

From the National Veterinary Institute, Stockholm  
and the Research and Development Laboratories, Astra Läkemedel AB,  
Södertälje, Sweden.

## STUDIES ON SUDDEN FATALITIES AMONG PIGLETS FOLLOWING PARENTERAL IRON THERAPY

By

*S. Lindvall, Gunilla Moberg and B. Nordblom*

LINDVALL, S., GUNILLA MOBERG and B. NORDBLOM: *Studies on sudden fatalities among piglets following parenteral iron therapy.* Acta vet. scand. 1972, 13, 206—217. — An investigation was carried out in order to clarify whether there is a correlation between the latent iron-binding capacity, UIBC, in the serum of suckling piglets and sudden fatalities occurring among these animals when they are treated with 250 mg trivalent iron in the form of a complex also containing dextrin, sorbitol, citric acid and lactic acid.

In all, 97 animals from 9 litters were used. By administering 100 mg oral divalent iron to 22 animals, the iron-binding capacity was saturated or appreciably reduced 3 hrs. after the oral treatment. After this time, the animals were treated with parenteral iron. Seventeen other animals were treated with 100 mg divalent iron and immediately afterwards with parenteral iron. Three hrs. later, the iron-binding capacity of the animals was exceeded. In 32 of the control animals, UIBC was high before the parenteral treatment. No fatalities were observed among the animals treated with parenteral iron.

Twenty-three of the animals had a high iron-binding capacity in spite of having diarrhoea. On parenteral treatment of these animals with the iron complex, no fatalities were observed which could be ascribed to the treatment.

The mechanism for the sudden fatalities among suckling piglets after parenteral administration of iron is discussed.

parenteral iron; oral iron; piglet; sudden fatalities; intestinal infections; serum iron; unsaturated iron-binding capacity; total iron-binding capacity.

It has been reported by Nilsson (1960), Henriksson (1962), Ueberschär (1966), Köhler (1966) and Behrens (1969) that fatalities have occurred in certain litters of piglets within 24 hrs. following treatment for anaemia by means of parenteral iron therapy.

Treatment with oral iron can also lead to sudden fatalities in certain litters of piglets (*Brag* 1957). It was established that the dead animals manifested a waxy degeneration of the muscle, and assumed that the reason for this muscle degeneration was a deficiency of vitamin E. *Lannek & Tollerz* (1962) have studied the role of vitamin E in the sensitivity of the animals to parenteral iron therapy. These authors demonstrated an increase in mortality in those litters having a deficiency of this vitamin. However, they did not preclude the possibility that other reasons than vitamin E deficiency could be responsible for the sudden fatalities.

The significance of vitamin E in sudden fatalities among piglets was also discussed by *Henriksson* and *Köhler*. The latter author assumed that vitamin E deficiency is of great importance in this connection, but he nonetheless considers that the immediate causes are of a more complex nature.

In the dead piglets which were examined by *Nilsson*, serious myocardial degeneration was ascertained. However, the author considers that the cause of death was not established, but he suspects some latent disorder which was aggravated by the treatment.

The pathological anatomical investigation of the cases described by *Ueberschär* showed that the dead animals had extensive oedema and focal necroses and that there was bleeding at the sites of injection. *Ueberschär* considers that the tissue toxic properties of the iron preparation are the cause of these changes, which are certainly responsible for the death of the animals. On the other hand, *Behrens* considers that the nature and course of the illness suggest acute iron poisoning and that the localized changes are either not responsible for the fatalities or responsible only to a limited extent. He rather considers that the fatalities are the result of a specific toxicity of the iron preparation and a particular susceptibility of certain litters or piglets. *Behrens* also considers that a causal relationship may exist between the total iron-binding capacity of the animals and the fatalities.

As with other parenteral preparations fatalities have also been observed in certain litters on using a complex of iron, dextrin, sorbitol, citric acid and lactic acid (Iroject, Astra, Sweden) for preventing anaemia in piglets (*Brag*, personal communication). In order to determine whether there is a correlation between the latent iron-binding capacity in serum and fatalities

among piglets treated with parenteral iron preparations, the latent iron-binding capacity was determined immediately before administration of the iron preparation. The experiments were carried out on suckling piglets on a farm where fatalities had been noted previously and on another farm where intestinal infections among the piglets had given rise to considerable problems. The latter farm was chosen because of the proposed correlation between iron injections, intestinal infection and fatalities. The iron-binding capacity of serum of piglets from litters from 2 other farms was saturated with iron and the animals were subsequently provoked by parenteral administration of the above-mentioned preparation.

## MATERIAL AND METHODS

### *Iron preparations*

The parenteral iron preparation has been described by *Högberg et al.* (1968). It contains 100 mg  $\text{Fe}^{3+}$  per ml in the form of a sterile solution of a complex of iron, dextrin, sorbitol, citric acid and lactic acid. In addition 0.3 % phenol is added to the solutions as a preservative.

Oral iron was administered to the animals in the form of a gelatin capsule containing ferrous sulphate corresponding to 50 mg  $\text{Fe}^{2+}$ . This capsule is dissolved within 3 min. by the gastric juice.

### *Animals and doses*

In the experiments, 9 litters comprising a total of 97 animals were used. The litters were from 4 experimental farms of varying size and with different feeding routines and hygienic standard.

*Litter 1 (farm A).* This litter — 12 animals (Nos. 1—12) — was a farm where fatalities had been noted previously on treatment with the above-mentioned iron preparation. Blood samples were taken from the jugular vein for determination of serum iron (SI) and unsaturated iron-binding capacity (UIBC), when the piglets were 3 days old. Immediately afterwards 250 mg  $\text{Fe}^{3+}$  was administered to all animals i. m. deep into the neck musculature (Table 1).

*Litter 2 (farm B).* Oral iron was administered to 7 out of 10 3-day old piglets (Nos. 13—22), the dose being  $2 \times 50$  mg  $\text{Fe}^{2+}$ . Three hrs. later, blood samples were taken from all the animals for determination of SI and UIBC. Immediately afterwards 7 of the animals were given a deep i. m. injection of 250 mg  $\text{Fe}^{3+}$  (Table 2).

*Litter 3 (farm C).* Three out of a litter of 10 5-day old piglets (Nos. 23—32) were treated with  $2 \times 50$  mg oral  $\text{Fe}^{2+}$  and 3 with  $2 \times 50$  mg oral  $\text{Fe}^{2+}$  + 250 mg  $\text{Fe}^{3+}$  i. m. deep into the neck musculature. Three hrs. later, blood samples were taken from all the animals for determination of SI and UIBC, and immediately afterwards 250 mg  $\text{Fe}^{3+}$  was administered i. m. deep into the neck musculature to the 7 piglets which had not previously received parenteral iron (Table 3).

*Litter 4 (farm C).* Three out of a litter of 10 4-day old piglets (Nos. 33—42) were treated with  $2 \times 50$  mg oral  $\text{Fe}^{2+}$  and 4 with  $2 \times 50$  mg oral  $\text{Fe}^{2+}$  + 250 mg  $\text{Fe}^{3+}$  i. m. deep into the neck musculature. Subsequently, the same procedure was adopted as for litter 3. This litter had gastro-intestinal trouble in the form of diarrhoea (Table 4).

*Litter 5 (farm C).* Four out of a litter of 11 3-day old piglets (Nos. 43—53) were treated with  $2 \times 50$  mg oral  $\text{Fe}^{2+}$  and 3 with  $2 \times 50$  mg oral  $\text{Fe}^{2+}$  + 250 mg  $\text{Fe}^{3+}$  i. m. deep into the neck musculature. Subsequently, the same procedure was adopted as for litter 3, except that SI and total iron-binding capacity (TIBC) were determined (Table 5).

*Litter 6 (farm C).* Four out of a litter of 11  $3\frac{1}{2}$ -day old piglets (Nos. 54—64) were treated with  $2 \times 50$  mg oral  $\text{Fe}^{2+}$  and 4 with  $2 \times 50$  mg oral  $\text{Fe}^{2+}$  + 250 mg parenteral  $\text{Fe}^{3+}$ . Subsequently, the same procedure was adopted as for litter 5 (Table 6).

*Litter 7 (farm C).* Four out of a litter of 10 3-day old piglets (Nos. 65—74) were treated with  $2 \times 50$  mg oral  $\text{Fe}^{2+}$  and 3 with  $2 \times 50$  mg oral  $\text{Fe}^{2+}$  + 250 mg parenteral  $\text{Fe}^{3+}$ . Subsequently, the same procedure was adopted as for litter 5 (Table 7).

*Litter 8 (farm D).* This litter, which consists of 11 4-day old piglets (Nos. 75—85), is from a farm where there had been considerable problems with intestinal infections among the piglets. At the time of treatment, the animals had diarrhoea. A blood sample was taken for UIBC determination, and then 250 mg  $\text{Fe}^{3+}$  was administered deep into the neck musculature (Table 8).

*Litter 9 (farm D).* This litter comprises 12 2-day old piglets (Nos. 86—97) and is from the same farm as litter 8. At the time of treatment, the animals had diarrhoea. Blood sampling and treatment was the same as for litter 8 (Table 9).

Post-mortem examinations and bacteriological tests were performed at the National Veterinary Institute from the 8 piglets which died during the experiments.

#### *Serum iron (SI)*

In litters 1—4, serum iron was determined according to the method described by *Lindvall & Andersson* (1961). In litters 5—7, the determination of serum iron was carried out using a Technicon autoanalyzer according to a method described by *Giovanniello et al.* (1967).

Table 1. Sex, serum iron (SI), unsaturated iron-binding capacity (UIBC), total iron-binding capacity (TIBC) and complications of piglets 4 days of age from litter 1.

| Piglet no. | Sex | $\mu\text{g Fe}/100 \text{ ml serum}$ |      |      | Complications |
|------------|-----|---------------------------------------|------|------|---------------|
|            |     | SI                                    | UIBC | TIBC |               |
| 1          | ♀   | —                                     | 155  | —    | none          |
| 2          | ♀   | 188                                   | 115  | 303  | none          |
| 3          | ♀   | 153                                   | 205  | 358  | none          |
| 4          | ♀   | 120                                   | 160  | 280  | none          |
| 5          | ♂   | 153                                   | 185  | 338  | none          |
| 6          | ♂   | 205                                   | 140  | 345  | none          |
| 7          | ♀   | 158                                   | 195  | 353  | none          |
| 8          | ♀   | 264                                   | 190  | 454  | none          |
| 9          | ♂   | 188                                   | 200  | 388  | none          |
| 10         | ♀   | 205                                   | 75   | 280  | none          |
| 11         | ♀   | —                                     | 215  | —    | none          |
| 12         | ♂   | 110                                   | 195  | 305  | none          |

#### *Latent and total iron-binding capacity (UIBC and TIBC)*

In litters 1—4, 8 and 9, the latent iron-binding capacity was determined according to a method described by *Cartwright & Wintrobe* (1949) and TIBC obtained by addition of SI and UIBC, while in litters 5—7, the total iron-binding capacity was first determined in a Technicon autoanalyzer according to *Giovannello et al.* and UIBC then obtained by subtraction of SI.

## RESULTS

### *Correlation between saturation of UIBC and the sudden fatalities*

On a farm where previous fatalities had occurred in connection with the administration of the iron preparation used in the experiments, the serum iron and iron-binding capacity in serum of the piglets of a new litter were investigated. Subsequently attempts were made to reproduce the previous fatalities by administering the same dose of the same batch of the preparation. It can be seen from the results given in Table 1, that these 12 piglets had high serum iron values, but in spite of this a high unsaturated iron-binding capacity. No fatalities were noted in this experiment.

Table 2. Sex, treatment, serum iron (SI), unsaturated iron-binding capacity (UIBC), total iron-binding capacity (TIBC) and complications of piglets 3 days of age from litter 2.

| Piglet no. | Sex | Blood sample taken           |   |                                     | $\mu\text{g Fe}/100 \text{ ml serum}$ |      |      | Complications |
|------------|-----|------------------------------|---|-------------------------------------|---------------------------------------|------|------|---------------|
|            |     | after<br>100 mg Fe<br>orally | after<br>100+200 mg Fe<br>oral.+parent. | before<br>250 mg Fe<br>parenterally | SI                                    | UIBC | TIBC |               |
| 13         | ♀   | —                            | —                                       | X                                   | 70                                    | 180  | 250  | none          |
| 14         | ♂   | —                            | —                                       | X                                   | 122                                   | 228  | 350  | none          |
| 15         | ♀   | —                            | —                                       | X                                   | 40                                    | 108  | 148  | none          |
| 16         | ♂   | X                            | —                                       | —                                   | 350                                   | 0    | 350  | none          |
| 17         | ♂   | X                            | —                                       | —                                   | 484                                   | 0    | 484  | none          |
| 18         | ♀   | X                            | —                                       | —                                   | 186                                   | 0    | 186  | none          |
| 19         | ♀   | X                            | —                                       | X                                   | —                                     | 0    | —    | none          |
| 20         | ♀   | X                            | —                                       | X                                   | 458                                   | 25   | 483  | none          |
| 21         | ♀   | X                            | —                                       | X                                   | 330                                   | 0    | 330  | none          |
| 22         | ♀   | X                            | —                                       | X                                   | 486                                   | 0    | 486  | none          |

Table 3. Sex, treatment, serum iron (SI), unsaturated iron-binding capacity (UIBC), total iron-binding capacity (TIBC) and complications of piglets 5 days of age from litter 3.

| Piglet no. | Sex | Blood sample taken           |   |                                     | $\mu\text{g Fe}/100 \text{ ml serum}$ |      |      | Complications |
|------------|-----|------------------------------|---|-------------------------------------|---------------------------------------|------|------|---------------|
|            |     | after<br>100 mg Fe<br>orally | after<br>100+250 mg Fe<br>oral.+parent. | before<br>250 mg Fe<br>parenterally | SI                                    | UIBC | TIBC |               |
| 23         | ♀   | —                            | —                                       | X                                   | 148                                   | 140  | 288  | none          |
| 24         | ♀   | —                            | —                                       | X                                   | 22                                    | 400  | 422  | none          |
| 25         | ♂   | —                            | —                                       | X                                   | 72                                    | 268  | 340  | none          |
| 26         | ♂   | —                            | —                                       | X                                   | 36                                    | 435  | 471  | none          |
| 27         | ♀   | —                            | X                                       | —                                   | 1440                                  | 0    | 1440 | none          |
| 28         | ♂   | —                            | X                                       | —                                   | 915                                   | 0    | 915  | none          |
| 29         | ♀   | —                            | X                                       | —                                   | 1224                                  | 0    | 1224 | none          |
| 30         | ♂   | X                            | —                                       | X                                   | 270                                   | 45   | 315  | none          |
| 31         | ♀   | X                            | —                                       | X                                   | 486                                   | 0    | 486  | none          |
| 32         | ♀   | X                            | —                                       | X                                   | 405                                   | 0    | 405  | none          |

In order to saturate the latent iron-binding capacity before the parenteral administration, a very large dose of oral iron was given to 22 piglets in litters 2—7. Tables 2—7 show that this dose was so large that the latent iron-binding capacity was substantially reduced or completely saturated 3 hrs. after the oral administration, at which time the animals received parenteral iron without any fatal side-effect occurring. When the parenteral

Table 4. Sex, treatment, serum iron (SI), unsaturated iron-binding capacity (UIBC), total iron-binding capacity (TIBC) and complications of piglets 4 days of age from litter 4.

| Piglet no. | Sex | Blood sample taken           |   |                                     | $\mu\text{g Fe}/100 \text{ ml serum}$ |           |      | Complications                      |
|------------|-----|------------------------------|---|-------------------------------------|---------------------------------------|-----------|------|------------------------------------|
|            |     | after<br>100 mg Fe<br>orally | after<br>100+250 mg Fe<br>oral.+parent. | before<br>250 mg Fe<br>parenterally | SI                                    | UIBC      | TIBC |                                    |
| 33         | ♂   | —                            | —                                       | X                                   | 45                                    | destroyed | —    | none                               |
| 34         | ♂   | —                            | —                                       | X                                   | 125                                   | 176       | 301  | none                               |
| 35         | ♀   | —                            | —                                       | X                                   | 185                                   | 246       | 431  | none                               |
| 36         | ♂   | —                            | X                                       | —                                   | 1056                                  | 0         | 1056 | very small and<br>weak piglet died |
| 37         | ♂   | —                            | X                                       | —                                   | 996                                   | 90        | 1086 | none                               |
| 38         | ♂   | —                            | X                                       | —                                   | 1056                                  | 0         | 1056 | none                               |
| 39         | ♀   | —                            | X                                       | —                                   | 1050                                  | 0         | 1050 | none                               |
| 40         | ♂   | X                            | —                                       | X                                   | 705                                   | 43        | 748  | none                               |
| 41         | ♀   | X                            | —                                       | X                                   | 549                                   | 0         | 549  | none                               |
| 42         | ♂   | X                            | —                                       | X                                   | no blood sample                       |           |      | none                               |

Table 5. Sex, treatment, serum iron (SI), unsaturated iron-binding capacity (UIBC), total iron-binding capacity (TIBC) and complications of piglets 3 days of age from litter 5.

| Piglet no. | Sex | Blood sample taken           |   |                                     | $\mu\text{g Fe}/100 \text{ ml serum}$ |      |      | Complications |
|------------|-----|------------------------------|---|-------------------------------------|---------------------------------------|------|------|---------------|
|            |     | after<br>100 mg Fe<br>orally | after<br>100+250 mg Fe<br>oral.+parent. | before<br>250 mg Fe<br>parenterally | SI                                    | UIBC | TIBC |               |
| 43         | ♀   | —                            | —                                       | X                                   | 85                                    | 205  | 290  | none          |
| 44         | ♀   | —                            | —                                       | X                                   | 117                                   | 180  | 297  | none          |
| 45         | ♂   | —                            | —                                       | X                                   | 62                                    | 361  | 423  | none          |
| 46         | ♀   | —                            | —                                       | X                                   | 87                                    | 161  | 248  | died          |
| 47         | ♀   | —                            | X                                       | —                                   | 740                                   | —    | 279  | none          |
| 48         | ♂   | —                            | X                                       | —                                   | 720                                   | —    | 414  | none          |
| 49         | ♂   | —                            | X                                       | —                                   | 740                                   | —    | 404  | none          |
| 50         | ♀   | X                            | —                                       | X                                   | 420                                   | 5    | 425  | none          |
| 51         | ♀   | X                            | —                                       | X                                   | 345                                   | 26   | 371  | none          |
| 52         | ♂   | X                            | —                                       | X                                   | 330                                   | 74   | 404  | none          |
| 53         | ♀   | X                            | —                                       | X                                   | 381                                   | 24   | 405  | none          |

iron preparation was given simultaneously with oral iron to 17 piglets from the same litters at the same time, values for iron in serum were obtained which exceeded the iron-binding capacity without any toxic symptoms appearing. For control purposes, 20 other piglets, which did not receive oral iron were

Table 6. Sex, treatment, serum iron (SI), unsaturated iron-binding capacity (UIBC), total iron-binding capacity (TIBC) and complications of piglets 3½ days of age from litter 6.

| Piglet no. | Sex | Blood sample taken           |   |                                     | µg Fe/100 ml serum |      |      | Complications |
|------------|-----|------------------------------|---|-------------------------------------|--------------------|------|------|---------------|
|            |     | after<br>100 mg Fe<br>orally | after<br>100+250 mg Fe<br>oral.+parent. | before<br>250 mg Fe<br>parenterally | SI                 | UIBC | TIBC |               |
| 54         | ♂   | —                            | —                                       | X                                   | 14                 | 365  | 379  | none          |
| 55         | ♀   | —                            | —                                       | X                                   | 17                 | 401  | 418  | none          |
| 56         | ♀   | —                            | —                                       | X                                   | 92                 | 363  | 428  | none          |
| 57         | ♂   | —                            | X                                       | —                                   | 992                | —    | 527  | none          |
| 58         | ♂   | —                            | X                                       | —                                   | 772                | —    | 592  | none          |
| 59         | ♀   | —                            | X                                       | —                                   | 972                | —    | 578  | none          |
| 60         | ♀   | —                            | X                                       | —                                   | 1040               | —    | 675  | died          |
| 61         | ♂   | X                            | —                                       | X                                   | 630                | —    | 534  | none          |
| 62         | ♂   | X                            | —                                       | X                                   | 621                | —    | 606  | none          |
| 63         | ♀   | X                            | —                                       | X                                   | 450                | 5    | 455  | none          |
| 64         | ♀   | X                            | —                                       | X                                   | 870                | 19   | 889  | none          |

Table 7. Sex, treatment, serum iron (SI), unsaturated iron-binding capacity (UIBC), total iron-binding capacity (TIBC) and complications of piglets 3 days of age from litter 7.

| Piglet no. | Sex | Blood sample taken           |   |                                     | µg Fe/100 ml serum |      |      | Complications |
|------------|-----|------------------------------|---|-------------------------------------|--------------------|------|------|---------------|
|            |     | after<br>100 mg Fe<br>orally | after<br>100+250 mg Fe<br>oral.+parent. | before<br>250 mg Fe<br>parenterally | SI                 | UIBC | TIBC |               |
| 65         | ♂   | —                            | —                                       | X                                   | 35                 | 444  | 479  | none          |
| 66         | ♂   | —                            | —                                       | X                                   | 78                 | 305  | 383  | none          |
| 67         | ♀   | —                            | —                                       | X                                   | 48                 | 399  | 447  | none          |
| 68         | ♂   | —                            | X                                       | —                                   | 592                | 22   | 614  | none          |
| 69         | ♀   | —                            | X                                       | —                                   | 688                | —    | 444  | none          |
| 70         | ♂   | —                            | X                                       | —                                   | 648                | —    | 581  | none          |
| 71         | ♀   | X                            | —                                       | X                                   | 396                | 73   | 469  | none          |
| 72         | ♂   | X                            | —                                       | X                                   | 486                | 18   | 504  | none          |
| 73         | ♀   | X                            | —                                       | X                                   | 510                | 60   | 570  | none          |
| 74         | ♂   | X                            | —                                       | X                                   | 435                | 87   | 522  | none          |

taken from the same litters and treated with parenteral iron at the same time as the other groups. Neither here did any fatalities occur that could be correlated to the iron treatment. Three piglets (Nos. 36, 46 and 60) died by internal bleeding during the blood sampling.



*Correlation between UIBC, infection and the sudden fatalities*

It was observed that the majority of animals that died after treatment with parenteral iron showed signs of intestinal disorder in the form of diarrhoea, and the post-mortem examination of these piglets revealed that in most cases there was an acute enteritis (*Brag, Nordblom*, personal communication). In order to study whether a correlation exists between UIBC intestinal infections and the sudden fatalities, experiments were carried out on a farm where there had been problems with enteritis of the piglets. It can be seen from Tables 8 and 9 that the iron-binding capacity before administration of parenteral iron was

Table 8. Unsaturated iron-binding capacity (UIBC) and complications of 4-day old piglets with intestinal infections from litter 8.

| Piglet no. | UIBC | Complications               |
|------------|------|-----------------------------|
| 75         | 425  | none                        |
| 76         | 412  | none                        |
| 77         | 285  | none                        |
| 78         | 525  | none                        |
| 79         | 410  | none                        |
| 80         | 360  | dead 2 days after treatment |
| 81         | 380  | none                        |
| 82         | 350  | none                        |
| 83         | 575  | none                        |
| 84         | 425  | none                        |
| 85         | 470  | dead 2 days after treatment |

Table 9. Unsaturated iron-binding capacity (UIBC) and complications of 2-day old piglets with intestinal infections from litter 9.

| Piglet no. | UIBC | Complications              |
|------------|------|----------------------------|
| 86         | 255  | none                       |
| 87         | 215  | none                       |
| 88         | 175  | none                       |
| 89         | 220  | dead 1 day after treatment |
| 90         | 275  | none                       |
| 91         | 200  | dead 1 day after treatment |
| 92         | 215  | none                       |
| 93         | 215  | dead 1 day after treatment |
| 94         | 200  | none                       |
| 95         | 225  | none                       |
| 96         | 140  | none                       |
| 97         | 100  | none                       |

high among these groups of animals in spite of most of the piglets having infection clinically manifested in the form of diarrhoea. The post-mortem examination of the dead piglets revealed nothing which suggests a connection between these fatalities and the treatment with parenteral iron. The cause of death of these piglets (Nos. 80, 85, 89, 91 and 93) has probably connection with an acute catarrhal enteritis. *E. coli*-infection was found (*Shreeve & Thomlinson 1970*).

#### DISCUSSION

On treating pregnant women for iron deficiency anaemia with an iron-sorbitol complex for parenteral use, *Scott (1962)* observed that 3 patients manifested side-effects. These patients had been treated at the same time with oral iron, which resulted in saturation of the transferrin, and iron from the parenteral preparation could not be bound to the transferrin, but gave rise to side-effects. According to *Behrens (1969)*, a causal relationship may exist between the total iron-binding capacity of animals and sudden fatalities. If this were the case, the piglets ought to be particularly sensitive to a large dose of parenteral iron after saturation of the transferrin with oral iron in analogy with *Scott's* results. However, the results of this investigation show that saturation of the transferrin does not give rise to any fatal side-effects on administering parenteral iron.

According to *Behrens*, one of the reasons for the fatalities is a specific toxicity of the iron preparation. He also considers that certain litters are especially susceptible, but that vitamin E deficiency may be ruled out as a cause of the fatalities as well as a specific infection on injection. *Köhler (1966)* investigated the dead animals with regard to infection and ascertained that fatalities occurred both in litters with a bacterial infection of the piglets as well as in litters where no infection could be established. However, he showed that in most cases there was a slight intestinal catarrh. In the present investigation, no fatalities could be established as a result of treatment with parenteral iron at the farm where intestinal infections had given obvious trouble. This supports the view that the bacterial infection found in certain of the dead piglets had nothing to do with the sudden fatalities. However, this does not rule out that the intestinal infection could have made the animals sensitive to the parenteral iron.

It was shown by *Beeson (1947 a)* that daily i. v. injections

of the same dose of bacterial pyrogens led to a decrease in the febrile reaction of the animals. The author considered that development of resistance was not a result of the production of specific humoral antibodies. On blocking the R-E system of such animals with colloidal thorium dioxide, *Beeson* (1947 b) found that the animals once again became sensitive to the bacterial pyrogens. He also showed that the pyrogenic substances were removed more quickly from the circulating blood of the animals, which were tolerant to pyrogens, than from that of normal animals and that blocking the R-E system caused retardation of this quicker elimination.

The various parenteral preparations, which were used at the time of the reported fatalities, have in common a high average molecular weight. The large dose of iron colloid which is administered to the piglets can temporarily block the R-E system of the animals. In animals exposed to toxins from a specific microorganism, which produces a large amount of toxin in the intestinal tract, such a blockade by the iron colloid might — in analogy with *Beeson's* (1947ab) results — be one possibility for increasing to a sufficiently high degree the risk for sudden fatalities to occur.

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## SAMMANFATTNING

*Studier över dödsfall hos spädkgrisar i samband med parenteral järnterapi.*

En undersökning har utförts med syfte att klargöra om någon korrelation föreligger mellan den latent järnbindande kapaciteten, UIBC, i serum hos spädkgrisar och plötslig död hos dessa djur, då de behandlas med 250 mg tvåvärt järn i form av ett komplex även innehållande dextrin, sorbitol, citron- och mjölksyra.

Nittioju djur fördelade på 9 kullar har använts. Genom att tillföra 100 mg tvåvärt järn peroralt till 22 andra djur är den järnbindande kapaciteten mättad eller kraftigt reducerad 3 timmar efter den orala behandlingen. Vid denna tidpunkt har djuren behandlats med parenteralt järn. Sjutton andra djur behandlades med 100 mg tvåvärt järn och omedelbart därefter med parenteralt järn. Tre timmar senare har djurens järnbindande kapacitet överskridits. Hos 32 av kontrolldjuren var UIBC hög före den parenterala behandlingen. Några dödsfall observerades ej hos de med parenteralt järn behandlade djuren.

Tjugotre av djuren hade trots diarré en hög järnbindande kapacitet. Vid parenteral behandling av dessa djur med järnkomplexet observerades inga dödsfall som kunde hänföras till behandlingen.

Mekanismen för plötslig död hos spädkgrisar efter parenteral järntillförsel har diskuterats.

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Reprints may be requested from: Sven Lindvall, Astra Läkemedel AB, S-151 85 Södertälje, Sweden.