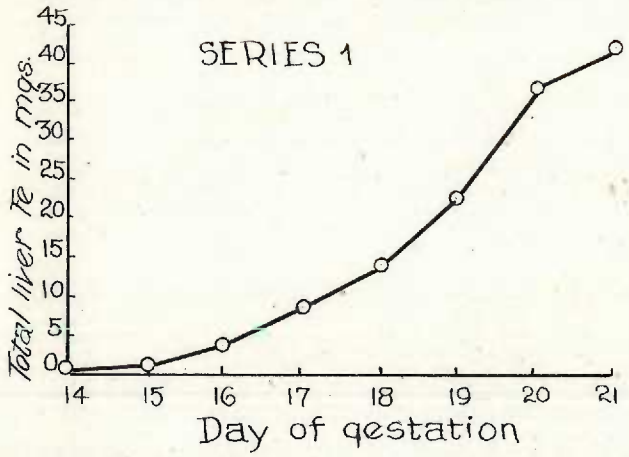


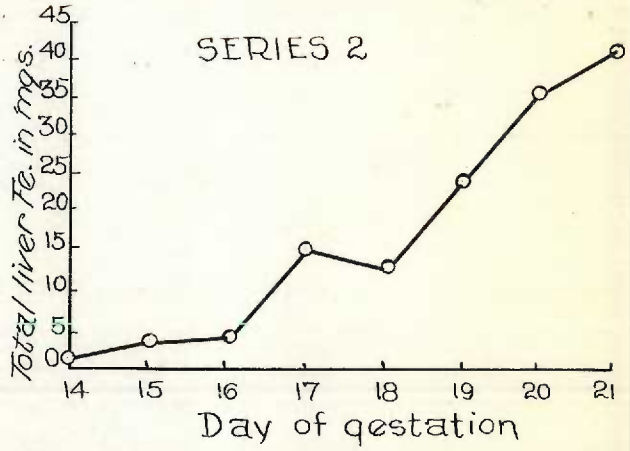


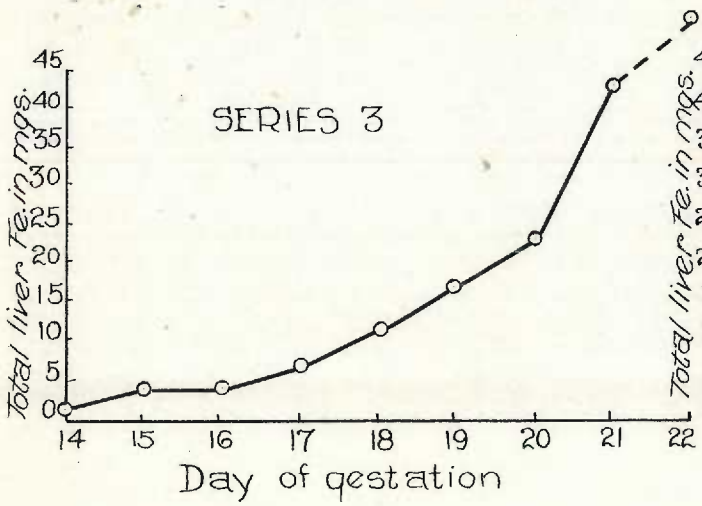


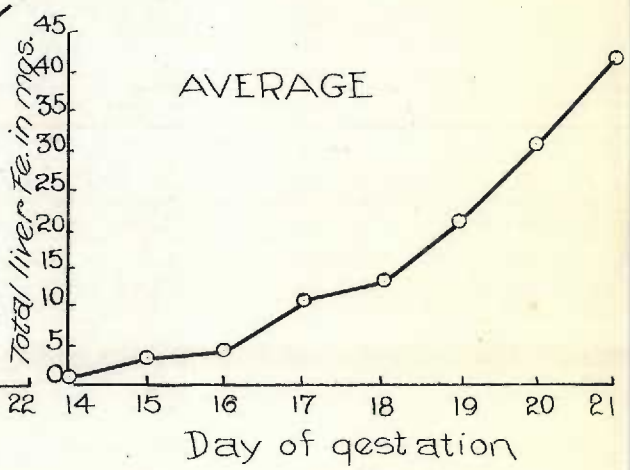
FETUSES' TOTAL LIVER IRON IN MGS. (Dry weight)

DAY	DIET # 1	DIET # 2	DIET # 3	AVERAGE
14	.00100	.00179	.00190	.00156
15	.00151	.00324	.00440	.00298
16	.00427	.00457	.00440	.00436
17	.00881	.01515	.00690	.01029
18	.01447	.01358	.01180	.01328
19	.02258	.02446	.01700	.02135
20	.03760	.03554	.02380	.03228
21	.04200	.04105	.04470	.04286
22	Day of birth		.05160	



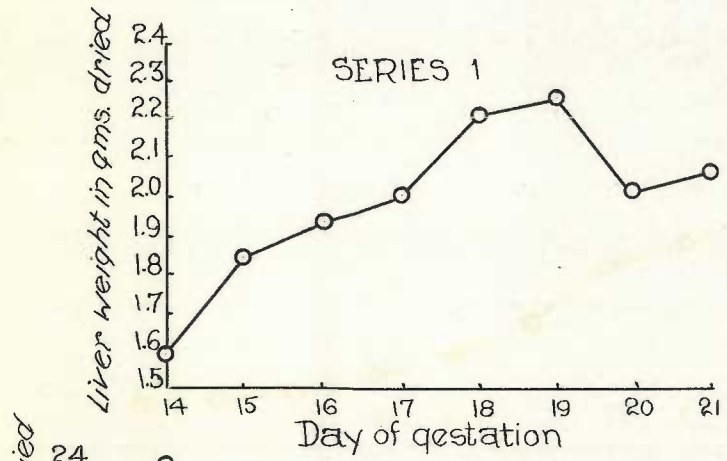


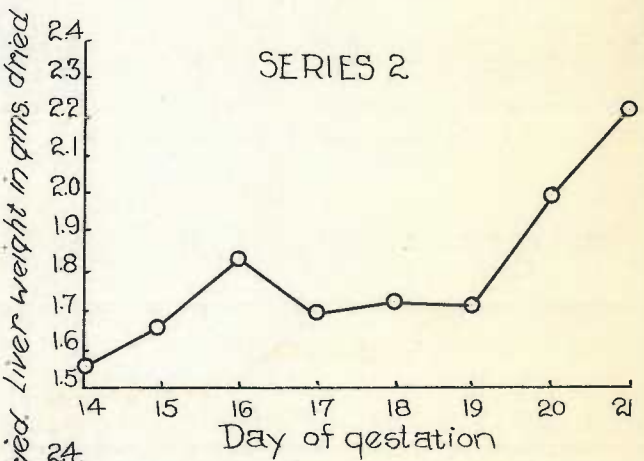


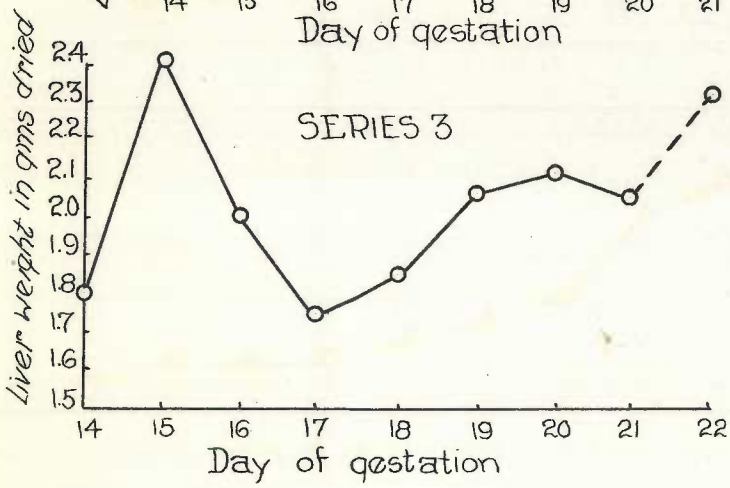


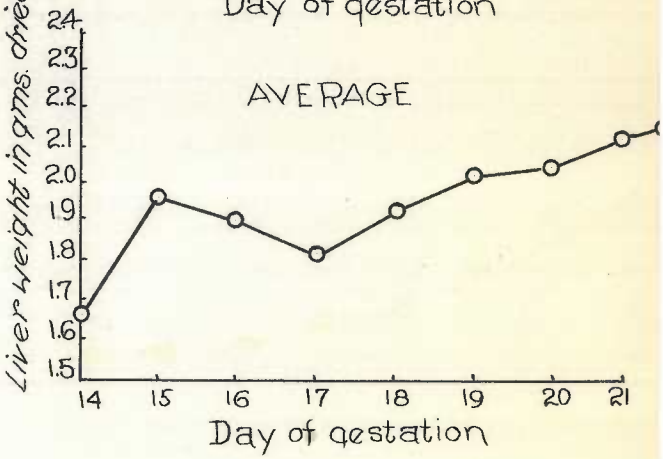
MOTHERS' LIVER WEIGHT IN GMS. (Dry weight)

DAY	DIET # 1	DIET # 2	DIET # 3	AVERAGE
14	1.596	1.577	1.804	1.659
15	1.850	1.670	2.412	1.977
16	1.924	1.848	2.002	1.925
17	2.002	1.702	1.764	1.823
18	2.202	1.735	1.867	1.935
19	2.260	1.714	2.082	2.019
20	2.009	1.999	2.126	2.045
21	2.084	2.224	2.066	2.125
22	Day of delivery		2.326	



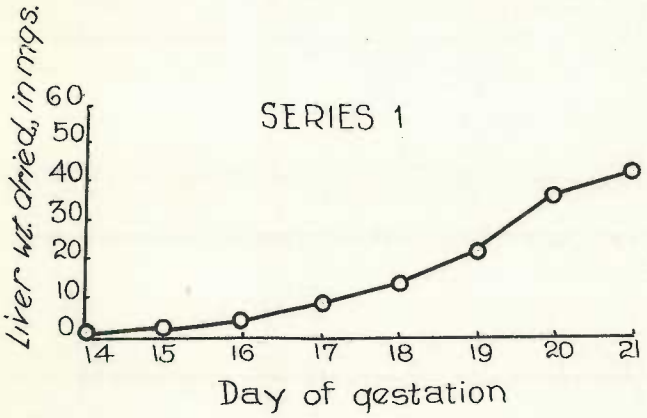


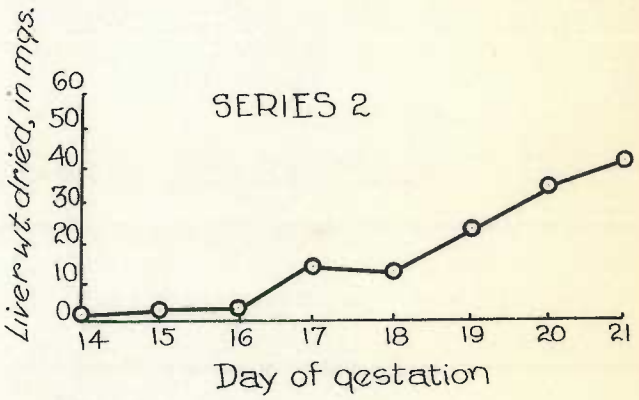


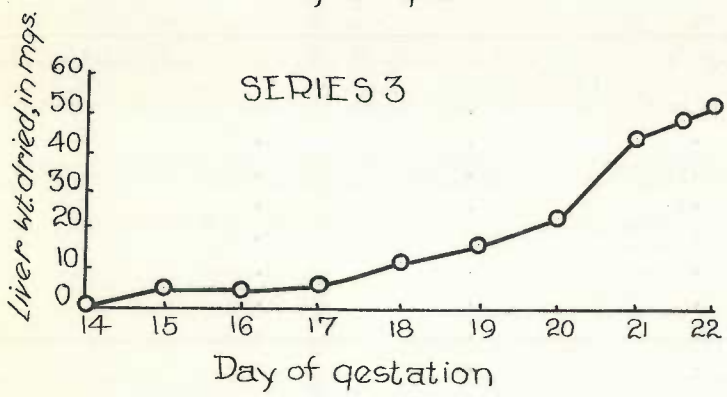


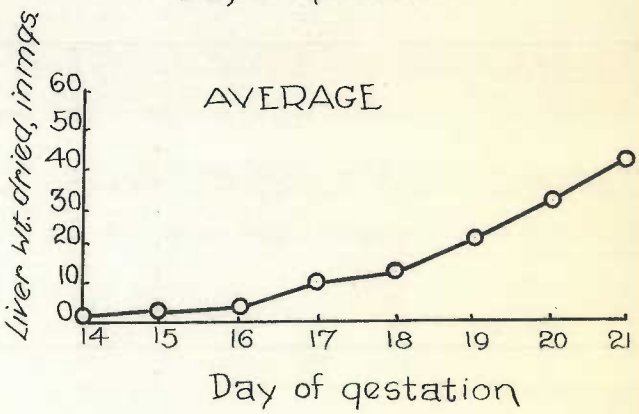
FETUSES' LIVER WEIGHT IN GMS. (Dry weight)

DAY	DIET # 1	DIET # 2	DIET # 3	AVERAGE
14	.00350	.00348	.00320	.00339
15	.00458	.00856	.00680	.00665
16	.00444	.00920	.00680	.00661
17	.00528	.01602	.00720	.00950
18	.01378	.01356	.01310	.01349
19	.02480	.02485	.02130	.02365
20	.04694	.03754	.03160	.03869
21	.05244	.06576	.05150	.05325
22	Day of birth		.05240	









FETAL DEATHS. In the first series, 83 per cent of the fetal deaths occurred on or before the 17th day. In the second series the per cent of fetal deaths at this time dropped to 77 and in the third series to 72. The average for the three series is 77 per cent. The peak of fetal deaths during this period occurred on the 17th day. Following the 18th day a second increase in fetal deaths took place with a peak on the 19th and 20th days. The curve of fetal deaths per 100 live fetuses shows no essential difference from that published in a previous report (92). It offers further evidence that intra-uterine crises occur which result in a pre-natal limitation of litters. That this represents another instance of a compensatory mechanism is highly probable. A lack of uniformity in distribution of the materials necessary for growth, hemoglobin synthesis, etc. to fetuses in the same uterus will decree death to those individuals unfortunate enough to receive minimum quotas of these essentials. Both the marked increase in the rate of growth of the fetus on the 17th day (84) and the initiation of movement which occurs at the same time (93) contribute to increasing the demand for oxygen and adequate means for its transport. This may well constitute the first crisis. If the rate of iron deposit which showed a marked increase on the 15th and 16th days is sufficient to meet the demands being made upon it, the crisis will be passed. A second crisis may develop as the result of a discrepancy occurring between the rate of liver growth

and that of iron accumulation. Reference to the curves will show that on the 18th day the liver showed a marked increase in its rate of growth. It is obvious that unless the total iron accumulation is sufficiently large it will not be possible to maintain a constant or growing concentration of this element in the liver. As a result a rather paradoxical situation arises, that is, the total iron in the liver increases but its concentration decreases. The individual will therefore suffer an iron deficiency in the face of an increasing iron deposit. Only those individuals who acquire iron at a sufficient rate to meet both these crises will be able to come to term. A third crisis, involving the fetal iron endowment, faces the infant after birth. This, however, will be discussed later under another subject. Thus it will be seen that a deficiency in the supply of those materials necessary for normal growth and development will prove to be the effective factor in limiting the size of a litter at a time in fetal development when this deficiency becomes the most marked.

Gonzalez (84) found that the left cornu contained 4.5 per cent more fetuses than the right one. Data from the experiments herein reported show that both cornu contain practically the same number of fetuses - right, 502 and left, 501. The death rate for the two cornu is also the same. Of the 43 prenatal deaths, 22 happened in the left cornu and 21 in the right. In this respect Gonzalez' results are not confirmed.

The particular place in the uterus seems to have little or no bearing in determining which fetuses will die. Thirty of

the fetuses dying occupied end positions, that is, were either at the extreme ovarian or uterine end of the tube. Six of the fetuses were found in central positions while seven of them lay in intermediate locations. The blood supply of the uterus might lead one to suspect that the point most impoverished would be the place where the largest number of fetuses would perish. The arterial circle formed by the uterine and ovarian arteries supplies the central portion of the uterine tubes with blood the most depleted. This does not correspond, however, with the locus where the largest number of deaths occur.

In the three series of animals observed there seemed to be an inverse ratio between litter size and pre-natal death. The largest litters - 8.1 and 8.7 - showed the smallest number of fetal deaths - 1.75 and 2.8 per cent -- while the smallest litter - 6.8 - was associated with the highest pre-natal mortality - 9.5 per cent.

MOTHERS' ERYTHROCYTES. In all three series there occurred a definite decrease in the number of red cells. Individual differences in the three curves are not very pronounced and probably do not amount to enough to be of statistical importance. As judged by the red cells, there appears to be little difference in the three diets. The average drop in red cells during the period under observation was nearly 14 per cent.

FETUSES' ERYTHROCYTES. The average curve for all groups shows a very definite and steady increase in red cells. The maximum reached was 1,800,000. Individual instances were recorded of counts over 2,000,000. The greatest scatter occurred in the animals of the second series. The fetuses of series III gave the smoothest curve. The highest red cell counts occurred in fetuses of mothers receiving Diet #2. On the 17th day the average for this group was 1,027,000 and on the 20th day it had risen to 1,874,000. Individual cases were observed with counts well over 2,000,000. Sure (94) observed a concentration of blood with a consequent increase in red cells and hemoglobin as a result of vitamin B deficiency. It is well established that a vitamin B intake restricted to that which may be drived from a diet containing 2 per cent yeast as the only source of this vitamin will not cause beri beri in the mother but will produce this condition in her young. While gross evidence of this deficiency first becomes apparent during the lactation period, there is no good reason for not believing that similar, though less marked, deficiency could not be manifested in less obvious ways during the period of gestation. The wide fluctuations in red cells and in hemoglobin during this period may be manifestations of such a deficiency.

MOTHERS' HEMOGLOBIN. Here, also, there is evidence of a progressive anemia. The difference between the initial level and the lowest levels attained, however, is not very great. The animals in the third series showed a definite decline in hemoglobin values while the mothers of the first two series were able to prevent any marked losses. Especially is this true in Series I. In this

instance the hemoglobin values were surprisingly constant and fluctuated within very narrow limits. One cannot escape the notion that when a series of values show so little fluctuation the processes operating to produce them are not being subjected very seriously to influences that would cause them to deviate from normality. The wide variations in Series II may be ascribed to at least two causes: (a) the blood concentration of the mother due to vitamin B deficiency and (b) the declining demand being made on the mother for hemoglobin building materials due to the marked pre-natal limitation in litter size.

FETUSES' HEMOGLOBIN. The fetuses in all three series showed a steady gain in hemoglobin. The curve of the animals in the second series showed the most erratic course. It reached a level somewhat higher than that attained by the animals of the third series. Here again one sees evidence of the blood concentration mentioned above in connection with erythrocyte counts. It seems reasonable to assume, in the light of previous experience, that these young animals are in a pre-beri beri condition. The curve they have established represents the maximal levels attained by those who were able to survive. Perhaps it represents equally well the minimal levels compatible with the maintenance of life.

The curve of the group in Series III shows a more rapid rise than did those established by the other groups. Furthermore the curve is more uniform in its ascent, reaches a peak sooner and shows a decided tendency to level off. The regularity in

the accumulation of fetal hemoglobin in this instance leads one to suspect that the increase followed some well-defined plan upon which no restrictions were placed. The similarity of the last three values suggests that the oxygen needs of the fetus on the 19th day and thereafter were satisfactorily met by a hemoglobin saturation of 72 per cent and that further increases were unnecessary. Here, as in the mothers' hemoglobin curve, there is evidence of an ability to manufacture hemoglobin not manifested in the other two groups. This cannot be due to a richer supply of iron since a review of the curves for iron deposit shows that Diet #5 excelled in this respect. Adequate iron reserves are not inconsistent with low hemoglobin values since it has been shown that, in the absence of sufficient copper, the body is unable to use iron in hemoglobin synthesis. Diet #1 is undoubtedly more efficient in providing for hemoglobin production. Diet #5 is relatively deficient in this respect although it possesses more iron. In view of the preliminary experiment cited above in regard to the value of cabbage extract and the light thrown upon this by Hart and his co-workers, it does not seem improbable that copper is the factor responsible for the variations in hemoglobin production noted above.

It seems desirable at this time to repeat the fact that the number of red cells and the amount of hemoglobin found in fetuses at the end of the gestation period must be very close, if not identical, to the values found immediately after birth.

If this may be considered true, then some explanation must be offered for the marked discrepancy that occurs between the blood values at the end of gestation as tabulated here and those found by other workers for the beginning of the lactation period. Sure (95) has accounted for differences in hemoglobin concentration in the nursing young on the basis of variations in maternal diets. Mention has been made earlier in this paper of the ability to raise fetal hemoglobin by supplementing the maternal diet with an alcoholic extract of cabbage. The ability of the maternal diet to bring about changes in the fetal level of hemoglobin seems, in view of the results just mentioned, to be the most likely explanation of the discrepancies mentioned above. If such powers can be associated with the maternal diet, then too much emphasis cannot be placed upon the necessity of so adjusting the food intake of an expectant mother that the developing fetus will be able to produce for itself a maximum amount of hemoglobin.

MOTHERS' LIVER IRON CONCENTRATION. The concentration of iron in the livers of mothers on all three diets showed a very definite decrease for the last three days of pregnancy. The average for all the animals showed an initial iron concentration of 110 mgs. This concentration is maintained with surprising success until the last three days when it dropped sharply to 74 mgs. The mothers in the third series showed the most success in maintaining the initial level. As a matter of fact, up to the 19th day these animals actually

gained in liver iron saturation. Furthermore the terminal drop was not as extensive as in the other groups. The animals receiving Diet #2 again showed a very erratic course with the curve finally reaching the low level of 63 mgs. This is a further demonstration of the struggle occurring in the maternal organism between the forces of iron mobilization and those concerned with the maintenance of the minimal iron concentration compatible with life. The demands of the fetus for iron will be honored by the maternal organism up to the point of development of a severe anemia. Presumably, however, there arrives a point in the depletion of maternal stores below which iron cannot be transferred to the fetus in adequate amounts with the result that it dies. Such a condition is represented on the 17th day in the maternal liver iron concentration and total liver iron curves. It will be noted that at this time a sharp rise in maternal iron occurs. It is associated with the time of greatest fetal mortality. The sudden reduction in iron demand thus brought about produced a backward surge in the flow of iron to the uterus with the resultant effect of a temporary rise in the maternal liver.

There are several factors which exert an influence on liver iron concentration. One of these is the size of the liver. The total iron remaining constant, its concentration will drop as the liver increases in size. Reference to the curves showing liver size reveals the fact that in all instances there occurred an increase in the size of the liver. Another factor is the

transfer of iron from the maternal tissues to those of the fetus. Reference to the appropriate curves shows that this occurred in nearly equal amounts in all three groups. A third factor is the utilisation of maternal iron for the synthesis of hemoglobin in the fetal tissues. A fourth factor is the presence in the maternal diet of available iron and other essentials such as copper which are necessary in blood building.

The sudden rise in liver iron concentration on the 20th day that occurred in the mothers of the first series finds its explanation in the drop in liver weight that occurred on the same day. Likewise the extensive drop in iron concentration in the livers of the animals on Diet #2 is accounted for by the marked rise in liver size that occurred at the same time. The total tranfer of iron from the mother to the fetus is practically the same in all three instances. This would minimize the effect of this factor on maternal liver iron concentration. The third factor has a definite influence on maternal liver iron concentration. It has been pointed out already that the fetuses in the first series were able to develop the most hemoglobin of the three groups. The utilization of maternal iron for this purpose would, in the first series, add to the maternal depletion while in the third series it would have a sparing action. This is reflected in the slight increase in maternal iron concentration in this series.

The influence of the fourth factor is difficult to assess. Obviously the benefits to be derived from Diet #3 over those coming from the use of Diet #2 must be ascribed to the larger amount of

yeast. The influence of yeast in correcting anemia of nutritional origin has been so adequately treated by Parsons (22) that it will not be necessary to discuss it here. The differences between Diet #1 and Diets #2 and #3 are still more complex. The chief purpose of this paper is not so much to assign specific benefits to particular factors, although this may be possible in many instances, but rather to demonstrate that changes in the maternal diet are responsible for differences in fetal hemoglobin production.

A question arises as to which represents a better index of depot iron, - the liver iron concentration or the total liver iron. Reference has already been made to a statement of Whipple's (87) that continued bleedings will not reduce the liver iron of dogs below 20 to 25 mgs. per cent. He spoke of this as the "irreducible minimum". The irreducible minimum as far as iron concentration is concerned represents a constant figure. No such estimate of total iron is possible because of the variation in size of livers. It seems much more appropriate, therefore, to think of depot iron in terms of iron concentration. The amount of iron available for transport to the fetus or for other purposes outside the depot will be that amount over and above the irreducible minimum. The rate at which the iron concentration drops will give some idea of the total quantity available.

With such considerations as the above in mind a review of the iron concentration curve of the mothers in Series II will yield interesting information. The iron concentration on the 17th

day was 128 mgs. per cent. Four days later it dropped to 64 mgs., exactly one-half the original amount. This represents the most rapid and extensive drop of the three series. Since the iron endowment of the three series of fetuses was nearly identical, the conclusion is justified that the total maternal iron was quite low. The figures on total iron for this group show that this is true. The lowered ability of the mothers in this group to transfer to their fetuses sufficient iron to attain and to maintain a high iron concentration has prepared the way for an increased post-natal death rate. As already related deaths among these animals during the nursing period was due both to beri beri and an associated anemia.

FETUSES' LIVER IRON CONCENTRATION. The peak of iron concentration in the fetal livers was close to 100 mgs. The average initial iron concentration of mothers' livers was 110 mgs. The final concentration of iron in the fetal livers was 80 mgs. while that of the mothers' was 74. From these figures it will be seen that the fetus is able to build up a maximum iron concentration in its liver to within 10 mgs. of that of the mother and that, by the end of the gestation period, it can exceed the mothers' iron by 8 per cent. On Diet #3 the fetal livers reached their highest concentration on the 17th day; on Diet #1 this occurred on the 18th day and on Diet #2 on the 19th day. The animals in the second series reached the lowest liver iron concentration of the three groups and required

a third less time in which to accomplish it. The fetuses in the third series were able to initiate a recovery in iron concentration before the end of gestation. This was due to the large maternal reserves; the acquisition of a greater total amount of iron; the production of less hemoglobin and a smaller increase in liver size.

The influence of copper in hemoglobin production has already been mentioned. Without this mineral in proper quantities the iron remains locked in the depots. It tends to increase in these places due to an inadequate outlet. Stroma and hemoglobin production in the fetal liver entails a certain amount of metabolic activity on the part of this organ. If this activity is lacking or diminished in amount it is reasonable to assume that there would occur corresponding changes in size. The smaller increase in liver size in the fetuses of this series may indicate a deficiency in activity of this sort and partially account for the greater concentration of iron.

The average curve for fetal iron concentration shows a decline beginning on the 18th day. Since the total iron is increasing at this time the decline must be due to a rate of liver growth greater than that of iron acquisition. Increases in the rate of hemoglobin production would also be effective in altering liver iron concentration. The curve of iron concentration for the animals in series three shows a second rise beginning on the

20th day. The fetuses of the second series do not show this. The only difference in the two groups lies in the increased amount of yeast the mothers of the third series were receiving. This illustrates again the remarkable influence of the maternal dietary on the ability of the fetus to produce hemoglobin or to acquire those substances necessary for its synthesis.

MOTHERS' TOTAL LIVER IRON. The average curve for all three groups shows an initial rise in total iron on the 15th day to the greatest total recorded. Reference to the individual curves shows that the animals of the first and third series were the only ones capable of showing this initial rise. That this does not represent an iron mobilization becomes evident when the curves for liver size are examined. The mothers of the third series were able to bring about a second rise in liver iron which took place on the 18th day. There is also a corresponding increase in liver size at this time. The correspondence between total liver iron and liver size impresses one with the fact that, concentration remaining unaffected, the liver iron must increase as size increases. A drop in total iron along with an increase in liver size will be reflected by a greater decline in iron concentration in the liver. The removal of maternal iron to meet the requirements of the fetus will accentuate this decline.

FETUSES' TOTAL LIVER IRON. All three groups show a fairly uniform increase in total liver iron. The maximum amount acquired was slightly greater than 40 mgs. The group getting Diet #3 was able to store the

most iron. It has already been pointed out that this represents an impaired outlet inasmuch as these animals were unable to produce as much hemoglobin as those in the first series. The high degree of uniformity in the three curves indicates that the factors controlling the transfer of iron from mother to fetus differ from those involved in hemoglobin production. In view of the higher pre-natal mortality in series II and the similarity of the three curves it seems probable that the higher fetal death rate is not directly related to iron transfer but to some other event associated with iron such as hemoglobin synthesis. The sudden and transitory rise in total iron in the fetuses of series II which occurred on the 17th day as the result of the high number of deaths at that time shows the flexibility of the adjustments regulating this transfer. Each fetus may be pictured as a minute pump whose duty it is to abstract from the maternal blood a certain amount of iron. The actual amount removed will be determined by the minimal requirements of the fetus and the richness of the maternal supply. The fetal requirements being uniform, the amount of iron removed must be uniform also or the fetus will die. Thus it will happen that each fetus will receive iron at a fairly uniform rate but the number of fetuses will depend upon the richness of the maternal supply. Such a concept will explain the similarity in the fetal total liver iron curves and the variations in litter size.

MOTHERS' LIVER WEIGHT (Dry). In general there is a tendency for the maternal livers to show an increase in size. This may represent a

compensatory hypertrophy. At any rate it has an adverse effect on liver iron concentration. The only way to offset this is to increase the available iron in the maternal diet.

FETUSES' LIVER WEIGHT (Dry). In all instances the fetal livers began increasing in size on the 18th day. From this time on weight increments were very rapid. The marked increase in size of the liver during this period undoubtedly accounts for the decline in concentration of liver iron which occurred in spite of an increase in total iron. The increase in total iron did not keep pace with liver growth. The fact that the fetuses in series I showed the least ill effects of these three conflicting factors is further evidence of the qualitative and quantitative importance of the maternal diet. The curve of liver growth of the fetuses in all three series is similar to that established by Gonzalez (84) for the entire body. The curves for body weights, liver weights, total iron, hemoglobin concentration and erythrocytes are quite similar. It is probable that the means for blood production, the ability of the blood to transport oxygen and the demand of the tissues for growth and activity develop in an entirely parallel manner.

FETAL CONDITION IMMEDIATELY PRIOR TO BIRTH. Five females were maintained on Diet #3 until the onset of labor. They were then anesthetized and the fetuses examined. The results are indicated in the charts by stippled lines. The number of red cells showed no further increase. The hemoglobin continued to increase at the usual rate. There was also a continuation of the gain in iron concentration and in total iron although the latter

had decreased markedly. There was no further gain in liver weight. During the last twenty four hours, then, the fetus made an actual gain in depot iron and in hemoglobin. The changes in the mother's were much more marked. The hemoglobin and red cells increased to levels almost equal to those at the beginning of the period of observation. The iron concentration of the liver and the total liver iron showed a remarkable gain. Furthermore these occurred in the face of a distinct gain in liver weight. It seems quite obvious from these figures that the rapid improvement in the mothers' condition which is usually noted post-partum actually is initiated a short time prior to delivery and that those changes incident to the onset of labor at first check and finally stop the gains being made by the infant.

INDIVIDUAL VARIATIONS IN LITTER-MATES. For purposes of discussion, only one litter will be selected. Other examples may be seen in the detailed tables at the end of the paper. The figures below were provided by 17 day old fetuses from female #74 of the third series. The arrangement of the figures in three columns is not intended to convey the idea that the values found in the same line were provided by the same fetus. While this is true for the red cells and hemoglobin, it is not so for the liver iron.

RED CELLS	HEMOGLOBIN PER CENT	MGS. IRON PER CENT
.570	25	92.6
.350	14	48.78
.650	26	153.0
.600	25	82.0
.630	32	99.3
.660	35	99.5
.470	38	105.6
.590	30	115.0
.410	41	93.3
.270	22	96.1

Purposely avoiding the extremes, it will be noted from the above that the hemoglobin varied from 22 to 38 per cent; the red cells from 350,000 to 630,000 and the iron from 82 to 115 mgs. per cent. The fetus containing the least amount of hemoglobin did not necessarily have the fewest red cells. The iron concentration was just as irregular. It seems apparent from these results that the factors regulating these different activities act independently of each other. There seems to be no correlation between these values and the position in the uterus or the cornu occupied. From the available evidence, the distribution of these values seems to be more fortuitous than otherwise. The position of the fetuses dying in utero suffers the same irregularity. While anemia with its resultant asphyxia or pre-natal beri beri may be actual causes of fetal death, no reason has been developed to explain why one fetus should succumb to the operation of these various lethal factors while another escapes.

DISCUSSION

The study of the three "pregnancy diets" herein reported offers several reasons for believing that still further improvements are capable of being effected. In the first place the red cell counts and the hemoglobin precentages of the fetuses at the end of gestation are not at the same level as the early neo-natal values reported by other investigators. Secondly, evidence was presented in this report that the simple addition of cabbage extract was sufficient to raise the hemoglobin from 72 to 88 per cent. There is reason to believe that

this is evidence of a copper deficiency. Further corroboratory proof of the inadequacy of the diets studied is provided by the following observation. Fifteen of the 42 females used in the first series received, in addition to Diet #1, 5 part of wheat germ. The blood and iron values of the animals that received the wheat germ differed in no respect from those not getting this addition with the possible exception of the mothers' hemoglobin. In this instance there was a slight increase. The chief effect of the wheat germ addition was observed in the number of fetal deaths. Of the six fetuses dying in utero in this series only one belonged to a mother getting wheat germ. It is believed that this observation should be considered as suggestive rather than as conclusive although the number of animals observed - 344 fetuses and 42 mothers - should lend considerable weight to the finding.

The nutritional discrepancies in the three dietaries studied seems to involve copper, iron, vitamin E and vitamin B. Any benefit derived from the use of these diets can be ascribed for the most part to increases in iron and vitamin B. Future work, involving larger series of animals and using methods as herein described for iron and vitamin B, must establish the values of copper and of vitamin E.

The ability of the organism to so adapt itself to changing conditions that it can continue transporting oxygen to the tissues in adequate amounts is nothing short of marvelous. Notwithstanding the extraordinary flexibility of this adaptive mechanism there are limits beyond which it breaks down and the continuation of life becomes impossible.

The tenacity with which the organism holds on to life after the compensating mechanism has broken is illustrated by the willingness it shows to endure relative degrees of oxygen starvation, reduction in functional capacity and other kinds of departures from normality. The inevitable appearance of death, however, shows that even this adaptation has its limits.

The transfer of oxygen by the blood to the tissues in amounts adequate to meet their needs is dependent upon several factors. The demand for an increased amount of oxygen is ultimately met by an hypertrophy of the erythron. The development of a polycythermia is not possible in the face of a deficient reserve in those materials necessary in the construction of red cells and hemoglobin. Furthermore, an increase in the number of red cells without a corresponding increase in blood volume will result in a rise in blood viscosity. This will place an added burden on the heart.

As already mentioned, the chief variations in the diets studied resided in the iron and vitamin B quotas. Small variations in copper and vitamin E undoubtedly had some influence. The chief complications liable to grow out of these "changing conditions" are those associated with the appearance of anemia and of beri beri. The decreased ability of an impoverished blood stream to carry oxygen is apparent. The part played by beri beri is not so obvious. When, however, one recalls that the heart is one of the chief structures damaged by a lack of vitamin B, the detrimental influence of beri beri

as a complication becomes apparent at once. It has already been pointed out that when the blood hemoglobin drops below a certain level - 50 per cent in humans - the cardiac output per minute must increase. In the cardiac damage associated with beri beri this rise in work performance becomes increasingly difficult. On the other hand, in the presence of fetal polycythemia and an increased blood viscosity, there still remains an increase in labor on the part of the heart. Thus it will be seen that in either extreme the heart has an added amount of work imposed upon it. If it is suffering from the changes produced as a result of vitamin B deficiency then the danger of fetal death from anemia is accentuated. If the deficiency is in vitamin B alone then the normal increase in blood viscosity will, sooner or later, cause death from cardiac failure. In either case the fetus will die of asphyxia and those changes associated with fetal asphyxia will develop.

The oxygen saturation of fetal blood indicates that the pressure of this gas in the placental blood is below the limit usually set as compatible with life (80 per cent saturated at a pressure of 48 mm.). This constitutes the initial stimulus to fetal hematopoiesis. The hematopoietic tissues do at least two things. They produce more red cells and hemoglobin. The hemoglobin appears to be in two forms, - one that resembles adult hemoglobin in its oxygen dissociation curve and another distinctly different in this respect to which the name fetal hemoglobin has been given. Perhaps, as Barcroft suggests, the type of hemoglobin differs as the tissue producing it differs. Thus there would be hemoglobin of the adult type produced by the bone marrow; hemoglobin of the fetal type produced by the liver and spleen and muscle

hemoglobin, a product of muscle-cell metabolism.

An increase in red cells is not necessarily followed by an corresponding increase in hemoglobin although this is usually what occurs. In the experiments reported in this study no great disparity in these two was noted. If there were adequate supplies of building materials, the demand for greater oxygen transport was met by an increased output of red cells and hemoglobin.

In view of the various functions of iron that have been set forth in this paper, tremendous importance must be attached to the stores of this mineral that must be built up in the liver. It goes without saying that a corresponding quantity of copper must be available also. The need of nuclear material for iron placess a growth value upon it. The presence of iron in intra-cellular cytochrome assigns to is great importance in intra-cellular oxidations. The necessity of iron in the three types of hemoglobin mentioned makes it indispensible in oxygen transport. For these reasons an iron reserve must be developed in order to enable the fetus to successfully overcome the various natural crises that it must meet either before or after birth.

Not all of the iron found in the liver can be regarded as depot iron. Presumably the same holds true for the spleen. A certain portion of this iron represents integral parts of the cellular structure and represents what Whipple was pleased to call "the irreducible minimum". According to him, iron must be present in excess of some 20 to 25 mgs. per cent before it can be considered depot iron. Even though iron may be present in the depots in amounts greater than the irreducible minimum

before it can be used in hemoglobin production, further stipulations must be met. Two of these demand the presence of copper and the availability of what Castle calls the "hematinic principle". Whipple's work suggests that there may still be another factor necessary for the unlocking of these iron reserves. Without these materials the depot iron increases for lack of an outlet and there is brought into existence the paradoxical situation of large iron reserves with low hemoglobin levels.

Variable amounts of vitamin B in maternal diets will invariably decree the development of beri beri in those fetuses or in those nursing young whose m thers received amounts below the minimum necessary for protection from this deficiency. The tragic thing about this situation is the failure of the mother to manifest any gross indication that such a deficiency exists. She does not develope clinical beri beri herself and by the time her baby shows the signs usually associated with this deficiency the disease is so far advanced that therapy is of little or no avail. Prophylactic measures are the only ones to employ. The vitamin B intake of the mother must be increased almost 400 per cent above her own protective dose in order to insure protection for her offspring.

There are at least three crises that must be met and passed before the baby can be considered as having a good chance to survive the nursing period. The first of these occurs on the 17th day of gestation. At this time the first heavy demand is placed upon the iron deposits. This is due to the initiation of movement, the sudden increase in rate of body growth and the consequent need for more blood

hemoglobin, nuclear material, etc. If the stream of iron coming from the mother coupled with the iron stored in the depots is sufficient to met this need the fetus will continue its existence and come to the time when it must face the second crisis. This is brought about by a marked increase in rate of liver growth which occurs on the 18th day. There does not seem to be a compensatory increase in the rate at which iron is being removed from the mother. The demands already established continue with the result that the liver iron decreases in concentration. By growth dilution the depot iron is reduced in the face of an increase in total iron. If the initial supplies are sufficient to meet this situation, the fetus is permitted to go on to term. The first crises takes out most of those with minimal reserves. The second crisis takes out a small intermediate group.

The fetuses coming to term have been reduced to those whose blood stream has proven itself adequate to meet the demands of oxygen transport placed upon it. The only test to which the iron depots have been subjected have been those imposed by the hematopoietic tissues and the requirements of cell division. They may have met these tests with a large reserve or with one extremely low. In either event the fetus is born and the third crisis develops due chiefly to the shutting off of the supply of iron from the mother. The time of appearance of this crisis will depend on the amount of depot iron, on the quantity of iron regained from the blood due to the change from fetal polycythemia, on the amount of growth dilution, on the demands for increased oxidation by greater activity and the requirements of temperature regulation and, finally, on the amount of iron received in the food.

Variations in neo-natal morbidity and mortality will be closely related to the amount of iron that is made available to the infant through that period when it is dependent upon milk or other iron-free foods for its nourishment. While there need be no particular concern in regard to the infant born with plentiful iron reserves, this does not hold for the child who comes into the world with a bare minimum. What is about to be said concerns an intermediate group - a group having a large enough iron reserve not to fall prey to the first two crises and, perhaps, not even the third one, but nevertheless a group whose depot iron is too low to place them in the strictly normal class. These individuals, even before birth, suffer from asphyxia. This results in an increased capillary permeability with resultant perivascular hemorrhages. This condition has been described elsewhere (96). Aside from the changes incident to bleeding in various parts of the body, the anemic infant suffers an increased susceptibility to respiratory infections. These conditions alone prescribe a very precarious existence for the infant born with low iron reserves.

Aside from a better understanding of some of the causes of early infantile deaths, the chief value of a study of this kind lies in the demonstration of the important bearing the maternal diet has in enabling the developing fetus to acquire the essentials for its existence. Almost as important as this is the realization that there may be a great variation in depot iron and that the blood hemoglobin at birth, unless it be very low, will give no indication of this. Out of a full appreciation of these facts should grow a realization that a large saving in human life may be made by placing emphasis on the proper feeding of expectant mothers.

CONCLUSIONS

1. Seventy seven per cent of fetal deaths occur on or before the 17th day following insemination. Reasons have been advanced for believing that this is due to failure on the part of the fetus to acquire, or of the mother to deliver large enough quantities of iron to provide for the needs of growth and activity both of which are greatly accelerated at this time. A second moderate rise in fetal mortality occurs on the 19th day due to exhaustion by growth-dilution of small reserves of iron.

2. The number of fetuses developing in each cornu is exactly the same. The death rate among the fetuses of each cornu is identical also. The position of the fetus in the uterus in relationship to blood supply, ovaries or cervix does not seem to have any bearing on fetal mortality.

3. The amount of yeast in the diet - other factors being constant - has an influence on litter size. With 2 per cent yeast the litters averaged 8.8 and with 8 per cent the average was 8.7 per cent. The size of the litter is directly related to fetal mortality. The litters of mothers receiving the 2 per cent yeast inclusion suffered a mortality rate of 9.5 per cent while those whose mothers got the 8 per cent quota had a death rate of 2.8 per cent. Although direct evidence is lacking it is probable that the deaths were due to anemia and beri beri.

4. There is an anemia which developed in mothers during pregnancy. It grows worse as gestation advances. Its severity is correlated with the diet - the better the diet, the less severe the anemia. A diet

containing 8 per cent yeast appears to enable the mother to store up a greater iron reserve than occurs with a lesser amount. Yet it is deficient in a factor possessed by the stock diet which promotes the utilization of iron for hemoglobin synthesis. Animals possessing a higher liver iron do not necessarily have high hemoglobin levels.

5. There was a steady rise in the number of red cells and the quantity of hemoglobin in the fetal blood during the last seven days of gestation. This rise was maintained even at the cost of fetal lives. The curves established by the poorest diet (#2) probably represent minimal values below which life cannot be maintained. The best of the three diets herein studied is susceptible to further improvement since the final fetal red cell and hemoglobin values are decidedly below those obtained from the newly born young of mothers receiving better diets.

6. High values for red cells and hemoglobin exist in the pre-beri beri state. This is misleading since it might be interpreted as representing a normal condition instead of one growing out of blood concentration.

7. The mothers showed a tendency to suffer a reduction in liver iron concentration throughout pregnancy. The better the diet the more they were able to maintain the initial concentration.

8. On the three diets used, the fetuses were able to build up a liver iron concentration close to 100 mgs. per cent. The better the diet the sooner and the higher the level attained. In general the iron concentration declined from the 18th day onwards. This was due to a greater rate in liver growth than in iron deposit. The animals of the third series showed a decided ability to change

declining values into ascending ones. There was a decided difference in liver iron concentration just prior to birth. The highest values were found in those animals whose mothers received the best diets. The fetus was able to build up a liver iron concentration greater than that of its mother.

9. On the whole there is a definite tendency for the maternal liver iron to decrease as pregnancy advances. The better the diet, the less the decrease.

10. The greatest increments in fetal iron began on the 17th day. The total acquired was nearly the same in all three series. This was accomplished at the expense of fetal livers. The constancy of the fetal requirement and the variability in maternal supply could work out in no other way. This conclusion coupled with that above in regard to the ability of a good maternal diet to enable the mother to hold high liver iron values places the responsibility for the fetal deaths herein described directly upon the quality of the mothers' food.

11. There is a slight but definite tendency for the maternal livers to become larger as pregnancy advances. This may be a compensatory hypertrophy. It serves to reduce the liver iron concentration and therefore the amount of depot iron. It creates another reason why there should be a plentiful supply of iron in the maternal diet.

12. The greatest accessions to fetal liver weight began on the 18th day. This is in marked contrast to the curves for red cells and hemoglobin in that the latter began their ascent on the 15th and 16th days. The latter constitutes the first drain on liver iron and the former the second.

13. The rapid improvement in the mother usually noted post-partum was actually initiated shortly before delivery. The rapid growth of the liver, the increases in red cells and in hemoglobin occurring in the fetus was stopped by the changes incident to the onset of labor but the deposition of iron continued. This iron was not derived from the mother, at least not in such large quantities since her liver iron showed a sharp rise. It is more probable that it was derived from a beginning hemolysis of fetal red cells which is known to exist for a few days after birth. These changes may be considered an anticipatory of birth.

14. Individual variation in liver iron, red cells and hemoglobin in litter-mates was quite marked. Pre-natal deaths may be limited to those individuals having unusually low values. Whether the distribution of these low values is purely fortuitous or dependent upon genetic or other factors poorly understood cannot be said.

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STOCK DIET 14 DAY

MOTHER	FETUS	RED CELLS	HB	LIVER WT.	MG. FE %	DRY WT.	TOTAL FE
#619		7.7900	86%	.8600	91.3		.7851
	L1,2	.16	9%	*.0111		11.26	*.0012
	R1,2	.11	5%				
	R3,4	.10	5%				
	R6	.11	3%				
	R5 Resorbed						
#624		7.2500	102%	1.9900	102.0		2.0298
	L1,2	.30	9%	*.0316		25.30	*.0083
	L3,4	.21	4%				
	L5,R1	.14	8%				
	R2,3	.06	2%				
	R4,5	.09	5%				
#631		9.0080	104%	1.7127	76.1		1.3033
	L1 Resorbed						
	L2,3	.168	3%	*.0380		21.06	*.0080
	L4,5	.080	3%				
	L6,R1	.064	1%				
	R2,3,4	.128	11%				
#634		8.1000	95%	1.5330	86.7		1.3290
	L1,2	.32	3%	*.0242		17.16	*.0041
	L3,4	.37	10%				
	R1,2	.26	2%				
	R3,4	.09	1%				
#636		8.5600	106%	1.8800	103.4		1.9440
	L1,2,3	.120	3%	*.0484		30.90	*.0150
	L4 Resorbed						
	L5,6,7	.026	1%				
	R1,2,3,4	.066	2%				

* This represents total for fetal livers

STOCK DIET 15 DAY

OTHER FETUS	RED CELLS	HB	LIVER WT.	MG. FE % DRY WT.	TOTAL FE
617	7.37	95%	1.86	107.9	2.0069
L1	.60	-	*.0242	65.5	*.0159
L2	.95	27%			
L3	.44	22%			
L4	.43	26%			
R1	.30	19%			
R2	.34	15%			
R3	.32	18%			
R4	.43	31%			
R5	.47	26%			
616	7.59	100%	1.72	113.6	1.9539
L1	.18	19%	*.0254	59.0	*.01498
L2	.44	20%			
L3	.33	18%			
R1	.30	18%			
R2	.39	21%			
R3	-	23%			
R4	.31	32%			
R5	.26	18%			
621	7.08	102%	2.01	115.4	2.31945
L1	.35	-	*.0086	68.5	*.01176
L2	.31	36%			
L3,4	.35	26%			
L5,6	.41	21%			
R1	.37	22%			
R2,3	.27	20%			
623	7.42	101%	2.09	102.0	2.1318
L1,2	.22	16%	*.0134	57.7	*.00775
L3,4	.30	5%			
L5,6	.16	5%			
L7,R1	.16	5%			
R2,3,4	.20	14%			
639	6.56	97.0%	1.57	133.9	2.10223
L1,2	.304	18%	*.0564	15.2	*.0009
L3,4	.400	9%			
R1,2	.296	12%			
R3,4,5	.176	8%			

*This represents total for fetal livers

STOCK DIET 16 DAY

MOTHER	FETUS	RED CELLS	HB	LIVER WT.	MG. FE	% DRY WT.	TOTAL FE
#615		7.52	119%	1.91	101.3		1.934
	L1	.60	-	*.0535		115.8	*.0620
	L2	-	53%				
	L3	.73	45%				
	L4	.91	-				
	R1	-	32%				
	R2	.51	45%				
	R3	.91	-				
	R4	.54	43%				
	R5	.73	62%				
	R6	-	-				
#620		7.05	101%	1.82	91.5		1.6653
	L1	.76	22%	*.0426		113.6	*.0484
	L2	.46	39%				
	L3	.74	44%				
	L4	Resorbed					
	R1	.75	48%				
	R2	.68	41%				
	R3	.89	57%				
#628		9.91	96%	1.73	82.4		1.4250
	L1	.26	25%	*.0200		80.6	*.0161
	L2	.50	32%				
	L3	(?)21	30%				
	R1	Resorbed					
	R2	.33	40%				
	R3	.25	35%				
	R4	.42	34%				
	R5	.32	35%				
#632		7.896	81%	2.50	115.4		2.885
	L1,2	.248	16%	*.0375		70.0	*.02624
	L3,4	.568	14%				
	L5,R1	.584	20%				
	R2,3	.332	15%				
	R4,5	.284	16%				
	R6	.352	17%				
637		6.760	91%	1.66	123.0		2.0420
	L1,2	.344	9%	*.0346		63.5	*.02196
	L3,4	.272	8%				
	R1,2	.136	6%				
	R3,4,5	.216	5%				

This represents total for fetal livers

STOCK DIET 17 DAY

MOTHER	FETUS	RED CELLS	HB	LIVER WT.	MG. FE	% DRY WT.	TOTAL FE
#609		6.97	101%	2.09	115.4		2.41186
	L1	1.38	60%	*.1943	117.2		*.22712
	L2	1.33	61%				
	L3	1.12	71%				
	L4	1.82	72%				
	L5	.79	76%				
	L6	1.00	62%				
	L7	1.07	78%				
	R1	1.22	81%				
	R2	1.12	52%				
#627		8.04	103%	1.94	95.2		1.84688
	L1	.47	30%	*.0576	80.04		*.04610
	L2	.62	4 0%				
	L3	.48	25%				
	L4	.46	43%				
	R1	.43	20%				
	R2	.38	35%				
	R3	.68	52%				
	R4	.43	29%				
	R5	.42	37%				
#62 5		6.28	86%	1.78	105.3		1.87434
	L1	.4 1	51%	*.0516	82.00		*.04235
	L2	.78	53%				
	L3	.60	26%				
	L4	.75	48%				
	R1	.76	50%				
	R2	.912	46%				
	R3	.792	47%				
	R4	.568	43%				
#633		6.6	90%	2.092	81.5		1.70498
	L1	.66	30%	*.0531	77.2		*.0410
	L2	.83	28%				
	L3	.55	36%				
	L4	.59	40%				
	L5	.60	35%				
	R1	.56	41%				
	R2	.70	49%				
	R3	.63	45%				
	R4	.72	27%				
	R5	.78	42%				
#641		6.91	110%	2.110	99.0		2.08890
	L1	.30	22%	*.0488	70.4		*.03435
	R1,2	.60	36%				
	R3,4	.49	27%				
	R5,6	.40	30%				
	R7	.45	35%				

* This represents total for fetal livers

STOCK DIET 18 DAY

MOTHER FETUS	RED CELLS	HB	LIVER WT.	MG. FE %	DRY WT.	TOTAL FE
#611	8.632	108%	2.34	117.6		2.75184
L1	2.00	64%	*.2327		134.2	*.30741
L2	1.50	50%				
L3	1.38	70%				
L4	1.59	62%				
L5	1.27	66%				
L6	1.61	86%				
L7	2.05	82%				
L8	1.45	52%				
R1	2.616	64%				
R2	1.50	85%				
R3	1.75	86%				
R4	1.704	65%				
R5	1.648	82%				
#612	7.544	64%	2.50	85.7		2.14250
L1	1.4	71%	*.2182		108.3	*.2418
L2	1.37	52%				
L3	1.52	72%				
R1	1.23	75%				
R2	1.72	69%				
R3	1.15	64%				
R4	1.17	80%				
R5	1.432	82%				
R6	1.528	83%				
R7	1.368	75%				
R8	2.032	90%				
#629	10.024	102%	1.76	63.6		1.11960
L1	.544	45%	*.0937		114.3	*.1071
L2	1.016	64%				
L3	1.008	47%				
L4	.560	27%				
L5	.832	55%				
R1	1.128	53%				
R2	1.200	59%				
R3	.832	56%				
R4	.728	48%				
#630	6.04	95%	1.9547	98.7		1.92900
L1	1.22	56%	*.0638		110.0	*.0702
L2	.70	57%				
L3	.50	47%				
L4	.36	25%				
R1	.66	47%				
R2	.82	55%				
#640	7.99	102%	2.4100	88.2		2.12562
L1	1.03	40%	*.0461		105.2	*.0495
L2	1.16	59%				
R1	.64	41%				
R2	1.31	52%				

This represents total for fetal livers

STOCK DIET 18 DAY (CONTINUED)

MOTHER	FETUS	RED CELLS	HB	LIVER WT.	MG. FE	% DRY WT.	TOTAL FE
#652		7.92	106%	2.2527	101.4		2.2848
	L1	.992	59%	*.1012	55.2		*.0559
	L2	1.000	35%				
	R1	.992	45%				
	R2	.760	49%				
	R3	1.280	44%				
	R4	.768	28%				
	R5	1.464	43%				
	R6	.984	58%				

* This represents total for fetal livers

STOCK DIET 19 DAY

MOTHER	FETUS	RED CELLS	HB	LIVER WT.	MG. FE %	DRY WT.	TOTAL FE
#610		4.8	85%	2.73	73.5		2.00655
	L1	1.86	86%	*.4702		104.35	*.43256
	L2	1.76	90%				
	L3	1.79	90%				
	L4	1.49	54%				
	L5	1.29	81%				
	L6	1.09	84%				
	L7	1.08	59%				
	R1	1.62	83%				
	R2	1.40	78%				
	R3	1.34	93%				
	R4	1.45	57%				
	R5	1.27	80%				
#622		7.54	100%	1.98	79.0		1.56420
	L1	1.41	75%	*.175		77.26	*.1352
	L2	1.36	73%				
	L3	1.15	65%				
	R1	.92	62%				
	R2	1.13	84%				
	R3	1.80	86%				
	R4	.96	75%				
#626		6.30	88%	2.37	105.6		2.50272
	L1	1.60	50%	*.1614		150.20	*.2424
	L2	1.42	59%				
	L3	1.18	57%				
	L4	1.31	79%				
	R1	.98	62%				
	R2	1.14	60%				
	R3	1.72	72%				
	R4	1.55	63%				
#644		5.13	105%	2.50	80.0		2.00000
	L1	1.10	58%	*.1827		34.71	*.0625
	L2	2.02	56%				
	L3	1.42	71%				
	R1	1.47	64%				
	R2	-	-				
	R3	1.88	71%				
	R4	1.49	51%				
	R5	1.87	67%				
	R6	1.70	68%				
#645		5.52	99%	1.82	55.5		1.01010
	L1	1.67	65%	*.175		87.88	*.1538
	L2	1.91	66%				
	L3	1.34	64%				
	L4	1.00	54%				
	R1	1.80	66%				
	R2	1.84	65%				
	R3	1.39	51%				
	R4	1.52	62%				
	R5	1.27	61%				

* This represents total for fetal livers

MOTHER	FETUS	RED CELLS	HB	LIVER WT.	MG. FE % DRY WT.	TOTAL FE
#613		7.28	103%	2.33	101.3	2.36029
	L1	2.16	61%	*.4736	87.3	*.41366
	L2	1.40	101%			
	L3	1.31	98%			
	L4	1.24	90%			
	R1	1.31	84%			
	R2	1.52	-			
	R3	2.232	-			
#614		7.18	100%	1.66	105.6	1.75300
	One resorbed					
#618		6.07	85%	1.82	87.2	1.58700
	L1	Removed, too small for recording, mother returned for few more days				
	L2	2.09	79%	*.3603	104.8	*.3750
	L3	1.65	71%			
	L4	1.27	-			
	R1	1.21	88%			
	R2	1.22	78%			
	R3	1.33	51%			
635		8.51	95%	1.825	124.0	2.26300
	L1	2.60	80%	*.2659	70.5	*.1876
	L2	2.03	96%			
	R1	1.71	77%			
	R2	1.83	70%			
	R3	1.69	73%			
	R4	1.31	50%			
643		6.69	85%	2.410	68.5	1.65085
	L1,2	1.05	38%	*.1891	116.2	*.22078
	L3,4	1.10	55%			
	L5,6	1.46	50%			
	L7,8	1.53	73%			
	L9	1.44	69%			
651	R1	9.04 1.75	98% 62%	-	-	-
	L1	1.616	56%	*.3037	29.1	*.0885
	L2	2.208	64%			
	L3	1.544	80%			
	L4	1.964	69%			
	R1	2.296	78%			
	R2	2.616	89%			
	R3	1.520	62%			

* This represents total for fetal livers

STOCK DIET 21 DAY

MOTHER	FETUS	RED CELLS	HB	LIVER WT.	MG. FE	% DRY WT.	TOTAL FE
#642		-	-	2.19	68.7		1.40453
	L1	1.824	62%	*.290		86.9	*.25201
	L2	1.312	72%				
	L3	1.640	51%				
	R1	.624	42%				
	R2	.760	55%				
	R3	2.000	81%				
	R4	.816	61%				
	R5	1.392	57%				
#647		6.06	102%	2.03	62.5		1.26875
	L1	1.30	80%	*.3078		99.41	*.03070
	L2	2.19	66%				
	R1	2.22	79%				
	R2	2.07	78%				
	R3	1.63	61%				
#648		6.89	98%	2.00	81.1		1.62200
	L1	1.56	78%	*.4095		50.5	*.02068
	L2	1.58	76%				
	L3	1.47	80%				
	R1	1.88	86%				
	R2	1.71	64%				
#649		7.19	100%	1.95	93.8		1.82910
	L1	1.55	75%	*.1616		84.16	*.01360
	R1	1.83	52%				
	R2	1.73	62%				
#650		7.44	95%	2.25	49.7		1.11825
	L1	2.42	95%	-		-	-
	L2	1.93	77%				
	L3	3.04	102%				
	L4	2.33	86%				
	R1	2.63	98%				
	R2	3.19	94%				
	R3	2.82	91%				
	R4	2.30	61%				

* This represents total for fetal livers

2% YEAST DIET 14 DAY

MOTHER	FETUS	RED CELLS	HB	LIVER WT.	MG. FE	% DRY WT.	TOTAL FE
#711		5.41	97%	1.5924	147.0		2.3108
	L1,2	.035	4%	*.0174	45.5		*.00764
	L3,4	.055	3%				
	L5,6	.100	2%				
	R1,2	.080	6%				
	R3,4	.120	5%				
#708		7.49	93%	1.8938	128.1		2.4241
	L1,3	.32	10%	*.0211	31.5		*.00666
	L2 Resorbed						
	R1,2,3	.110	9%				
#716		6.92	92%	1.5188	147.1		2.2342
	L1,2,3	.10	5%	*.0145	19.3		*.0028
	R1,2,3,4	.09	4%				
#666		7.29	90%	1.5480	80.0		1.2380
	L1,2	.16	8%	*.0322	48.5		*.0156
	L3,R1	.10	5%				
	R2,3,4	.11	5%				
#671		7.98	107%	1.3345	117.6		1.5680
	L1,2	.08	3%	*.0429	24.7		*.0106
	L3,4	.09	2%				
	L5,6	.08	2%				
	R1,2,3	.12	3%				

* This represents total for fetal livers

2% YEAST DIET 15 DAY

MOTHER	FETUS	RED CELLS	HB	LIVER WT.	MG. FE	% DRY WT.	TOTAL FE
#714		6.87	96%	1.5071	138.9		2.09336
	L1,2	.17	13%	*.0448		35.1	*.01575
	L3,4	.23	11%				
	R1 Resorbed						
	R2,3,4	.16	10%				
#721		8.42	101%	1.8316	87.2		1.59720
	L1,2	.22	9%	*.0474		32.9	*.0156
	L3,4	.36	10%				
	L5 Resorbed						
	L6,R1	.16	11%				
	R2 Resorbed						
#718		7.23	104%	1.5923	129.2		2.05720
	L1,2	.17	11%	*.0490		38.8	*.01904
	L3,4	.34	15%				
	R1,2	.35	11%				
	R3	.35	12%				
	R4 Resorbed						
#669		6.96	100%	1.6002	99.0		1.58400
	L1,2	.22	10%	*.0768		39.2	*.02976
	L3,4	.16	3%				
	R1,2	.17	5%				
	R3,4	.10	2%				
#675		6.38	105%	1.8227	133.3		2.42800
	L1,2	.13	4%	*.0951		41.2	*.0392
	L3,R1	.08	3%				
	R2,3	.10	4%				
	R4,5	.10	5%				

* This represents total for fetal livers

2% YEAST DIET 16 DAY

MOTHER	FETUS	RED CELLS	HB	LIVER WT.	MG. FE	% DRY WT.	TOTAL FE
#700		7.10	120%	2.1334	98.0		2.14200
	L1	.50	37%	*.0805(?)	141.1(?)		*1.136(?)
	L2	.92	32%				
	L3	1.01	40%				
	L4	1.08	30%				
	L5	.61	21%				
	R1	.91	52%				
	R2	1.09	37%				
#696		6.80	107%	2.1926	75.8		1.66199
	L1,2	.64	26%	*.0625		80.0	*.04998
	L3,4	.87	32%				
	L5,6	.50	28%				
	R1,2	.67	30%				
#695		6.57	110%	1.7141	76.9		1.31814
	L1	.35	20%	*.035		88.8	*.03108
	L2	Resorbed					
	R1	.50	19%				
	R2	Resorbed					
	R3	.32	9%				
	R4	.20	5%				
	R5	Resorbed					
	R6	.52	25%				
#676		6.97	145%(?)	1.5532	137.0		2.12800
	L1,2	.12	10%	*.0512		17.2	*.00882
	R1,2	.27	13%				
	R3,4	.17	6%				
#677		7.92	116	1.6504	128.2		2.11500
	L1,R1	.15	5%	*.0494		28.9	*.01436
	R2,3	.27	12%				
	L2,3	Resorbed					

* This represents total for fetal livers

(?) These seemed so aberrant that they were omitted from the averages. It should be remembered, however, that these values may be alright in view of blood concentration occurring in Vitamin B deficiency.

2% YEAST DIET 17 DAY

	MOTHER	FETUS	RED CELLS	HB	LIVER WT.	MG. FE	% DRY WT.	TOTAL FE
#701		6.17	95%	2.0466	84.0			1.71900
	L1	Resorbed						
	L2		2.66	77%	*.2833	102.9		*.2917
	L3		1.63	67%				
	L4		2.36	60%				
	R1		2.41	75%				
	R2		2.36	72%				
	R3		1.62	50%				
	R4		1.69	64%				
#694		8.38	107%	2.3931	86.05			2.05926
	L1	Resorbed						
	L2	Resorbed						
	R1		1.21	35%	*.0256	95.9		*.02454
	R2		1.24	39%				
	R3	Resorbed						
#699		7.82	114%	1.3974	122.7			1.71460
	L1	Resorbed						
	L2	Resorbed						
	L3		1.32	47%	*.0671	99.0		*.06643
	L4		1.01	38%				
	R1		1.38	45%				
	R2		1.50	46%				
	R3		1.27	40%				
#673		7.736	113%	1.3281	190.4			2.52500
	L1,2		.176	19%	*.0423	59.1		*.02500
	L3,4		.160	13%				
	R1		.200	8%				
	R2		.192	4%				
	R3	Resorbed						
#678		8.360	109%	1.3477	158.4			2.13000
	L1,2		.408	15%	*.0318	69.8		*.02222
	L3		.360	14%				
	L4		.240	12%				
	L5	Resorbed						
	R1		.304	15%				
	R2	Resorbed						
	R3	Resorbed						

* This represents total for fetal livers

2% YEAST DIET 18 DAY

OTHER FETUS	RED CELLS	HB	LIVER WT.	MG. FE % DRY WT.	TOTAL FE
697	7.25	105%	2.2740	113.6	2.58340
L1	.84	19%	*.0784	86.7	*.0680
L2	Resorbed				
L3	1.05	30%			
L4	.7	24%			
R1	.5	20%			
R2,3	.71	14%			
R4,5	.49	22%			
R6	.55	15%			
R7	.41	25%			
704	7.24	106%	1.8300	104.2	1.90680
L1	1.90	57%	*.0867	119.3	*.10336
L2	1.55	30%			
L3	.88	-			
717	4.89	92%	1.6661	102.0	1.69942
L1	.67	42%	*.0883	108.7	*.09600
L2	Resorbed				
L3	.71	33%			
R1	.96	49%			
R2	.95	41%			
R3	.77	40%			
R4	.86	30%			
R5	1.03	48%			
R6	.70	35%			
670	7.656	108%	1.3671	123.0	1.68100
L1	.400	21%	*.0668	62.3	*.04165
L2	.370	19%			
L3	.73	31%			
L4	.60	35%			
R1	.51	17%			
R2	.64	16%			
R3	.57	-			
R4	.64	31%			
654	6.310	100%	1.5399	79.0	1.21700
L1	1.17	33%	*.0812	81.5	*.06620
L2	1.04	10%			
L3	1.18	31%			
R1	1.02	34%			
R2	1.80	39%			
R3	.66	39%			
R4	1.02	25%			

* This represents total for fetal livers

2% YEAST DIET 19 DAY

MOTHER	FETUS	RED CELLS	HB	LIVER WT.	MG. FE	% DRY WT.	TOTAL FE
#698		6.02	110%	1.8215	65.2		1.18762
	R1	2.60	75%	*.1886	103.2		*.1948
	R2	1.93	70%				
	R3	2.28	74%				
	R4	1.62	70%				
	R5	2.10	65%				
#715		7.09	101%	1.6346	125.0		2.04320
	L1	Resorbed					
	L2	1.21	62%	*.0827	121.9		*.1008
	L3	1.18	-				
	R1	1.82	73%				
	R2	Resorbed					
	R3	Resorbed					
#722		8.07	99%	1.9364	87.2		1.68850
	L1	1.6	54%	*.1534	97.79		*.1500
	L2	1.7	34%				
	L3	1.45	32%				
	R1	.58	32%				
	R2	1.32	51%				
	R3	1.33	51%				
#668		6.82	109%	1.4570	100.0		1.45700
	L1	1.51	45%	*.1061	84.20		*.0893
	R1	1.42	35%				
	R2	1.14	39%				
	R3	1.26	34%				
	R4	1.39	38%				
	R5	1.07	38%				
	R6	1.01	44%				
#674		6.12	107%	1.7230	147.0		2.53500
	L1	1.69	38%	*.1096	66.1		*.0724
	L2	.81	10%				
	L3	1.35	12%				
	L4	.89	29%				
	L5	1.08	16%				
	R1	1.46	49%				

* This represents total for fetal livers

2% YEAST DIET 20 DAY

MOTHER	FETUS	RED CELLS	HB	LIVER WT.	MG. FE	% DRY WT.	TOTAL FE
709		6.44	115%	2.5547	68.8		1.7576
	L1	1.85	83%	*.3445	89.4		*.3081
	L2	1.54	70%				
	L3	2.49	69%				
	L4	1.87	79%				
	L5	1.86	50%				
	L6	2.31	79%				
	L7	2.59	77%				
	R1	2.24	78%				
712		6.68	96%	2.1336	64.0		1.3655
	L1	2.81	85%	*.474	96.6		*.4580
	L2	2.00	83%				
	L3	2.39	79%				
	L4	2.41	78%				
	L5	2.15	69%				
	R1	1.74	50%				
	R2	1.93	73%				
	R3	1.76	69%				
	R4	1.60	-				
713		5.06	62%	1.9716	46.0		.9069
	L1	1.93	80%	*.2965	116.0		*.3462
	L2	1.57	60%				
	L3	1.47	70%				
	L4	1.61	71%				
	R1	1.85	81%				
	R2	1.12	55%				
	R3	1.89	72%				
	R4	1.14	63%				
	R5	1.09	60%				
653		8.35	108%	1.5999	44.4		.7100
	L1	2.21	67%	*.1738	-		-
	L2	1.70	62%				
	L3	1.01	60%				
	L4	1.71	42%				
	R1	1.73	59%				
	R2	1.89	60%				
	R3	1.57	65%				
655		5.61	85%	1.7383	96.8		1.6830
	L1	1.99	60%	*.1927	44.6		*.0859
	L2	1.93	61%				
	R1	2.18	53%				
	R2	1.80	55%				
	R3	1.79	59%				
	R4	2.26	51%				

* This represents total for fetal livers

2% YEAST DIET 21 DAY

MOTHER	FETUS	RED CELLS	HB	LIVER WT.	MG. FE	% DRY WT.	TOTAL FE
# 710		5.91	79%	2.7026	40.0		1.08104
	L1	1.89	77%	*.6408		92.2	*.5913
	L2	1.68	88%				
	L3	1.84	81%				
	L4	2.11	72%				
	L5	2.08	77%				
	L6	2.06	70%				
	R1	2.09	73%				
	R2	.91	82%				
	R3	1.38	62%				
	R4	1.58	83%				
#719		6.99	100%	1.7550	57.5		1.00910
	L1	1.23	50%	*.4427		74.45	*.3296
	L2	1.24	54%				
	L3	1.10	63%				
	L4	1.52	51%				
	R1	1.33	60%				
	R2	1.87	61%				
	R3	Resorbed					
	R4	1.48	64%				
#672		6.09	102%	1.6040	90.0		1.44400
	L1	2.21	60%	*.4789		66.80	*.3200
	L2	1.43	57%				
	L3	.99	55%				
	L4	1.71	60%				
	L5	1.47	62%				
	R1	.98	80%				
	R2	.99	85%				
	R3	1.70	60%				
	R4	1.51	52%				
#667		5.61	100%	2.3393	46.3		1.11200
	L1	1.84	60%	*.3674		51.8	*.19035
	L2	2.18	53%				
	L3	1.51	51%				
	L4	2.20	65%				
	R1	2.55	68%				
	R2	1.96	63%				
	R3	2.20	72%				
	R4	2.02	71%				
#707		6.11	110%	2.7224	83.3		2.26770
	L1	2.04	75%	*.3666		75.72	*.2776
	L2	2.62	81%				
	R1	2.08	84%				
	R2	1.99	78%				
	R3	2.00	89%				
	R4	1.55	62%				
	R5	2.12	74%				

This represents total for fetal livers

8% YEAST DIET 14 DAY

THER FETUS	RED CELLS		HB	LIVER WT.	MG. FE% DRY WT.	TOTAL FE
8	6.87	115%		1.883	98.7	1.858
L 1,2	.04		2%	*.024	46.0	*.011
L 3,4,5	.08		4%			
R 1,2	.24 (?)		11% (?)			
R 3,4,5	.07		3%			
9	6.70	98%		2.055	84.3	1.732
L 1,2	.07		2%	*.035	41.5	*.015
L 3,4	.13		6%			
L 5,6	.08		4%			
R 1,2,3	.11		3%			
0	6.38	107%		1.827	161.2	2.945
L 1,2	.13		4%			
L 3,4	.09		5%	*.035	54.5	*.019
L 5,6	.11		3%			
R 1,2	.05		4%			
R 3,4,5	.07		5%			
2	7.05	98%		1.557	115.4	1.796
L 1,2	.21		7%	.003	88.2	.0024
L 3,4	.11		10%	.0025	115.4	.0046
L 5,6,7	.13		8%	(L6) .003	75.0	.0020
				(L5) .003	164.8	.0018
				(L7) .0035	105.6	.0036
R 1,2	.13		4%	(R1) .0035	57.3	.0020
				(R2) .0035	81.1	.0028
8	6.14	89%		1.702	90.9	1.547
L 1,2,3,4	.09		5%	(L1) .004	50.0	.0020
				(L2) .0035	57.7	.0020
				(L3) .0035	55.5	.0019
				(L4) .004	84.7	.0033
R 1,2	.07		8%	.004	75.0	.0030
R 3,4,5	.13		3%	(R3)		
				(R4) .005	57.8	.0028
				(R5) .0035	78.9	.0027

This represents total for fetal livers.

8% YEAST DIET 15 DAY

OTHER	FETUS	RED CELLS		HB	LIVER WT.	MG. FE% DRY WT.	TOTAL FE
41		9.52	100%		1.864	109.5	2.041
	L 1,2	.08		5%	*.054	40.8	*.021654
	L 3,4,5	.124		9%			
	R 1,2	.308		14%			
	R 3,4	.180		12%			
26		8.56	105%		2.081	125.0	2.601
	L 1,2,3	.132		8%	*.038	25.8	*.0098
	R 1,2	.112		5%			
	R 3,4,5	.110		7%			
37		5.34	101%		2.958	113.6	3.360
	L 1,2	.07		5%	*.062	51.3	*.0318
	L 3,4	.08		3%			
	L 5,6	.08		7%			
	R 1,2,3	.19		10%			
43		6.16	111%		2.126	84.3	1.792
	L 1,2	.14		6%	(11) .012	58.8	.0070
					(12) .011	73.2	.0080
	L 3,4	.11		10%	(13) .009	95.5	.0085
					(14) .011	72.5	.0079
	L 5,6	.20		17%	(15) .013	56.3	.0073
					(16) .011	98.7	.0108
	R 1,2	.20		20%	(21) .012	82.9	.0099
					(22) .011	115.4	.0126
	R 3,4	.19		21%	(23) .012	109.5	.0131
					(24) .011	82.9	.0091
31		8.25	108%		3.032	133.9	4.059
	L 1,2	.14		8%	(11) .007	64.9	.0045
					(12) .006	103.4	.0062
	L 3,4	.06		4%	(13) .006	103.6	.0062
					(14) .006	98.7	.0059
	L 5 Resorbed						
	R 1,2,6	.21		18%	(21) .004	130.7	.0052
					(22) .006	107.5	.0064
					(26) .004	145.7	.0058
	R 3,4,5 Resorbed						

This represents total for fetal livers.

8% YEAST DIET 16 DAY

OTHER	FETUS	RED CELLS		HB	LIVER WT.	MG. FE/	DRY WT.	TOTAL FE
31		5.99	95%		1.688	84.3		1.4229
	L 1	.35		20%	.006		108.1	.0064
	L 2 Resorbed							
	L 3	.43		25%	.005		77.7	.0038
	L 4	.30		23%	.005		96.7	.0049
	R 1	.27		15%	.006		83.8	.0050
	R 2	.26		15%	.006		84.3	.0050
	R 3	.27		13%	.005		89.8	.0044
28		5.41	100%		2.153	115.4		2.485
	L 1	.19		20%	*.032		77.7	*.0243
	L 2	.43		22%				
	L 3	.17		15%				
	R 1	.22		12%				
	R 2	.21		22%				
	R 3	.25		22%				
	R 4	.25		23%				
	R 5	.23		15%				
	R 6	.36		24%				
64		7.45	101%		2.206	163.0		3.5957
	L 1,2	.20		21%	*.099		71.4	*.0702
	L 3,4	.16		20%				
	L 5,6,7	.23		37%				
	R 1,2	.22		21%				
	R 3,4	.18		28%				
	R 5,6	.30		34%				
65		7.61	107%		2.115	103.4		2.1869
	L 1,2	.30		29%	(L1).008		78.5	.0062
					(L2).010		89.3	.0089
	L 3,4	.24		29%	(L3).006		115.4	.0069
					(L4).006		113.0	.0067
	L 5,6	.32		44%	(L5).005		72.1	.0036
					(L6).005		104.9	.0052
	R 1,2	.30		31%	(R1).008		88.2	.0072
					(R2).007		102.0	.0071
	R 3,4	.25		34%	(R3).005		96.0	.0049
					(R4).009		103.4	.0093
66		7.76	104%		1.850	135.1		2.4993
	L 1,2	.28		28%	* .083		37.5	*.0308
	L 3,4	.36		33%				
	R 1,2	.33		30%				
	R 3,4	.28		39%				
	R 5,6,7	.27		29%				

* This represents total for fetal livers.

8% YEAST DIET 17 DAY

OTHER	FETUS	RED CELLS		HB	LIVER WT.	MG. FE% DRY WT.	TOTAL FE
30		6.45	100%		2.102	187.5	3.9412
	L1	.63		21%			
	L2	.48		24%			
	L3	.45		21%			
	L4	.66		27%			
	L5	.59		31%			
	L6	.59		37%			
	R1	.56					
	R2	.44		25%			
	R3	.62		31%			
	R4	.66		31%			
	R5	.53		32%			
32		5.75	98%		1.409	68.2	.9609
	L1	.51		28%	.004	132.4	.0052
	L2	.58		19%	.007	75.0	.0052
	R1	Resorbed					
	R2	.54		22%	.006	86.7	.0052
	R3	.38		18%	.006	79.1	.0047
	R4	.55		17%	.006	85.7	.0051
	R5	Resorbed					
33		5.05	99%		1.670	105.6	1.7635
	L1	.75		40%	*.094	104.9	*.0981
	L2	1.01		32%			
	L3	.56		28%			
	L4	.89		34%			
	L5	.70		30%			
	L6	.66		31%			
	L7	.56		29%			
	R1	.84		28%			
	R2	.89		22%			
68		6.04	96%		1.624	104.1	1.6905
	L1	.51		4%	*.045	96.8	*.0344
	L2	.41		25%			
	L3	.50		25%			
	L4	.32		34%			
	R1	Resorbed					
	R2	.38		19%			
	R3	.30		20%			
	R4	.55		30%			
	R5	.47		29%			
74		7.75	109%		2.016	105.6	2.1288
	L1	.57		25%	.008	92.6	.0074
	L2	.35		14%	.007		
	L3	.65		26%	.009	153.0	.0137
	L4	.60		25%	.008	82.0	.0065
	R1	.63		32%	.009	99.3	.0089
	R2	.66		35%	.007	99.5	.0069
	R3	.47		38%	.009	105.6	.0094
	R4	.59		30%	.009	115.4	.0103
	R5	.41		41%	.008	83.3	.0066
	R6	.27		22%	.007	96.1	.0067

* This represents total for fetal livers.

8% YEAST DIET 18 DAY

OTHER	FETUS	RED CELLS		HB	LIVER WT.	MG. FE% DRY WT.	TOTAL FE
21		5.89	99%		2.098	49.5	1.0385
	L1	.65		28%	*.128	50.5	*.0639
	L2	.77		34%			
	L3	.92		35%			
	L4	.92		36%			
	R1	.90		40%			
	R2	1.09		35%			
	R3	.86		33%			
	R4	.86		43%			
	R5	1.24		54%			
35		5.96	105%		1.930	168.5	3.2520
	L1	.92		44%	*.143	105.6	*.1494
	L2	1.20		48%			
	L3	1.20		47%			
	L4	1.19		44%			
	R1	1.16		43%			
	R2	.79		52%			
	R3	1.06		44%			
	R4	.99		46%			
	R5	1.12		55%			
67		6.66	110%		1.791	85.2	1.5259
	L1	1.60		60%	*.109	64.5	*.0693
	R1	1.19		43%			
	R2	.89		39%			
	R3	.93		48%			
	R4	1.12		38%			
	R5	.98		38%			
	R6	.82		46%			
69		7.65	98%		2.000	182.9	3.6580
	L1	.52		39%	.008	87.2	.0069
	L2	.93		44%	.011	130.3	.0143
	L3	.70		Clotted	.009	88.2	.0079
	L4	.47		42%	.009	128.1	.0115
	L5	.61		46%	.011	137.6	.0151
	R1	.49		48%	.011	115.4	.0126
	R3	.78		41%	.012	118.1	.0141
	R2	.39		32%	.012	104.9	.0125
75		7.49	104%		1.518	127.0	1.9278
	R1	.79		35%	.009	97.6	.0087
	R2	1.10		46%	.011	98.5	.0108
	R1	1.14		38%	.011	111.1	.0122
	L2	.90		44%	.011	111.1	.0122
	L3	.64		32%	.010	307.6	.0307
	L4	.98		51%	.008	112.4	.0089

* This represents total for fetal livers.

8% YEAST DIET 19 DAY

MOTHER	FETUS	RED CELLS	HB	LIVER WT.	MG. FE	% DRY WT.	TOTAL FE
#23		6.64	102%	2.213	170.4		3.7709
	L1	1.02	51%	.016	167.6		.0268
	L2	1.12	42%	.011	98.0		.0107
	L3	1.29	40%	.016	87.9		.0140
	L4	1.16	40%	.010	80.0		.0080
	R1	1.02	35%	.017	125.0		.0212
	R2	.84	28%	.023	75.0		.0172
	R3	.86	38%	.013	105.6		.0137
#53		6.77	99%	2.111	92.2		1.9463
	L1	1.172	34%	*.1800		65.5	.1239
	L2	.984	35%				
	L3	1.192	45%				
	R1	1.192	31%				
	R2	1.052	41%				
	R3	1.088	35%				
	R4	1.092	46%				
#54		8.52	96%	1.741	125.0		2.1762
	L1	1.252	61%	*.182		53.6	.0972
	L2	1.028	39%				
	L3	1.172	45%				
	R1	1.144	49%				
	R2	1.096	46%				
	R3	1.176	51%				
	R4	1.224	47%				
	R5	1.192	49%				
	R6	1.184	45%				
55		6.52	94%	1.953	56.5		1.1024
	L1	1.608	49%	*.188		94.9	*.1773
	L2	1.448	50%				
	L3	1.448	47%				
	L4	1.146	37%				
	R1	1.312	45%				
	R2	1.268	46%				
	R3	1.324	52%				
	R4	1.288	54%				
	R5	1.368	51%				
70		7.10	95%	2.395	142.8		3.4200
	L1	1.81	57%	.030		82.0	.0246
	L2	1.61	44%	.023		112.7	.0259
	L3	1.45	42%	.026		77.7	.0202
	R1	1.62	37%	.026		79.4	.0206
	R2	1.44	55%	.021		85.7	.0179
	R3	1.23	47%	.020		82.4	.0164
	R4	1.36	46%	.029		76.9	.0223
	R5	1.31	52%	.024		87.2	.0209

This represents total for fetal livers

8% YEAST DIET 20 DAY

MOTHER	FETUS	RED CELLS	HB	LIVER WT.	MG. FE	% DRY WT.	TOTAL FE
49		8.456	95%	2.639	94.9		2.5044
	L1	1.568	70%	*.355	93.2		*.330
	L2	1.631	64%				
	L3	1.492	57%				
	L4	Resorbed					
	R1	1.520	63%				
	R2	1.592	55%				
	R3	1.690	49%				
	R4	1.564	54%				
	R5	1.530	63%				
	R6	1.528	66%				
	R7	1.576	56%				
50		6.208	112%	1.718	62.5		1.0737
	L1	1.484	45%	.032	106.3		*.1548
	L2	1.828	49%	.029	92.0		
	L3	1.208	50%	.029	93.8		
	L4	1.484	48%	.026	83.3		
	L5	Resorbed					
	R1	1.714	41%	.032	66.1		
	R2	1.182	38%	.032	74.6		
56		7.664	99%	2.190	71.4		1.5636
	L1	1.952	52%	*.400	46.7		*.186
	R1	1.784	65%				
	R2	1.332	45%				
	R3	1.608	52%				
	R4	1.376	50%				
	R5	1.316	45%				
	R6	1.604	46%				
	R7	1.624	61%				
	R8	1.104	46%				
	R9	1.392	57%				
62		6.584	90%	1.646	82.4		1.3563
	L1	1.640	43%	.023	66.1		.0152
	L2	1.560	37%	.021	80.2		.0168
	L3	1.680	40%	.021	82.0		.0172
	L4	1.520	55%	.014	86.2		.0120
	R1	1.180	42%	.023	86.7		.0199
	R2	1.492	56%	.025	127.0		.0337
	R3	1.568	clotted	.022	25.4		.0055
	R4	1.692	61%				
	R5	1.472	56% (R4,5)	.032	72.8		.0116
63		6.160	98%	2.441	142.8		3.4857
	L1	1.425	58%	*.294	77.7		*.2286
	L2	1.450	75%				
	L3	1.510	67%				
	L4	1.385	56%				
	L5	1.580	74%				
	L6	1.485	64%				
	R1	1.330	66%				
	R2	1.500	46%				
	R3	1.810	60%				

*This represents total for fetal livers

8% YEAST DIET 21 DAY

MOTHER	FETUS	RED CELLS	HB	LIVER WT.	MG. FE	% DRY WT.	TOTAL FE
#51		5.504	103%	2.170	37.4		.8115
	L1	2.100	65%	*.470	82.9		*.3888
	L2	1.788	60%				
	L3	1.950	72%				
	L4	1.896	64%				
	L5	1.820	66%				
	L6	1.712	58%				
	L7	1.920	80%				
	L8	1.752	56%				
	R1	2.088	61%				
#29		5.272	95%	1.735	73.9		1.2821
	L1	1.704	60%	.045	133.9		.0602
	L2	1.748	57%	.045	103.4		.0465
	R1	1.836	56%	.045	60.3		.0271
	R2	1.868	72%	.047	43.9		.0206
	R3	1.672	50%	.047	79.0		.0371
	R4	2.024	59%	.038	125.0		.0475
	R5	Resorbed					
#52		7.792	82%	2.112	93.8		1.9810
	L1	1.984	56%	.048	89.3		.0428
	L2	1.756	49%	.037	150.0		.0555
	L3	1.924	54%	.049	100.0		.0490
	L4	1.292	44%	.043	140.1		.0602
	R1	1.244	51%	.053	200.0		.1060
	R2	1.628	53%	.041	86.2		.0353
	R3	1.500	55%	.041	140.1		.0574
	R4	1.736	53%	.057	46.9		.0267
#71		5.640	82%	2.328	111.1		2.5864
	L1	2.08	52%	*.381	60.2		*.2296
	L2	1.89	51%				
	L3	2.03	52%				
	R1	1.80	55%				
	R2	1.99	65%				
	R3	2.03	67%				
	R4	1.84	50%				
#72		6.490	83%	1.987	124.0		2.4638
	L1	2.33	70%	*.603	89.3		*.538
	L2	1.94	72%				
	L3	1.68	60%				
	L4	2.17	75%				
	L5	1.79	71%				
	L6	1.53	70%				
	L7	2.09	80%				
	L8	1.95	77%				
	R1	2.00	79%				
	R2	1.69	76%				

* This represents total for fetal livers

8% YEAST DIET 22 DAY

OTHER FETUS	RED CELLS	HB	LIVER WT.	MG. FE	% DRY WT.	TOTAL FE
57	5.848	90%	1.978	125.0	2.4725	
L1	1.968	67%	.070	93.2		.0652
L2	1.960	60%	.089	70.1		.0623
L3	1.932	74%	.085	74.6		.0634
L4	2.000	68%	.094	89.3		.0839
L5	1.820	84%	.087	49.0		.0426
R1	1.896	64%	.062	93.8		.0581
58	7.410	106%	2.220	147.1	3.2656	
L1	1.72	74%	*.476	107.1		*.509
L2	1.85	83%				
L3	2.43	81%				
L4	2.17	112%				
R1	2.33	68%				
R2	1.99	77%				
R3	2.05	73%				
R4	1.56	81%				
R5	1.58	80%				
R6	2.05	90%				
59	7.350	110%	2.406	51.0	1.2270	
L1	2.14	70%	.028	137.9		.0386
L2	1.17	77%	.052	94.9		.0493
L3	1.81	73%	.048	85.2		.0408
L4	2.07	68%	.048	98.4		.0423
R1	1.91	70%	.039	108.7		.0423
R2	1.03	60%	.040	120.0		.0480
R3	.59	25%	.043	200.0		.0860
R4	1.93	85%	.044	104.9		.0461
R5	1.87	66%	.043	118.1		.0507
60	6.770	102%	2.385	230.0	5.4855	
L1	1.88	40%	*.404	90.9		*.3670
L2	2.02	35%				
L3	2.00	46%				
L4	1.71	43%				
R1	1.95	54%				
R2	2.07	49%				
R3	1.26	40%				
R4	1.72	50%				
R5	1.81	52%				
R6	1.40	38%				
73	7.490	97%	2.741	67.0	1.8364	
L1	2.06	79%	*.603	116.2		*.6996
L2	2.10	77%				
L3	2.13	80%				
L4	1.84	76%				
L5	1.91	79%				
R1	1.79	74%				
R2	1.76	68%				
R3	1.71	72%				
R4	1.59	72%				
R5	1.51	75%				
R6	1.44	71%				
R7	1.25	68%				

This represents total for fetal livers