CLINICAL ASPECTS OF BEJEL*†

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In the summer of 1951, Dr. E. H. Hudson reviewed the early stages of the WHO/UNICEF sponsored bejel campaign in Iraq (Hudson, 1951). I will attempt to carry the story a step further.

Bejel was fully described by Hudson (1928) who was working amongst the Arabs of Syria. The infection appeared to be well known by the Bedouin, and the local name "bejel", which Hudson retained, originally probably meant "sores". Its possible identity with syphilis, yaws, pinta, and other treponemal diseases was made the basis of Hudson's unionist view (Hudson, 1928, 1946). This is still controversial and the exact relationship of the non-venereal treponematoses to each other and to syphilis has yet to be determined. It is probably true that there is hardly a sign of these treponemal diseases which has not been described at one time or another in syphilis. Nevertheless each of these conditions gives a fairly constant and typical clinical pattern, recognizable as such. One is justified in keeping these infections under separate headings until further evidence decides the issue. The individual patient may pose considerable diagnostic difficulties at times, usually from syphilis; but the more accurate the clinical and epidemiological data, the less often is one left in doubt.

We have experts on Bosnian endemic syphilis, yaws, pinta, and also bejel—but large-scale comparative studies by the same observers on all or most of these conditions have yet to be undertaken. The task is a forbidding one owing to the vast distances which separate most of the areas of treponematosis from each other and the relative inaccessibility of some of them to ordinary forms of transport. The WHO with its accumulated experience is probably in the best position to tackle this work and close the wide gaps in our knowledge; it appears to be fully alive to this aspect of treponematosis.

Research and routine laboratory procedures have not been of much help in either unifying or differentiating the treponematoses. Turner (1947) found cross-protection between experimental syphilis and yaws, but McLeod and Magnuson (1951), working with the same strain of yaws spirochaete, failed to produce significant cross immunity. Recently, Turner (1952) compared treponemata from venereal syphilis—including strains sent by our team from Baghdad, and endemic syphilis from Bosnia, with yaws and bejel from several sources. The syphilis strains behaved in the same way in the rabbit as other syphilis strains have done in the past; yaws showed a longer incubation period with the development of less indurated lesions. Bejel occupied an intermediate position. The Nichols strain induced good immunity against the syphilis treponemata from Baghdad and Bosnia. Results in the bejel and yaws experiments were less clear-cut. Immobilizing antibodies have been found in yaws and bejel in much the same way as in venereal syphilis. I performed a hundred luetin skin tests ("Luotest") in all stages of bejel, and found approximately the same results as in lues, i.e. negative in the early stages, usually positive later on. Morphologically, neither the electron nor the ordinary microscope have so far been able to differentiate these treponemata, but admittedly more work in this sphere is necessary. The so-called Universal Reaction of Kahn—a flocculation test with lipid antigen using different NaCl concentrations—was found to differentiate between yaws and syphilis serum (Kahn, 1951) but not between pinta, bejel, and syphilis (Kahn, 1952; Kail, 1952). Routine serology in bejel is thought to give rather lower titres than a corresponding stage of syphilis would lead one to expect (Tuomioja, 1951). It is hoped that syphilitic sera from various countries will soon become available for large-scale comparisons.

To summarize, the clinical picture of the variously named treponemal diseases is fairly distinct, but it cannot yet be said with any certainty whether they are simply different manifestations of the same disease, modified by environmental and immunological factors, or whether the undoubted differences

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lie with the infecting organisms. The fact of the essentially non-venerable nature of all the treponematoses but syphilis, must also be mentioned here, as it has variously been held to account for some of the differences in its subsequent course. This would not, however, explain why bejel, pinta, and yaws are all clinically distinct, as they are usually contracted non-venerally.

Turning more exclusively to bejel, it has hitherto been associated with the Middle East only, but recent reports suggest a wider distribution. Thus, "njovera" (Willcox, 1951) in Southern Rhodesia, and a report of a similar treponematosis in Bechuanaland (Murray, 1952) appear to be closely allied to bejel. I was able to confirm bejel in Southern Persia (Csonka, 1951a) and believe that other foci will come to light now that increasing attention is being given in the medical literature to treponemal diseases.

Present Investigations

The present paper is based on 3,507 cases of bejel which were seen by our team during my 9-month stay in Iraq. Many observations are in line with those of Hudson and other earlier workers, and they are now receiving their first statistical evaluation on a large scale.

Onset.—Mainly in childhood; 25 per cent. acquired it before the age of 6 years, and 66 per cent. before the age of 16 (which is, incidentally, the customary age of marriage for girls). The extremes of age were 5 months and 75 years respectively. There was no evidence that it is a venereal disease though in rare instances such transmission appears to be possible.

Sex Ratio.—Females preponderated slightly over males (1:1:1). As more males presented themselves for examination (1 female to 1:2 males), the female preponderance might be more significant. Girls have to look after the children in the family, thus maintaining a close contact with the most infectious element in the population, and this might possibly be a factor in the sex distribution.

Some lesions of bejel have a characteristic sex ratio of their own; thus skin gummata and periostitis were commoner in males, possibly because they are more frequently exposed to minor trauma which acts as a precipitating and localizing factor. Gummata of the nose and throat, on the other hand, were three times more common in females.

Incubation Period.—Not known; but human experimental work (Akrawi, 1949) and isolated clinical observations suggest that it is similar to venereal syphilis. The incubation period in inoculated rabbits is on the long side—up to 4 months having been reported (Rizk and others, 1951).

Caustive Organism.—Morphologically identical with T. pallidum and as easily demonstrated from early lesions.

Appearance.—Clinically the resemblance to certain stages of syphilis is striking, though the lesions are apparently confined to skin, mucous membranes, and the skeleton.

Primary Sores.—These are extremely rare—thus differing from syphilis, yaws, and pinta—but they can occur in special circumstances. We saw two lactating women with chancres of the nipples, which were dark-field positive. These mothers had been infected by their own infants, who were then 5-6 months old and had in turn been infected by neighbours' children (Csonka, 1951b). Three further cases with possible primary lesions in the mouth or lips were seen. Even when all are included, it amounts to only 0:1 per cent. of our material. Akrawi (1952) reports similar cases, and believes that the non-sexual contact in bejel leads to the transfer of fewer organisms than in venereal lues and is a factor in the virtual absence of the primary lesion. As yet this interesting theory is unproven.

As the first signs of bejel correspond with secondary syphilis, confusion of terminology is apt to occur. To start the description of bejel with a "secondary" stage is not satisfactory; to call the initial lesions "primary" bejel, on the other hand, would destroy the helpful parallelism with syphilis. In this paper, therefore, the early manifestations of up to 4 years' duration are called early bejel, and the subsequent course late bejel.

Mucous Patches.—These were the commonest initial lesions in our cases. The greyish-white oral patches (274 cases) teemed with the causative treponemata. Hudson (1946) and later Akrawi (1949) suggested that the common drinking vessel which passes unwashed from mouth to mouth, especially in the hot season, is a factor in the spread of bejel. The possibility of insect vectors has also been raised by these authors.

Stomatitis.—The high incidence of angular stomatitis in the young villager was noted by many, and Akrawi (1949) believes that it may condition the mucous membrane to subsequent treponemal infection. In my experience it may occasionally be an early manifestation of bejel itself. One group of these patients was given vitamin B complex, another penicillin injections. Surprisingly, some of the patients responded to one, some to the other treatment, and a few to neither. This led to dark-field studies in angular stomatitis. A few showed typical treponemata and these cases were also sero-positive and responded to penicillin. I did not find the organisms in the group which responded to vitamin B. The third group was found to need vitamin B and penicillin before the condition cleared completely. It appears therefore, that bejel can mimic
angular stomatitis on rare occasions, and that it may be superimposed on vitamin B deficiency in others. Looking at it from the serological viewpoint, 45 per cent. of 105 patients with angular stomatitis as the only lesion gave positive serum tests, against 32 per cent. in a control group identical in number, age, and geographical location. None of the patients or controls gave a bejel history, but they all came from endemic areas. The difference is not spectacular but it is felt that at present all patients with angular stomatitis in infected areas should have the benefit of penicillin.

Skin Rashes.—Either with or soon after the appearance of the mucous patches a proportion (155 cases) showed generalized skin rashes comparable to those seen in secondary lues (Fig. 1). Though we did not see macular rseola, this may have been due to the difficulty in spotting the faint rash on the dark skin of the villager.

Otherwise it is noteworthy that hypertrophic lesions, which are rarely seen nowadays in syphilis, were an everyday occurrence and by no means confined to the moist areas of the skin.

Anogenital Condylomata were found in nineteen patients with skin rashes and were invariably dark-field positive.

Pigmentary Changes were seen in 49 patients consisting of depigmentations and pigmented patches. The former are similar to those seen in pinta. Favoured areas for depigmentation are the periphery of the extremities, genitals, shoulders, nipples, and trunk. The areas are usually symmetrical and well defined (Fig. 2). We found, as did Rein (1951) when investigating pinta in Mexico, that penicillin given early induced satisfactory repigmentation; treatment given late appeared to be ineffective. The pigmented patches were seen in eight patients and were not associated with depigmentation. The colours ranged from light brown to bluish-grey. As yet we do not know whether they involute under treatment.

Hoarseness.—Another sign of early bejel is hoarseness (82 cases). I performed a small number of laryngoscopies which showed either diffuse erythema or actual mucous patches—a picture also seen in secondary laryngeal syphilis. It responded dramatically to penicillin.

Skeletal Involvement.—An important group of signs and symptoms which often started early and sometimes continued for years affected the skeleton either as simple ostealgia (164 cases) or frank osteoperiostitis (30 cases). The most favoured sites were the tibia and fibula, followed by radius, ulna, and femur. In contrast to yaws, no bony lesions of hands, feet, or skull have been seen by us to date. The bone pain was often worse
at night, and was usually accompanied by tenderness of the affected bones. Both bone pain and osteoperiostitis (Fig. 3) affected the limbs on the right side about twice as commonly as on the left. Possibly this is due to more frequent traumata on the active side. This factor may also be responsible for the preponderance of males over females (2:1) in cases of periostitis, as already mentioned. In the ostealgia group the ratio was only 1:2:1 in favour of males. Radiology showed that a large number of those with ostealgia had no apparent structural abnormalities of the bones and the minority had slight osteoperiostitis. Sometimes this was confined to the upper or middle third of the fibula alone and this explains our inability to palpate these abnormalities, though the patient often accurately directed our attention to the localized painful bone. Penicillin brought fairly quick relief and deformities improved gradually. Initial exacerbation of symptoms was sometimes complained of and may have been in the nature of a Herxheimer reaction. We gained the impression—rightly or wrongly—that a larger dosage of penicillin was necessary to get as satisfactory results as with skin lesions. We had little doubt that much that went under the label "bejel bone pain" was possibly due to other causes such as malaria, occupational stress and strain, malnutrition, and anaemia, as well as malingering in order to obtain the much valued penicillin injection. It is therefore not surprising that this heterogeneous group gave the highest percentage of sero-negative reactions and perhaps some of the "treatment failures" might rightly be due to misdiagnosis. In those with bone pain only, 25 per cent. were sero-negative against 3 per cent. in those with bone pain and periostitis. Ostealgia and osteoperiostitis are considered to be part of the same fundamental process and the different sex distribution, as already mentioned, points also to our diagnostic difficulties. When field work becomes more static, this is clearly one of the problems to be further investigated.

**Latency.**—At any time after the stormy beginning of bejel, the condition might become asymptomatic. It was most unusual for the mucous patches and generalized skin rashes to last more than 2 to 3 years and most patients passed into latency within 4 years of the onset. Some appeared to be clinically and serologically cured, others showed merely a positive blood test as token of past bejel. In a third group, some of the lesions recurred, gradually changing their character to approximate to the gummatous stage as seen in late "benign" syphilis. Fig. 4 (opposite) records the distribution of the various signs of bejel found during our survey in 1951 before treatment had been given. It covers over 3,500 patients and it is hoped that this cross-section of the therapeutically untouched infection may give information on the natural history of bejel.

In this diagnostic survey the early stages are probably over-represented, as expectation of life in the bejel areas is short (largely because of malaria, dysenteries, malnutrition, tuberculosis, and bilharzia). Many will not reach an age when late bejel or spontaneous cure can be expected to occur. It also became evident that a number of latent or cured patients escaped our attention due to the difficulty in persuading asymptomatic patients to be examined. For these reasons, and because our information is a cross-section rather than a longitudinal one, only a guess can be hazard to the "natural history" of bejel. This guess suggests that at least one-third of patients would become symptomatically and serologically cured, provided they live long enough; one-third would show positive blood tests only, and one-third would be inconvenienced by late symptoms and signs. Bejel is probably not fatal, though it may lead to serious complications, as the remarkable patient of Dr. L. G. Jones bears witness (p. 104).

**Late Bejel.**—Some 30 per cent. of our cases showed active late lesions, and of these skin gummata (215 cases) were commonest, followed by nasopalatal destruction (113), late periostitis (74), laryngeal involvement (59), and pigmented changes (57). Ostealgia (621) was the predominant symptom but is probably due to several causes, only one of which is bejel. Of the rare manifestations, juxta-articular nodes (4) were of interest. Leukoplakia of the mouth was seen in 24 patients, sixteen of whom were males, but some doubt was felt about its relation to bejel. The late symptoms may emerge gradually from early ones, or be separated by a latent asymptomatic phase of variable duration.

**Fig. 3.—Osteoperiostitis of radius and ulna with overlying healing late skin lesions.**
**Skin Gummata.**—These were slightly more common in males (1.2:1) and appeared from 6 years onwards. The majority developed between 20–30 years of age. Sometimes the area involved was strikingly large and sometimes the underlying bones became diseased in the process. As gummata tended to "burn out" their scars became an even better diagnostic landmark than the original sores had been (Fig. 5). They were typically atrophic, non-contractile, and depigmented, often surrounded by hyperpigmentation and retaining the geometrical pattern of the sores.

![Gummatus plaque. Healed with scarring after one injection of 1-2 mega units P.A.M.](image)

The distribution of gummata seems to show that areas commonly exposed to trauma were sites of election (Fig. 6).
Nasopalatal Destruction.—Lesions of the nasal septum, palate, and larynx were found to be three times as common in women than men for reasons unknown. Although the lesions were sometimes seen separately, this “triad” was frequent enough to merit attention (Fig. 7). Chronic sinusitis often complicates this unsightly condition, and as Grin (1952), working with endemic syphilis in Bosnia, points out, disabilities like these are taken lightly in socially depressed areas ridden with other diseases, but as soon as living conditions improve, these deformities assume a much greater importance with the individual. It is therefore interesting to note that at present the average villager in Iraq rates bejel as a mild disease, and is much more concerned with malaria, dysentery, bilharzia, and other diseases. This attitude is reasonable enough, but did nothing to help our work in these communities.

Skeletal Involvement is similar to that found earlier, though the proportion of ostealgia to osteoperiostitis is twice as high as in early bejel and other possible differences have been noted. The gross deformities of early osteoperiostitis were unusual in the later stages.

Pigmentary Changes.—Often start early in the infection, and attain their full development at this stage and apparently become irreversible.

Hyperkeratosis of Feet was seen in two patients and cleared completely after a single penicillin injection.

Juxta-articular Nodes were seen in four patients (Fig. 8).

Late Latency (732).—This is the largest single group and, by our definition, a clear bejel history of more than 4 years’ duration, without signs of activity at the time of diagnosis, had to be obtained. Ideally, visceral bejel should be excluded by lumbar punctures and radiographs of the heart and great vessels. This was done in the minority, but most had merely a thorough physical and serological examination. Serology therefore attained its maximum usefulness in this type of case, though one realizes that the results did not necessarily reflect the state of activity. In practice we were often confronted by asymptomatic persons of over 40 years of age who gave a clear history of childhood bejel and were sero-positive. Should one treat this group or presume them cured, with the reservation that they should be re-examined during the periodical surveys? These latent cases also deserve careful observation from another angle. Grin (1952), suggests that gummata in endemic areas are often the result of superinfection of the sensitized host. This theory is not new, but, if confirmed, would add additional importance to the elimination of all infectious foci, to check not only the appearance of fresh cases but also of late lesions. To my mind, the evidence is not yet sufficient and it is hoped that the large material in Iraq may contribute to this issue.

Neurological and Cardiovascular Involvement

A great deal of interest has long been shown in the question as to whether the treponematoses, other than syphilis, give rise to neurological and cardiovascular involvement. Bejel is not an exception and, here as elsewhere, the answer is not yet known. Reports of a few patients with usually minor visceral involvement, did not altogether exclude syphilis as a cause (Akrawi, 1949; Hoff, cited by Akrawi, 1949). Clinical examination of many thousands in the remote parts of Iraq by our teams has failed to detect a single case. Radiography of the cardiovascular system in seventy patients with late untreated bejel was equally negative. Lumbar punctures were unfortunately not too popular, and I was able to collect only 43 fluids,
coming from selected cases, especially those with abnormal neurological signs. Of these, 36 were completely normal, three had increased cells only (11, 11, and 17 lymphocytes), one had protein of 55 mg. per cent. but was 70 years of age, which may account for the slightly raised value; two were reported to have a minimal increase in globulin. It is significant that none of these fluids had more than one abnormal test and none was impressively wrong. The 43rd fluid however, was very different. It came from a young man in his twenties who had been admitted to a district hospital as a case of acute bejel. He certainly hailed from a "bejel village" and presented himself with mucous patches and erosive lesions of the scrotum. In addition, he complained of nocturnal headaches. Clinical examination did not add anything relevant, and, in particular, venereal disease was denied. The cerebrospinal fluid gave a strongly positive Wassermann reaction, raised cells, and protein. All signs and symptoms disappeared after treatment. This was indeed exciting—until we took a more careful history, when he admitted to having contracted syphilis whilst in the army, when he had received only rudimentary treatment. The lesions had been relapsing for some time, but he was ashamed to tell us the truth at first. This case taught us a helpful lesson, as this patient might well have gone down in print as suffering from "neurobejel".

At this early stage of our survey one cannot be dogmatic about visceral bejel. All one can say at present is that failure to find clinical evidence of neuro- and cardiovascular bejel, supported so far by radiography and cerebrospinal fluid examinations, might mean that the incidence of such involvement is either low or absent, or that the extent of lesions is minimal. A few cases of optic atrophy were seen, but cerebrospinal fluid and other investigations failed to connect it with bejel. It would obviously be most desirable to have autopsies of patients coming from the distant bejel areas where syphilis is not a practical problem. With this in mind all pathological departments were circularized, but disappointingly, permission for autopsy is difficult to obtain.

**Differential Diagnosis**

As bejel resembles certain stages of venereal syphilis closely enough to make differentiation at times impossible, the presence of the latter in significant numbers in bejel areas is of some moment. Histories of patients where illicit contacts are concerned, are notoriously unreliable. As none of the laboratory aids could help us in the differenti-
of 5-6 months, were seen. On the other hand, saddle noses, sabre tibias, and late skin lesions were commonly seen in young people. Could they be of congenital origin? I feel that as bejel is often acquired at a very early age when bone growth is most active (unlike acquired syphilis), vulnerable parts of the skeleton are open to infection. A similar state exists in congenital syphilis. Our failure to find Hutchinsonian teeth, Moon's molars, and other dystrophies suggests that bejel has its onset after the second dentition teeth are comparatively grown and set and no longer vulnerable to infection—that is, some time after birth. The bejel of early childhood resembles congenital syphilis in some respects (saddle nose, etc.) only because the onset in both infections is so little separated in time, so that the two diseases act at a similar stage upon the developing host. This makes childhood bejel more like congenital syphilis, than the acquired type.

It is not denied that congenital bejel may occur, especially when mothers-to-be are infected rather late and remain infectious during pregnancy; but usually, by the time the first child is born, bejel has been present for 7-8 years on an average, and can be considered non-infectious.

The miscarriage rate proved of little help, as it was enormously high both in affected and unaffected women from these rural areas. Our information on this point may be inaccurate, as women did not like to admit miscarriages or stillbirths and attached shame to their occurrence.

Epidemiology

The factors which maintain bejel as an endemic infection must be investigated, if only to guide mass-eradication of the disease by the most effective means. Some of these, such as the common drinking vessel and low standards of hygiene, have already been mentioned. Insect vectors remain a possibility (as in yaws) and here two observations may be relevant:

1. Most bejel is found near water, be it river, marsh, or lake. Partly this is due to the fact that many more people cluster around the water-ways than in the less fertile areas away from it. However, in the north of the country, where this factor is less operative, I found a steep decline of bejel even a few miles inland, although the racial characteristics, size of villages, standard of hygiene, etc., appeared to be identical with those of the "bejel villages" near the water (Csonka, 1952).

2. A decided increase in the number of early cases occurs with the coming of spring. Insects, especially flies, are especially prevalent near water with the coming of the warm season. However, our observations may be explained on a climatic basis. Thus in the warm season, near water, a hot humid atmosphere is generated which is apparently conducive to the occurrence and spread of yaws. Incidentally, we have not found any bejel at an altitude of over 1,500 ft., but unfortunately other factors, such as different standards of hygiene may be obscuring the picture.

Flies and climate aside, and leaving it very much an open question, we learned in practice which communities were most likely to have bejel and which did not. Distance from towns proved quite reliable: i.e., bejel increased as we moved further away from the towns with their better hygiene, and simple treatment facilities.

As Hudson has often pointed out, even a small school or primitive dispensary was sufficient to clear a belt free from bejel; the first by teaching the rudiments of hygiene, the latter by means of a few injections of bismuth, which though inadequate to cure the individual, was sufficient to render him non-infectious to others.

Proximity to water has already been mentioned. Although most bejel is found in one particular tribe—the Djibours—this was thought to be because this large tribe conforms more completely than any other to the geographical and hygienic conditions favourable to bejel.

This point was dramatically illustrated in a few villages where Kurds and Djibours lived side by side. The former, with their superior hygienic standards, were almost free of bejel, although surrounded by infectious cases amongst the Djibours.

Archaeological Research

I examined a few crates of skeletons and individual bones, estimated to be 3,000 to 4,000 years old, and now reposing in the museums of Baghdad, but no evidence of osteoperiostitis was found.

Results of Treatment

The effects of "one-shot" doses of 1-2 mega units of PAM, give a fair hope that this treatment will prove adequate. The rate of healing was prompt in all stages, and of 237 patients seen 12 months after treatment, only nine (3.6 per cent.) could be classed as failures. Most of these had skeletal bejel and for some time now the dosage for this type of case has been doubled to 2-4 mega units PAM. It is expected that 25,000 people will have been treated by the end of 1952. A small number of patients treated with aureomycin, chloramphenicol, or terramycin gave encouraging results, however. Penicillin is clearly the drug of choice.

Serologically, there was a steady decline in the titres, 31 per cent. becoming negative after 12
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months. Dr. Jones, the present Adviser, noted in a recent report (Jones, 1952) that in an endemic area which had been lightly treated a year ago, there was an 85 per cent. reduction of new cases. It seems certain that annual, or better still 6-monthly, "sweeps" with the "penicillin broom" will clear the bulk of bejel, especially if contacts as well as cases can be included. However, there is danger in these spectacular results, for a complete and easy solution of the whole problem might be wrongly expected. But all our experience shows that lack of hygiene is a fundamental factor in maintaining bejel, and therefore a rural hygiene project should be combined with penicillin teams to secure permanent results. The authorities responsible for the planning in the WHO are fully alive to this aspect of treponemal control (Reynolds and Guthe, 1952).

Summary

Some clinical and epidemiological aspects of bejel, a non-venereal treponematosis found amongst the rural Arab population of some Middle-Eastern countries, are described on the basis of 3,507 cases seen in Iraq under the auspices of the bejel campaign sponsored by WHO/UNICEF. The infection commonly, though not exclusively, affects children and adolescents of both sexes, and imitates closely the secondary and benign tertiary stages of venereal syphilis. It involves mainly the mucous membranes, skin, and bones. Primary lesions were found only in exceptional circumstances and in the present material no obvious cases of neural or cardiovascular involvement came to light, but such visceral complications remain a possibility. No evidence of congenital transmission was found; the apparent similarity of certain features with congenital syphilis are discussed.

The "natural history" of untreated bejel is suggested on the basis of a clinical cross-section of over 3,500 consecutive cases.

The relationship of bejel to syphilis and other treponemal diseases is still uncertain, but in practice it responds, like all the others, to penicillin. The first results with the newer antibiotics are satisfactory, though penicillin remains the drug of choice for mass-treatment. The raising of hygienic standards in the bejel areas is considered essential to consolidate the good, early results achieved by mass-treatment with penicillin.

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