microscopic examination of the wounds prior to giving ascorbic acid showed the presence of the characteristic non-banded extracellular fibrils previously described[6]. Within 24 h after ascorbic acid administration, this fibrillar material was entirely replaced by characteristically banded collagen fibrils, most of which were of similar diameter.

Thus the extracellular material which is labelled 24 h after ascorbic acid administration can be clearly identified as collagen, and the intensity of labelling is similar to that seen in the fibrillar material which could not previously be identified as collagen. These results are consistent, therefore, with the conversion, extracellularly, of the non-collagenous fibrillar material present in scurvy, to collagen, following ascorbic acid administration.

We are aware that these results again raise the possibility of the presence of an extracellular collagen procursor in scurvy in which *in situ* hydroxylation of proline and lysine might occur. Since this remains a controversial issue, we are attempting to extract this material and identify its amino-acid content, in the hope of increasing our understanding of this complex situation.

The work here was supported in part by grant (*H*–3174) of the National Institutes of Health.

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Prediction of Spontaneous Hereditary Diabetes Mellitus in Chinese Hamsters by Means of Elevated Alpha-2 Serum-levels

Clinical and pathological observations on Chinese hamsters (*Cricetulus griseus*) with spontaneous hereditary diabetes mellitus have been reported previously in several papers[1–7]. Generally speaking, the disease in Chinese hamsters is primarily pancreatogenic, with degranulation, hydropic degeneration and deficiency of β-cells. Other forms of pathological expression noted in symptomatic animals are glomerulosclerosis, arteriosclerosis, increased periodontal breakdown, and proneness toward the formation of adenocarcinomas of the pancreas.

Elevated serum α-2 levels several times greater than normal (3–8 per cent) have been reported[8] in diabetic hamsters, or in families with a high incidence of spontaneous diabetes. When symptomatic members of these high incidence families were randomly hybridized by single or double crosses involving two or four grandparents of diabetic background, normal α-2 values were re-established. At the time when this investigation was reported, many animals had high α-2 values with no clinical evidence of diabetes. In this communication we shall show that with but a few exceptions these non-symptomatic high α-2 hamsters afterwards developed chemical diabetes while the low α-animals generally remained symptom-free.

Both diabetic and non-diabetic inbred animals were obtained from the colony maintained at the Children's Cancer Research Foundation. The methods in breeding and maintaining the animals have already been described[9]. Animals were observed for a period of at least 250 days, and in some cases longer, for evidence of diabetes. Only animals showing prolonged glycosuria were considered as confirmed diabetics.

Blood was obtained by cardiac puncture and the α-2 serum-levels were determined by the Spinco model *R* system of paper electrophoresis, using their recommended procedures.

For purposes of analysis, the hamsters were divided into three groups consisting of: (1) those which were never diabetic (within 250 days); (2) those which had no initial symptoms, but later developed diabetes; and (3) those which were diabetics or showed initial glycosuria, and later were confirmed as diabetics. The condition of the animals at the time when the electrophoretic analysis was run was the point of reference for the above categories. These results are given in Table 1.

Table 1. Relationship of Serum Paper Electrophoretic α-2 Levels with the Diabetic State in 89 Chinese Hamsters*

Serum α-2 (%)	No diabetes	Confirmed diabetes: No initial symptoms	Confirmed diabetes: Initial symptoms and/or established diabetes
3–5	8	0	0
6–10	18	5	6
11–15	1	7	10
16–20	1	6	7
21–25	1	2	10
26–30	0	2	4
31–35	0	0	1
Total	29	22	38

* All animals observed for at least 250 days.

It will be observed that out of the 29 which did not develop diabetes, 26 animals had α-2 levels of less than 10 per cent, the majority (18 animals) giving levels between 6 and 10 per cent. Only three animals gave levels above 10 per cent. It is conceivable that if these latter animals were observed for a longer period—up to a year—diabetic symptoms might have developed.

In the 22 animals showing no initial symptoms, none was observed in the 3–5 per cent group, in contrast to the previous group where 8 animals were found to have the lowest α-2 levels. There were 13 initially non-symptomatic animals in the 11–20 per cent α-2 interval.

Similarly, the 38 animals with established diabetes or initial symptoms, such as glycosuria, and later confirmed as diabetics, showed no members in the 3–5 per cent α-2 group. There were 27 animals in the 11–25 per cent α-2 interval.

These results show a high degree of association between the active diabetic state in Chinese hamsters and the serum α-2 level. Some overlap occurred in the 6–10 per cent α-2 interval between the non diabetics, the initially non-symptomatic, and the symptomatic groups. Most of the initially non-symptomatic high α-2 animals (above 10 per cent) were later confirmed as diabetics when observed for a period of 9 months.

The possible prognostic implications of elevated α-2 levels in selected groups of high diabetic risk, such as overweight new-borns, is being investigated by a variety of techniques.

This work was supported in part by a grant (*G*–21307) from the National Science Foundation, and grants *A*–4468, *E*–1560(*C*4) and *A*–6339 from the U.S. National Institutes of Health.

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