Hyperostosis of the spine in an adult population

Its relation to hyperglycaemia and obesity

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Osteoarthritis is a common disorder in middle-aged and older people (Kellgren and Lawrence, 1958; Lawrence, de Graaff and Laine, 1963; Anderson and Duthie, 1963; Roberts and Burch, 1966; Lawrence, 1969). Hyperostosis of the spine is a special form of osteoarthritic spondylosis. This condition was first described in the 19th century, but became better known after Forestier and Rotes-Quérol (1950) rediscovered this clinical entity and called it 'senile ankylosing hyperostosis of the spine'. Hyperostotic spondylosis occurs mostly in elderly people and is characterized by the formation of prominent bony bridges between the vertebrae. The thoracic spine is most frequently affected, but involvement of the cervical and lumbar spine is not uncommon. The bony bridges are usually most marked on the anterior surfaces of the vertebrae and differ from the bridges occurring in ankylosing spondylitis, which are flatter in contour.

Boulet, Serre, and Mandin (1953) and Ott, Schwenckenbecher, and Iser (1963) reported that the prevalence of hyperostotic spondylosis was high in middle-aged and elderly patients with diabetes mellitus, and this finding has been corroborated by several other studies of hospitalized patients. The prevalence of hyperostotic spondylosis in middle-aged and elderly diabetics has been reported to be 20 to 50 per cent. (Schilling, Schacherl, Camp, and Bopp, 1965; Hájková, Středa, and Škrha, 1965; Julkunen, Kärävä, and Viljanen, 1966). The prevalence of hyperostosis in diabetics has been reported to increase with age and duration of disease (Hájková and others, 1965; Bywaters, Doyle, and Oakley, 1966). On the other hand, a manifest or 'chemical' diabetes mellitus has been found in 40 to 60 per cent. of patients with hyperostotic spondylosis (Einaudi and Viara, 1960; Ott and others, 1963; Schilling and others, 1965).

In contrast to the results of the studies mentioned above, Klunker (1964) did not find any definite correlation between the occurrence of hyperostosis and decreased glucose tolerance in an unselected

series of patients attending a rheumatological clinic. In a series of 1,258 policemen, aged 30 to 69 yrs, Julkunen, Pyörälä, and Lehtovirta (1968) did not find a significant relationship between the occurrence of hyperostotic spondylosis and the degree of hyperglycaemia defined by means of 2-hour blood glucose level in an oral glucose tolerance test, although there was a trend to an increased occurrence of the disease in those men who had a 2-hour blood glucose level of 120 mg./100 ml. or more.

Hyperostotic spondylosis is often found also in acromegaly with or without diabetes (Julkunen and others, 1966). Hyperostotic spondylosis and endocranial hyperostosis have been found to occur more often together than expected (Schoen, Eggstein, and Vogt, 1969a; Hájková, Středa, and Škrha, 1971). This may refer to some metabolic disorder causing hyperostotic manifestations.

Schilling and others (1965) suggested that hyperostotic spondylosis is associated with obesity. Schoen, von Oldershausen, and Vogt, (1969b) reported an increased occurrence of hyperostotic spondylosis, particularly in obese diabetics. Julkunen and others (1966), however, found no definite association between obesity and hyperostotic spondylosis in hospitalized patients with diabetes mellitus. It is well known that there is a high degree of correlation between obesity and disorders of carbohydrate metabolism. Most relevant information about the relative contributions of obesity and hyperglycaemia in the pathogenesis of hyperostotic spondylosis can be obtained from a study of a non-selected population sufficiently large to yield an adequate number of subjects with this condition. The present study, which records an epidemiologic approach to this problem, was carried out in connection with a multiphasic screening examination in six communities in Finland.

Study population and methods

POPULATION

There were 12,858 persons aged 15 years or over, 6,151

men and 6,707 women. The screening examination was offered to all persons in the population register, the average response rate in the six communities being 83 per cent. (range 76.4 to 91.2). The response rate was slightly lower for men than women, the difference being about 5 per cent.

Three of the six communities are located in East Finland and three in West Finland (Fig. 1). Mouhijärvi and Juuka are rural agricultural communities, Kauttua and Pankakoski industrial communities, whereas Vammala and Nurmee-Porokylä are small country towns without industry.

FIG. 1 Location of the six study communities. Their entire adult population, 12,858 persons in all, were examined in regard to hyperostotic spondylosis, glucose tolerance, and obesity.

METHODS

Social class was determined according to a national classification described by Rauhala (1966); for the purposes of this study, all farmers were classified into a separate group and presented as social class 4. Information on the subjective heaviness of the daily work was collected by self-administered questionnaire.

The anthropometric measurements were: standing height without shoes (cm.); weight in clothes—men without jacket—(kg.); triceps skinfold thickness measured to the nearest mm. with the Harpenden calliper on the dorsum of the right arm, at the level midway between the tip of the acromial process and the tip of the elbow. A weight-height index was calculated as weight in kg./height in cm.—100.

As a part of the multiphasic screening programme an

oral glucose tolerance test was carried out on all persons without previously diagnosed diabetes mellitus. The test was preceded by at least 4 hours fasting. A glucose dose of 40 g./sq.m. of body surface area was given as a 20 per cent. glucose solution. One hour after the administration of glucose a sample of venous blood was taken into a heparinized tube. Plasma was separated immediately and frozen. The frozen samples were sent to the central laboratory of the Division where plasma glucose was determined by ferricyanide reduction method in the Auto-Analyzer (Technicon Auto-Analyzer Methodology N-2b).

X-ray examination of the chest was performed by taking postero-anterior and lateral exposures on 10 × 10 cm. films. The lateral view was used for the assessment of the presence of hyperostotic spondylosis in the thoracic spine. The presence of at least two typical complete prominent bridges between vertebrae (Fig. 2) was required for the diagnosis of hyperostotic spondylosis

FIG. 2 Hyperostotic spondylosis with typical prominent bony bridges between vertebrae of thoracic spine. The presence of at least two bridges was required for the diagnosis in the study.

Hyperostotic bridges are quite different from the bridges developing in ankylosing spondylitis (Fig. 3). Bridges typical of ankylosing spondylitis occurred in only nine cases in the entire series, six men and three women.

ANALYSIS OF DATA

For the purpose of analyses on the possible role of glucose tolerance and obesity in the hyperostosis of the spine, a control was matched for each case. The matching was performed with regard to sex, age, occupation, and place of residence. No subject with the slightest sign of hyperostotic formations in the thoracic spine was accepted to serve as a control. Thus 94 male and 70 female pairs were obtained. χ^2 -test with Yates' correction and the procedure described by Mantel and Haenszel (1959)

were applied in the statistical comparison of prevalences, with the exceptions mentioned in the presentation of the results. Student's t-test and the Wilcoxon test were used in the testing of statistical significance of the differences of the means and medians, respectively.

FIG. 3 Bony bridges in ankylosing spondylitis.

Results

PREVALENCE OF HYPEROSTOSIS OF THE SPINE

The total number of persons showing hyperostotic bridges in the thoracic spine was 164, the youngest being 43 years of age. The prevalence of hyperostosis is given in Table I for men and women by age group beginning at 40 years, separately for the populations studied in East and West Finland. The prevalence of hyperostosis was higher in men than in women, particularly in age groups above 60 years. The

differences of prevalence between men and women in all age groups combined were statistically significant in the entire series ($\chi^2_1 = 9.0$; $P < 0.005$) and in the West Finland population ($\chi^2_1 = 8.5$; $P < 0.005$). Especially in the older age groups the prevalence of hyperostosis was higher in the women of East Finland than in those of West Finland (for all age groups combined $\chi^2_1 = 3.7$; $0.1 > P > 0.05$).

The analysis of the possible role of occupational factors in the development of hyperostosis was restricted to men. When the prevalence rates of hyperostotic spondylosis in men aged 50 years or over were broken down by social class, the relative distributions did not show any significant difference between the populations from the Eastern and Western parts of the country. Thus it seemed to be justified to combine the prevalence rates within the social classes (Fig. 4, overleaf). These crude prevalence rates of hyperostosis of the spine show significant differences between the social classes; but in addition to the prevalence rate the social strata also proved to be age dependent. When the effect of age was controlled, the differences of the prevalence rate between the social classes disappeared.

The heaviness of work was reported by the hyperostotic men to be light or heavy as often in East as in West Finland. The pattern of deviations from the intermediate groups both to the directions of heavy and light were similar in the age groups 50 years or over. Therefore the prevalence rates within the classes of heaviness of work were combined. In regard to subjective judgement about their work, the hyperostotics were fairly equally distributed into classes of heavy and light (Fig. 5, overleaf).

GLUCOSE TOLERANCE AND ANTHROPOMETRIC MEASUREMENTS

Plasma glucose

In order to compare the prevalence of definitely

Table I Prevalence of hyperostosis (HO) in men and women in East and West Finland

Sex	Age (yrs)	East		West		Total series	
		Number HO/Total	Per cent.	Number HO/Total	Per cent.	Number HO/Total	Per cent.
Men	40-49	1/490	0.2	2/557	0.4	3/1,047	0.3
	50-59	11/444	2.5	14/468	3.0	25/912	2.7
	60-69	24/290	8.3	23/272	8.5	47/562	8.4
	70-	12/84	14.0	7/86	8.2	19/170	11.2
	All ages	48/1,308	3.7	46/1,383	3.3	94/2,691*	3.5
Women	40-49	1/546	0.2	2/680	0.3	3/1,226	0.2
	50-59	11/515	2.1	6/503	1.2	17/1,018	1.7
	60-69	16/344	4.7	14/360	3.9	30/704	4.3
	70-	14/141	10.0	6/149	4.0	20/290	6.9
	All ages	42/1,546	2.7	28/1,692	1.7	70/3,238*	2.2

* $\chi^2_1 = 9.0$; $p < 0.005$.

FIG. 4 *Prevalence of hyperostotic spondylosis by social class. All farmers are included in Class 4. The relative contribution of hyperostotics aged 70 years or more is shown by shading.*

impaired glucose tolerance in the hyperostotic subjects and in the matched control subjects, the definition of 'hyperglycaemia' was arbitrarily chosen to be a 1-hour plasma glucose level of more than 250 mg./100 ml. in oral glucose tolerance test or the presence of previously diagnosed diabetes. The prevalence of 'hyperglycaemia' was higher in hyperostotic subjects than in control subjects both in men and women (Table II). The differences in the prevalences between hyperostotic and control subjects were statistically significant both in men ($\chi^2_1 = 4.35$; $P < 0.05$) and in women ($\chi^2_1 = 4.00$; $P < 0.05$) assessed by Mantel-Haenszel test, after excluding from the analysis those pairs which were concordant with regard to either presence or absence of 'hyperglycaemia' and including only discordant pairs, as recommended for case-control studies by Pike and Morrow (1970).

Table II *Prevalence of 'hyperglycaemia' in hyperostotic subjects and in matched controls*

Sex	Men	Women
Hyperostotic subjects	18/94 19.1 per cent.	20/70 28.6 per cent.
Control subjects	7/94 7.4 per cent.	9/70 12.8 per cent.

Men: $\chi^2_1 = 4.35$; $P < 0.05$.
Women: $\chi^2_1 = 4.00$; $P < 0.05$.

Table III (opposite) shows the mean and median values as well as the standard deviations and the 10th and 90th percentiles for 1-hour plasma glucose in the hyperostotic and control subjects after excluding pairs with one or both members with previously verified manifest diabetes. In the 40 to 59-year age group

FIG. 5 *Prevalence of hyperostotic spondylosis by subjective heaviness of work. The relative contribution of hyperostotics aged 70 years or more is shown by shading.*

of women the mean and median values for plasma glucose were significantly higher in hyperostotic subjects than in controls. The same trend was evident also in the ≥ 60 -year age group of women and in both age groups of men, although the differences were not statistically significant.

Exclusion of fifteen pairs in which one or both members were previously diagnosed diabetics might have decreased the differences in the degree of hyperglycaemia between the hyperostotic subjects and control subjects. Therefore, the previously diagnosed diabetics, on whom glucose tolerance test was not carried out, were given an arbitrary 1-hour plasma glucose value of 400 mg./100 ml. which was the highest value observed in this series. These analyses of the data revealed more accentuated trends, but the results were essentially the same as in the previous analyses with exclusions.

Thus it is evident that impaired glucose tolerance is related to the occurrence of hyperostotic spondylosis. As stated above, the prevalence of hyperostotic spondylosis was higher in men than in women, particularly in West Finland, and in women the condition was more common in East than in West Finland. However, the glucose tolerance of these population groups did not explain the differences observed in the prevalence rates.

The mean and median of 1-hour plasma glucose values were calculated for the entire population aged 40 years or over (2,691 men and 3,238 women). The age group specific plasma glucose values showed no definite difference between men and women, but were higher in West than in East Finland both in men and women.

Table III 1-hour plasma glucose in hyperostotic subjects and in matched controls after excluding pairs containing previously diagnosed diabetics

Age (yrs)	Sex	No. of pairs	Hyperostotic subjects					Control subjects					P-value	
			Mean	S.D.	Median	P ₁₀	P ₉₀	Mean	S.D.	Median	P ₁₀	P ₉₀	t-test	Wilcoxon
40-59	M	24	174.4	59.3	175.5	102.5	276.0	157.4	47.6	143.5	98.0	232.5	0.40	0.60
40-59	F	19	211.0	72.7	214.0	119.0	296.0	153.0	61.1	128.0	97.0	248.5	0.02	0.05
> 60	M	62	189.0	68.0	186.5	108.0	282.0	175.3	49.2	174.0	112.0	244.0	0.40	0.40
> 60	F	44	193.5	68.5	184.5	111.0	300.0	184.4	47.7	176.5	124.5	259.0	0.60	0.40

P₁₀; P₉₀ = 10th and 90th percentiles.*Weight-height index*

The hyperostotic subjects and control subjects were similar with regard to height. In none of the groups did the difference in the mean values exceed 2 cm.

Diabetes in middle-aged and elderly persons may be associated either with weight loss or with excessive weight gain. Consequently, the weight-height index in hyperostotic and control subjects was evaluated both in the entire matched series and after excluding pairs with previously known diabetes.

As shown in Table IV, the weight-height index was significantly higher in hyperostotic subjects than in controls in both men and women in all age groups. After excluding pairs with one or both members with previously diagnosed diabetes, the difference in the 40 to 59-year age group of men became statistically even more significant ($P < 0.001$).

The observed regional differences in the prevalence rate of hyperostotic spondylosis in women could not be explained by regional differences in the measurements for obesity. The sex and 10-year age group specific means and medians of weight-height index were of the same magnitude or higher in West than in East Finland (2,691 men and 3,238 women). Women were more obese than men in both West and East Finland.

Triceps skinfold thickness

In the entire matched series the triceps skinfold thickness in men tended to be greater in hyperostotic subjects than in controls, the difference in the median values being statistically significant in the ≥ 60 -year age group of men (Table V). In women the same trend is evident only in the ≥ 60 -year age group. After excluding pairs with one or both members

Table IV Weight-height index in hyperostotic subjects and in matched controls

Age (yrs)	Sex	No. of pairs	Hyperostotic subjects					Control subjects					P-value	
			Mean	S.D.	Median	P ₁₀	P ₉₀	Mean	S.D.	Median	P ₁₀	P ₉₀	t-test	Wilcoxon
40-59	M	28	1.18	0.15	1.16	1.02	1.33	1.04	0.19	1.01	0.83	1.28	0.01	0.01
40-59	F	20	1.36	0.18	1.38	1.10	1.62	1.16	0.16	1.15	0.93	1.38	0.01	0.01
> 60	M	66	1.14	0.16	1.14	0.94	1.35	1.03	0.13	1.01	0.92	1.19	0.001	0.001
> 60	F	50	1.32	0.21	1.33	1.04	1.60	1.17	0.20	1.17	0.93	1.47	0.001	0.001

P₁₀; P₉₀ = 10th and 90th percentiles.**Table V** Skinfold thickness in hyperostotic subjects and in matched controls

Age (yrs)	Sex	No. of pairs	Hyperostotic subjects					Control subjects					P-value	
			Mean	S.D.	Median	P ₁₀	P ₉₀	Mean	S.D.	Median	P ₁₀	P ₉₀	t-test	Wilcoxon
40-59	M	28	10.5	4.5	11.0	4.5	16.5	8.3	4.5	7.0	3.0	13.0	0.10	0.10
40-59	F	20	26.4	10.6	25.0	17.0	41.5	23.6	7.2	23.5	12.0	31.0	0.40	0.60
> 60	M	66	9.8	5.0	9.0	3.5	15.5	8.1	5.0	7.0	3.0	16.0	0.10	0.05
> 60	F	50	23.8	8.5	23.0	14.0	34.5	20.8	7.5	20.0	12.0	31.0	0.10	0.05

P₁₀; P₉₀ = 10th and 90th percentiles.

with previously diagnosed diabetes, the difference in the skinfold thickness between hyperostotic and control subjects became statistically more significant in both age groups of men ($P < 0.005$ and < 0.02), whereas the difference in the oldest women decreased and was not statistically significant.

The statistical analyses were repeated after the logarithmic transformation of skinfold values, which decreased the skewness of their distribution. The results, however, remained essentially unchanged.

Correlation of glucose tolerance to obesity

To discover whether the measurements for glucose tolerance and obesity are dependent on each other in this series, an approach based on quartiles was selected, because the distributions of 1-hour plasma glucose value, weight-height index, and triceps skinfold thickness were considerably skew. The number of persons in the matched series were cross-tabulated in quartiles based on plasma glucose value and quartiles based on weight-height index, in separate series with and without hyperostotic spondylosis. Persons with previously diagnosed manifest diabetes were included in the highest plasma glucose quartile. Firstly, the homogeneity of each sex and age group specific table was tested by means of χ^2 -test or Fisher's exact test. Secondly, summary tables were constructed combining the numbers of corresponding cells from the age-specific tables and likewise tested for homogeneity. In regard to plasma glucose and triceps skinfold thickness, similar cross-tabulations and tests were performed.

There was no definite correlation of glucose tolerance to weight-height index or triceps skinfold thickness in hyperostotic women or in any group in the control series (Table VI).

In hyperostotic men there was a trend to positive correlation between glucose tolerance and measure-

ments for obesity; this was most evident in the age group of ≥ 60 years. In hyperostotic men the correlation of 1-hour plasma glucose to triceps skinfold thickness (Table VII) was stronger both in the entire series ($\chi^2_1 = 5.17$; $P < 0.025$) and in the oldest age group ($\chi^2_1 = 6.15$; $P < 0.025$) than the correlation of plasma glucose to weight-height index (entire series $\chi^2_1 = 2.72$; $0.1 < P < 0.05$. ≥ 60 -years $\chi^2_1 = 2.18$; $P > 0.1$).

Discussion

Since the main purposes of this study were to determine the prevalence rate of hyperostotic spondylosis and to clarify the possible role of certain factors in its aetiology, a strict diagnostic criterion was applied.

There had to be at least two typical and fully-developed bony bridges between the vertebrae of the thoracic spine. A single, prominent bony bridge between the vertebrae may originate from previous trauma of the spine, which is not very rare. The prevalence rate presented for hyperostotic spondylosis based on the criterion used in this study certainly underestimates the actual occurrence of the condition. However, employing this criterion, the results are, according to our experience, repeatable and practically free from observer error. In fact, all forms of severity, from advanced hyperostotic spondylosis to none at all, are observed in the general population. However, for analytical purposes, this continuous series of different expressions of the same condition is extremely difficult to handle reliably without limitation by clear-cut definition. Furthermore, the application of the selected criterion in the case-control design enables one to find the greatest difference between the series, as it is easy to exclude persons with any minor hyperostotic formations from serving as controls.

As expected, the prevalence rate of hyperostotic

Table VI *Distribution of men in control series according to age/group/specific quartiles for 1-hour plasma glucose and triceps skinfold thickness.*

Figures in bold type represent the number of subjects below and above the median

Skinfold	1-hour plasma glucose				Total
	Q ₁	Q ₂	Q ₃	Q ₄	
Q ₁	6	5	5	5	21
Q ₂	5	6	7	2	20
Q ₃	7	6	5	9	27
Q ₄	5	7	5	9	26
Total	23	24	22	25	94

$\chi^2_1 = 0.17$; $P = 0.7$.

Table VII *Distribution of hyperostotic men according to age/group/specific quartiles for 1-hour plasma glucose and triceps skinfold thickness.*

Figures in bold type represent the number of subjects below and above the median

Skinfold	1-hour plasma glucose				Total
	Q ₁	Q ₂	Q ₃	Q ₄	
Q ₁	9	4	6	2	21
Q ₂	6	12	4	7	29
Q ₃	5	3	4	8	20
Q ₄	3	5	9	7	24
Total	23	24	23	24	94

$\chi^2_1 = 5.17$; $P = < 0.025$.

spondylosis was found to rise steeply with age and the rise was more accentuated in men than in women. As a whole, the condition was definitely more common in males. There were surprisingly marked regional differences in the prevalence rate of this condition in women. The youngest men and women with hyperostotic spondylosis were in their forties, not a single case being found in 6,929 persons aged 15 to 40 years. Whatever the aetiological factors causing hyperostotic spondylosis may be, either they do not operate before middle-age or the 'incubation period' of the condition is very long. Thus the information based on the present status of persons with or without hyperostotic spondylosis must be interpreted with caution.

Both hyperglycaemia and obesity were found to be related to the development of hyperostotic spondylosis in this study on a large unselected population. Obesity was very strongly associated with hyperostotic spondylosis, thus confirming the observation of Schilling and others (1965) made in a clinical series.

Obesity is known to be often associated with decreased glucose tolerance which is not necessarily a true manifestation of diabetes, but a metabolic disorder reversible after successful weight reduction. On the other hand, excess weight gain may be a factor leading to the manifestation of genuine diabetes mellitus. Studies on unselected groups of young and middle-aged men and women (Abrams, Jarrett, Keen, Boyns, and Crossley, 1969; Epstein, 1970; Pyörälä, Siltanen, Punsar, Lehtovirta, Nikkilä, Pelkonen, and Taskinen, 1971) have shown that there is a significant positive correlation between blood sugar response in oral glucose tolerance test and relative body weight. Therefore, the correlation of 1-hour plasma glucose to the weight-height index and triceps skinfold thickness was also analysed in the present series to find out whether the association of decreased glucose tolerance with the development of hyperostotic spondylosis was due merely to obesity with concomitant impairment of glucose tolerance. A significant positive correlation between 1-hour plasma glucose and triceps skinfold thickness and a correlation between plasma glucose and weight-height index was found in men with hyperostotic spondylosis, whereas there was no such correlation in women with hyperostotic spondylosis or in the control groups of both sexes. This may be due to the fact that in old age many persons tend to lose weight. The lack of correlation between glucose tolerance and obesity in the hyperostotic women of all ages despite the strong relationship between decreased glucose tolerance and hyperostotic spondylosis suggests that the

contributions of these two factors to the aetiology of hyperostotic spondylosis are at least partly independent of each other.

These factors, however, could not explain the principal differences in the prevalence rates observed in this study. Either the influence of impaired glucose tolerance and obesity on men is different from that on women in the development of hyperostotic spondylosis or, as suggested by the regional differences in male : female ratio, some unknown factors are responsible for these variations.

The distribution of hyperostotic spondylosis by social class was uneven, but the differences disappeared when the confounding effect of age was taken into account.

The social strata in Finland have changed considerably during the past decades, but more farmers have remained in their present occupation than other workers. The somewhat higher prevalence in farmers may reflect the role of physical strain in the aetiology of hyperostotic spondylosis, but the patients' own assessment of the heaviness of their work showed no definite relation to hyperostotic spondylosis.

Summary

The prevalence of hyperostotic spondylosis in the general population was studied in connection with a multiphasic screening examination of 12,858 persons over 15 years of age. The youngest persons with this disorder were in their forties. The prevalence increased steeply with age to 8.4 per cent. in men and 4.3 per cent. in women in the 60 to 69-year age group.

The relationship of impaired glucose tolerance and obesity to the occurrence of hyperostotic spondylosis was studied by forming a pair-matched control series. The prevalence of overt or chemical diabetes was significantly higher in the hyperostotic subjects than in the controls. After excluding pairs in which one or both members had previously diagnosed diabetes, the plasma glucose level 1 hour after oral glucose load was significantly higher in the 40 to 59-year group in women with hyperostotic spondylosis than in the corresponding control group, but this difference was not significant in older women or in men. The weight-height index was significantly higher in both men and women with hyperostosis than in the corresponding controls in all age groups. Triceps skinfold thickness was significantly greater in men with hyperostosis than in controls.

The analyses of intercorrelations between glucose tolerance and obesity in the series suggest that decreased glucose tolerance and obesity contribute, in part at least, to the development of hyperostotic spondylosis independently of each other.

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