Characteristic Aspects of Iron Metabolism in Piglets

By Kou FURUGOURI

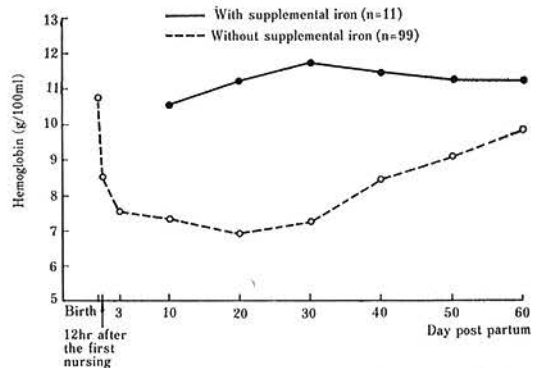Department of Animal Physiology, National Institute of Animal Industy

In recent years, confinement rearing of a large number of sows is becoming popular, aiming at labor saving and hygiene. As a result, piglets are apt to suffer from trace element deficiency, particularly iron, being without contact with soil as a supply source of minerals. McGowan and Crichton (1923)[1] revealed that piglet anemia is caused by iron deficiency, and since then many studies on preventive measures have been carried out to meet practical demand. However, effect of iron treatments practiced as preventive measures is not fully understood on theoretical basis because mode of occurrence of anemia is still unknown due to lack of basic information on iron absorption and metabolism in piglets.

The present study was carried out to make clear the mode of occurrence of piglet anemia in relation to iron metabolism.

Note: Supplemental iron group was injected 1 ml of iron-dextran (100mg iron) intramuscularly at 3 and 10 days of age, respectively. Pigs were weaned at 30 days of age.

Fig. 1. Changes in hemoglobin concentration from birth to 60 days of age

Note: Supplemental iron group was injected 1 ml of iron-dextran (100 mg iron) intramuscularly at 3 and 10 days of age, respectively. Pigs were weaned at 30 days of age.

Changes in hemoglobin and stored iron[2]-[6]

At the time of birth, hemoglobin content of piglets was at the same level as normal value of adult, but with ingesting maternal colostrum it decreased rapidly, reaching 70% of the original value at 3 days of age and further continued to decrease (Fig. 1).

Intramuscular injection of 1 ml of iron-dextran (100 mg iron) given at 3 and 2 days of age restored the hemoglobin to the value of birth and that level was maintained throughout the nursing period. With un-injected piglets, hemoglobin turned to increase gradually only after the supply of iron from creep feed began.

Such a rapid decrease in hemoglobin occurring immediately after birth has a close relation to mortality of newborn piglets, and even during the nursing period growth retardation takes place if hemoglobin level lower than 8 g/dl lasts long.

At birth, serum protein level is about 3.0 g/dl, showing hypoproteinemia, but as piglets absorb intact maternal colostrum from gastrointestinal tracts, serum protein reaches the level of adult (6.0–7.0 g/dl) at 12 hr after the first nursing. This nonselective absorption ceases 10 to 36 hr after the first nursing. During that period, immunoglobulin, consist-

ing 50% of protein of maternal colostrum, is absorbed by piglets, and which gives them disease-resistance.

On the other hand, a rapid absorption of colostrum into piglets' blood and resultant increase of plasma volume induces physiological anemia, followed by a typical iron deficiency anemia caused by an increasing demand of iron associated with a rapid growth of piglets.

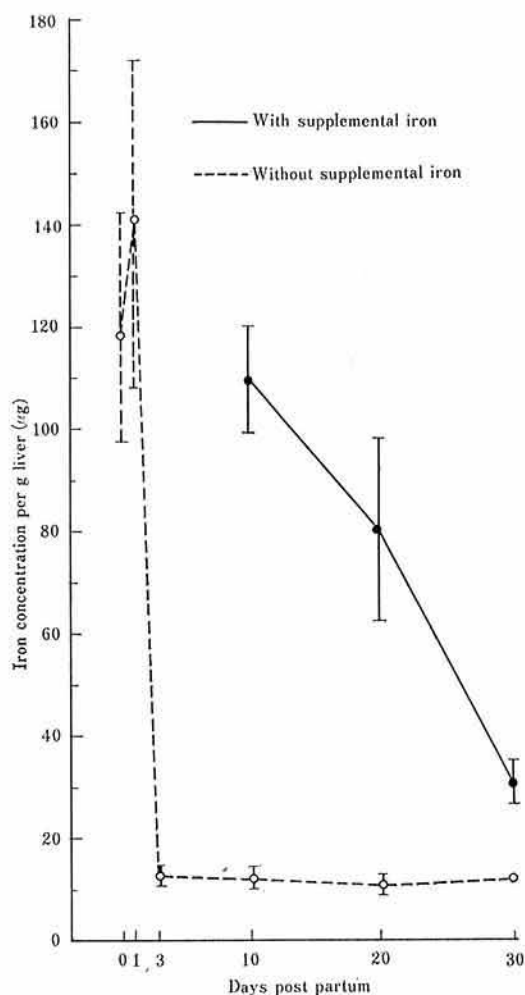In this connection, iron store in the liver was examined. As shown in Fig. 2, stored

iron, abundant at birth, began to decrease at 3 days of age and disappeared at 10 days of age. By injecting iron-dextran (100 mg iron) at 3 days of age, the iron store was restored to the original level at 10 days of age, but marked mobilization occurred after 20 days of age. Thus, iron store was exhausted in a short time, inducing iron deficiency anemia, although there was some time lag between trends of iron store and of hemoglobin. Such a remarkable mobilization was not observed with other minerals stored in the liver.

From the data on hemoglobin and stored iron, balance sheet of iron was calculated. Against the daily iron requirement of about 10 mg/head, availability of iron is (1) about 15 mg of stored iron at birth, (2) reutilization of iron less than 1 mg/day released by red cell destruction, and (3) about 1 mg/day of iron supplied from colostrum. It indicates that the availability can hardly meet the requirement, and as such iron deficiency occurs in a short period under normal iron metabolism of piglets.

Ferrokinetics[7), 8)]

Plasma iron turnover and tissue retention of radioactivity in piglets starved for 24 hr

Fig. 2. Nonheme iron concentration in the liver in piglets from birth to 30 days of age. Values are given as mean ±SE.

Note: Supplemental iron group was injected 1 ml of iron-dextran (100 mg iron) intramuscularly at 3 days of age.

Table 1. Plasma iron turnover in piglets from birth to 35 days of age

Days of age	^{59}Fe clearance half time min	Plasma iron turnover[1)] mg/day/100 ml whole blood
Birth	23[2)]	1.63
1	18	3.22
3	18	2.69
10 (Without supplemental iron)	16	2.23
10 (With supplemental iron)	30**	5.44**
35 (Weanling)	43	2.44

1) $\dfrac{\text{Plasma iron } (\mu g/100 \text{ ml})}{^{59}Fe \text{ clearance half time (min)}} \times \dfrac{100-\text{Ht}}{100}$ (mg/day/100 ml whole blood)

2) Mean from values of 6 to 8 piglets

** Significantly different from the corresponding value without supplemental iron (P<0.01)
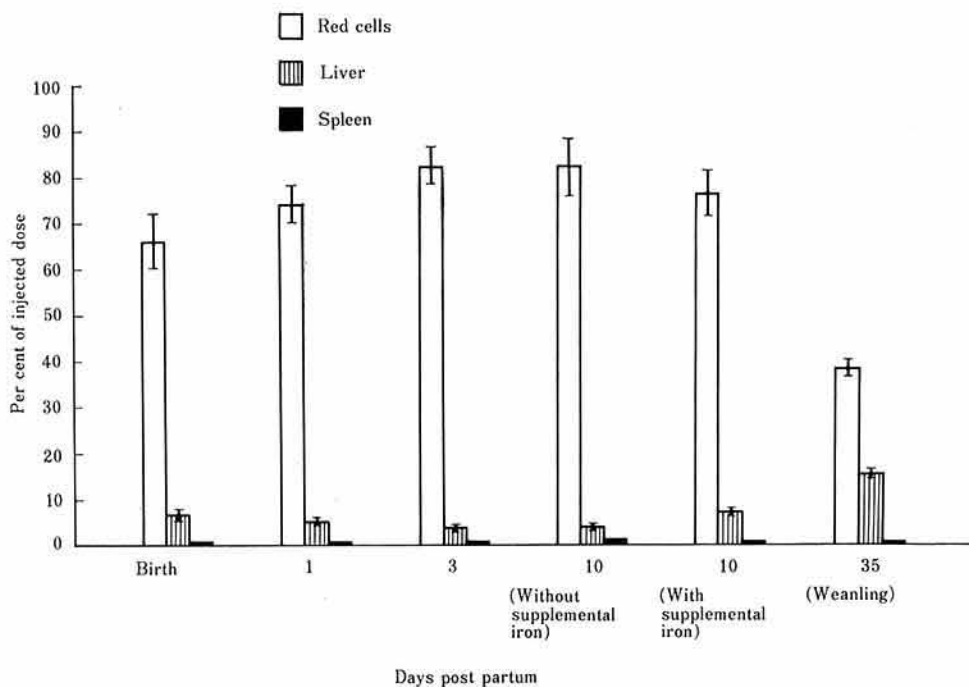
Fig. 3. Tissue retention of radioactivity by piglets starved for 24 hr after the intravenous injection of ^{59}Fe-labelled plasma. Values are given as mean±SE.

Note: Supplemental iron group was injected 1 ml of iron-dextran (100 mg iron) intramuscularly at 3 days of age. Pigs were weaned at 30 days of age.

Fig. 4. Changes in total iron-binding capacity and plasma iron from birth to 35 days of age. Values are given as mean±SE.

Note: Supplemental iron group was injected 1 ml of iron-dextran (100 mg iron) intramuscularly at 3 days of age. Pigs were weaned at 30 days of age.
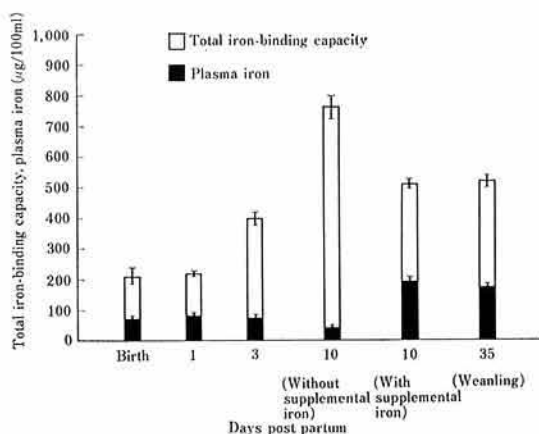
after the intraveous injection of ^{59}Fe-labelled plasma are shown in Table 1 and Fig. 3. The ^{59}Fe clearance half time (T 1/2) was found to be about 20 min during a period from birth to 10 days of age, far shorter than 1 to 1.5 hr observed with growing pigs.

Plasma iron turnover showed high value except slightly lower value at birth. On the other hand, most of ^{59}Fe injected was utilized by red cells with only a very small amount taken up by liver, spleen and erythroid marrow. Thus, erythropoietic activity of piglets was considerably higher than that of growing pigs.

Iron transport from tissue to plasma[9)-11)]

Changes in iron-binding capacity of transferrin, iron carrier protein in plasma, and plasma iron are shown in Fig. 4. Total iron-binding capacity of transferrin was very low at birth and 1 day of age, but it started

increasing at 3 days of age, reaching the level of adult at 10 days of age. On the other hand, plasma iron, being affected by transferrin level, showed low values in the neonatal period which still more lowered when no iron treatment was given in nursing period.

Table 2. Changes in iron metabolic pattern of piglets

Item	Period	
	Neonatal	Nursing
Iron store	high	low
Erythropoiesis	high	high
Plasma iron turnover	high	high
Plasma transferrin	low	high
Plasma iron	low	low
Hemoglobin	high → low (after nursing)	low

The above results are summarized in Table 2. Although the metabolic pattern in the nursing period is apparently of iron deficiency, that of neonatal period is peculiar in that the concentration of iron stored in the liver is high, while the level of plasma transferrin and plasma iron is low in spite of high erythropoietic activity and high plasma iron turnover. This seems to be caused by a restricted transport of iron from stored iron to plasma owing to the low plasma transferrin value. To examine further this process, hepatic xanthine oxidase and plasma ferroxidase, which are related to cell-to-plasma iron transfer, as well as plasma transferrin and plasma ceruloplasmin were studied. As shown in Fig. 5, all these substances were very low at birth and 1 day of age, particularly ceruloplasmin (a principal component of plasma ferroxidase) was only 0.3% of that of 10 days of age. Such shortage of enzyme and protein involved in metabolic system of stored iron restricts the mobilization of stored iron, despite the high erythropoietic activity.

However, rapid and steady increases in plasma ferroxidase and transferrin were observed from a few days after the first nursing. In parallel to this change, stored
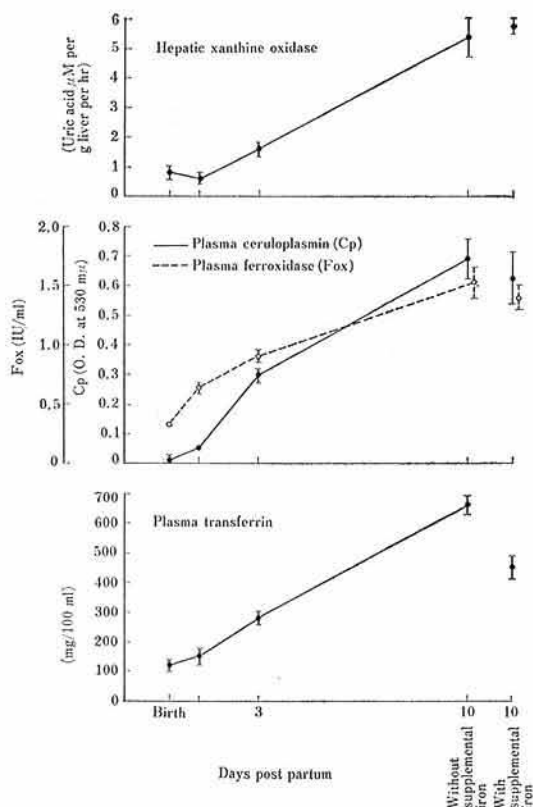

Fig. 5. Changes in hepatic xanthine oxidase, plasma ceruloplasmin, ferroxidase and transferrin. Values are given as mean±SE.

Note : Supplemental iron group was injected 1 ml of iron-dextran (100 mg iron) intramuscularly at 3 days of age.

iron in the liver was released. Evidently, the rate of transport of iron from storage cells to erythropoietic organ through plasma was accelerated due to the increases of iron-releasing enzymes and plasma transferrin, and eventually, as a result of iron store exhaustion due to a great demand of iron in the nursing period, hemoglobin synthesis slowed down and iron deficiency anemia appeared.

The increases of enzymes and proteins related to iron transfer were not attributable to a passive transfer from colostrum, but to the intense production of these substances in the liver that occurred after ingesting maternal colostrum.
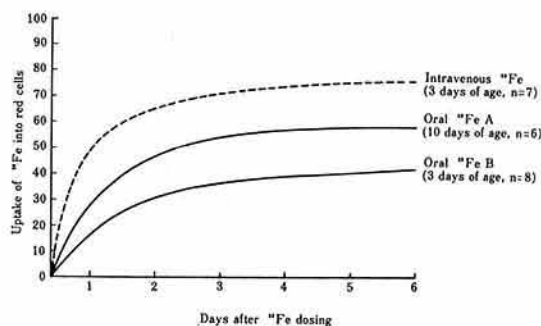
Fig. 6. Uptake of radioactivity into red cells of piglets nursed for 6 days after ^{59}Fe dosing

Note: ^{59}Fe-ferric citrate in a dose of $1-2\mu$ ci per kg body weight was administered with 8 mg of carrier iron by stomach tube. 48 mg of ferric citrate (8 mg iron) was administered orally per day for 5 days after ^{59}Fe dosing.

Iron absorption from intestine[12]

Rate of intestinal absorption of iron in the nursing period was determined by using red cell radioiron (^{59}Fe) method. As shown in Fig. 6, utilization of ingested iron by red cells of piglets, receiving 8 mg of iron per day, reached a plateau level (40 to 60%) at 5 days after ^{59}Fe dosing, whereas the utilization of injected iron (^{59}Fe-labelled plasma) was 70–80%. Only a minute quantity of ^{59}Fe was deposited in nonheme iron in the liver. Thus, efficiency of intestinal absorption of iron in the nursing period is very high, and the absorbed iron is quickly utilized by red cells.

By using tied-off intestine segments *in vivo*, the development of intestinal functions related to iron absorption was studied. Proximal segments of the small intestine in newborn piglets showed a high absorption activity for iron which was maintained throughout the neonatal period. This result is conflicting with the fact that iron transport system is not well developed in the newborn piglets. Further study will be made on physicochemical properties of iron in circulating system, especially portal vein.

Conclusion

Piglet anemia comprises two phases: it starts from physiological anemia which is caused by a rapid increase of plasma volume due to absorption of intact maternal colostrum, and is followed by iron deficiency anemia, which occurs based on inbalanced demand-supply relation caused by an increasing iron requirement to meet a rapid growth in the nursing period. These two phase occur successively in a very short time.

Occurrence of iron deficiency anemia is closely related to the development of iron metabolic function. Namely, newborn piglets have a particular pattern of iron metabolism: activity of intestinal absorption of iron and erythropoietic activity are very high, whereas enzymes and protein related to iron transfer from stored iron to plasma are extremely low.

In the early stage of nursing, the iron transfer system develops with increases of enzymes and protein in that system, resulting in an accelerated transfer of iron from tissue to erythropoietic organ through plasma. This, together with the increase of iron requirement caused by rapid growth of piglets, induces iron deficiency anemia. Therefore, it is necessary to start supplying iron to piglets at least in a few days after birth.

References

1) McGowan, J. P. & Crichton, A.: On the effect of deficiency of iron in the diet of pigs. *Biochem. J.* 17, 204–207 (1923).
2) Furugouri, K. & Tohara, S.: Studies on iron metabolism and anemia in piglets. I. Relationship between growth and anemia. *Bull. Nat. Inst. Anim. Ind.*, 21, 35–52 (1970) [In Japanese with English summary].
3) Furugouri, K. & Tohara, S.: Studies on iron metabolism and anemia in piglets. II. Blood volume and mean corpuscular constants. *Bull. Nat. Inst. Anim. Ind.*, 24, 75–82 (1971) [In Japanese with English summary].
4) Furugouri, K. & Tohara, S.: Effects of anemia on growth in piglets. *Jap. J. Swine Res.*, 8, 57–66 (1971) [In Japanese with English summary].

5) Furugouri, K.: Developmental changes in the nonheme iron composition of the liver and spleen in piglets. *J. Anim. Sci.*, **36**, 265–270 (1973).

6) Furugouri, K.: Influence of anemia on iron, copper, zinc and manganese contents of the liver in piglets. *Jap. J. Swine Res.*, **10** 5–11 (1973) [In Japanese with English summary].

7) Furugouri, K.: Kinetics in iron metabolism in piglets. *J. Anim. Sci.*, 38, 1249–1256 (1974).

8) Furugouri, K.: Effect of fasting of ferro-kinetics in piglets. *Jap. J. Vet. Sci.*, **36**, 441–445 (1974).

9) Furugouri K.: Plasma iron and total iron-binding capacity in piglets in anemia and iron administration. *J. Anim. Sci.*, **34**, 421–426 (1972).

10) Furugouri, K., Akita, T. & Himeno K.: Postpartum changes in transferrin in sow milk and piglet's blood serum. *Bull. Nat. Inst. Anim. Ind.*, 27, 27–34 (1973) [In Japanese with English summary].

11) Furugouri, K.: Nonheme iron mobilization from the liver in piglets. *Jap. J. Vet. Sci.*, 36, 255–261 (1974).

12) Furugouri K. & Kawabata, A.: Iron absorption in nursing piglets. *J. Anim. Sci.* 41, (In press, 1975).