

# Electrophysiological changes during episodes of the Kleine-Levin syndrome

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**SYNOPSIS** Diurnal EEGs of a 17 year old male with the Kleine-Levin syndrome revealed moderate diffuse abnormalities and stage REM at sleep onset during attacks. Overnight, stages 3, 4, and REM of sleep were decreased, but sleep onset REM stage was not seen. These records returned to normal between attacks.

Kleine (1925) and Levin (1929) described in three young men the occurrence of repeated attacks of somnolence, personality disturbances, and gluttony. Alterations in sexual behaviour were noted in two cases. Critchley (1962) found 15 previously reported observations and added 11 personal cases of a clinical syndrome described as 'periodic hypersomnia and megaphagia in adolescent males'. A review by Fresco *et al.* (1971) indicated that, although a spectrum of clinical manifestations and a variable course characterized this illness, which could affect individuals of either sex, periodic episodes of hypersomnia were the prime and essential feature of the Kleine-Levin syndrome. Furthermore, it appears that the diagnosis is often difficult and not likely to be made early, particularly during the first episode.

We observed, in a young man with the Kleine-Levin syndrome, a variety of electrophysiological changes, including rapid eye movement (REM) sleep in short diurnal electroencephalograms (EEGs) during attacks, but not during asymptomatic intervals. Very little attention has been directed to the EEG features of sleep of patients with this illness. The following report describes our findings.

## METHODS

The patient was observed carefully for manifesta-

tions of the syndrome. In particular, the presence or absence of hyperphagia, hypersexuality, truculence, and withdrawn behaviour (prolonged latent responses, monosyllabic answers, or refusals to answer) were monitored.

EEGs were recorded during diurnal wakefulness and sleep with eight- or 16-channel electroencephalographs utilizing the International 10-20 system of electrode placement, and included bipolar and referential montages. Each tracing lasted a minimum of 30 minutes. In particular, the waking parieto-occipital rhythm and EEG activity slower than the average frequency of this rhythm were assessed. Also, all-night sleep polygraphic records were taken with the patient comfortably in bed in a sound-proofed laboratory. All recordings during sleep included an electrooculogram (EOG), from electrodes placed above and lateral to one eye, and a submental electromyogram (EMG). The nocturnal records were made and scored according to the recommendations of Rechtschaffen and Kales (1968).

## CASE REPORT

A 17 year old white male was essentially healthy until he was brought to another hospital in April 1973 because of the sudden onset of continuous somnolence. Although he was not hospitalized, he remained for the next 13 days in this state. His appetite for sweets increased greatly and he became openly amorous toward women, to the embarrassment of his family. He recovered spontaneously.

Five months later he was again observed to become somnolent and uncommunicative. He was hospitalized elsewhere without definite diagnosis for the next four months and did not respond to phenothiazines or electroconvulsive treatments. EEGs

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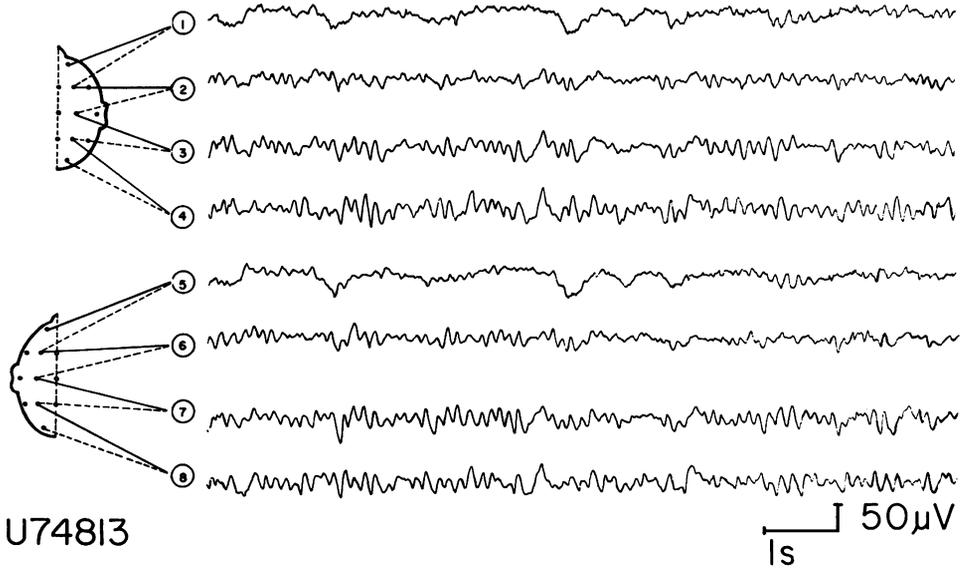


FIG. 1 *Abnormal diurnal waking EEG recorded during symptomatic period.*

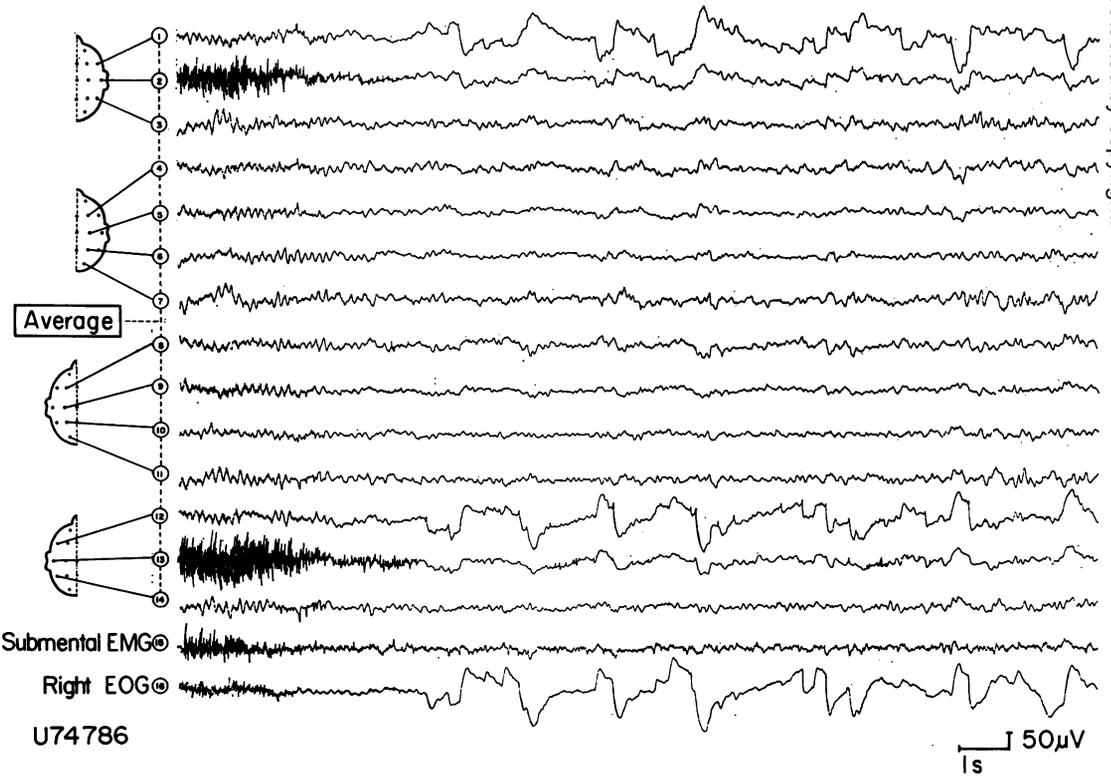


FIG. 2 *Sleep onset REM stage of sleep in a diurnal EEG recorded during an attack.*

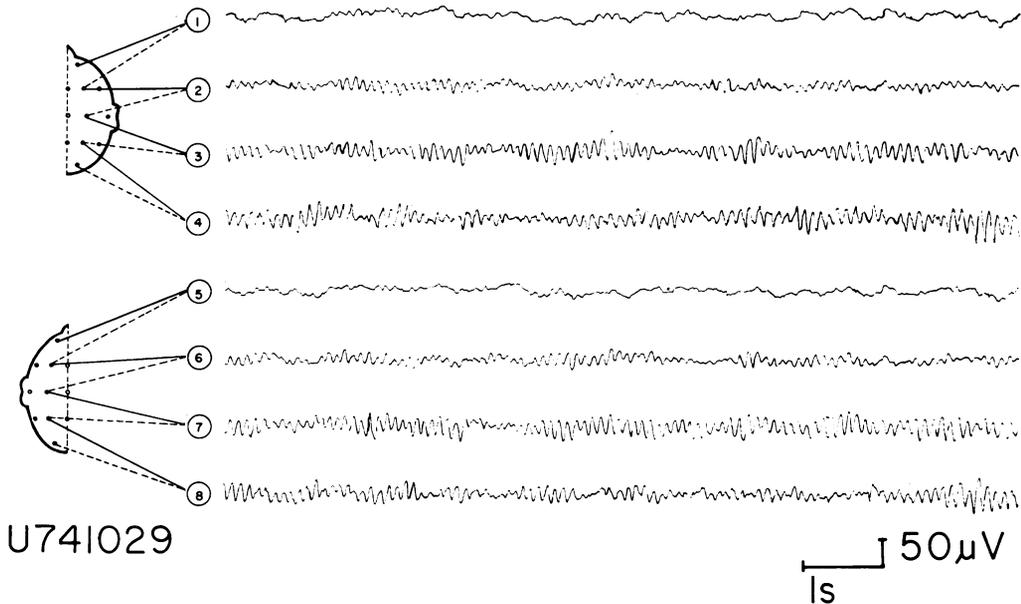


FIG. 3 Normal diurnal waking EEG recorded during an asymptomatic interval.

were said to show 'some excessive slowing', although his behaviour at the times of recording was not apparent from the hospital records. The patient was transferred to the University of Washington Hospital in January 1974. He was withdrawn, verbally unresponsive, and heavily medicated with phenothiazines. All drug therapies were stopped. Within three weeks he became a pleasant and interactive person and was discharged with 'no current psychiatric diagnosis'. In June 1974 he had another attack and was again admitted to the psychiatry service of the University of Washington Hospital. His somnolence, truculence, hyperphagia, withdrawn behaviour, and aggressive, amorous sexual episodes were quite apparent and the diagnosis of the Kleine-Levin syndrome was suggested.

Shortly thereafter, an EEG was performed during wakefulness and sleep. The technologist noted that the patient was very lethargic, uncommunicative, and would fall asleep when not stimulated. When he appeared to be awake (Fig. 1), a posterior rhythm of 7–8 Hz and 25–65  $\mu$ V was seen intermixed with a moderate number of 1.5–6 Hz arrhythmic potentials of similar or slightly higher voltage. This rhythm was attenuated by opening the eyes. Occasional posterior sharp transients were also noted, as are typically seen in healthy youths. A small number of fairly rhythmic 4–6 Hz waves was detected over the middle and anterior regions, mostly during drowsiness. Infrequent, diffuse 2–6 Hz arrhythmic waves

were induced by noises during light sleep or at arousal. The patient could not cooperate to hyperventilate adequately, and intermittent photic stimulation induced a prominent posterior driving response. This record was felt to demonstrate moderate generalized abnormalities.

The patient, when not stimulated, promptly fell asleep. In this EEG, after six minutes of stage 1 sleep and arousals associated with body movement, typical rapid eye movement (REM) sleep patterns suddenly appeared. These consisted of diffuse low voltage (15–50  $\mu$ V) EEG activity, primarily in the theta range, associated with sudden decrease in submental tonic EMG and prominent and frequent rapid eye movements (Fig. 2). Also, EMG bursts suggestive of clonic activity were detected intermittently and over the scalp. The patient spontaneously awoke twice and on both occasions within less than three minutes went back into REM sleep.

EEG records were repeated over the next 11 weeks, during which the patient had a spontaneous remission lasting one month followed by recurrence of symptoms. This last attack terminated within three days after beginning the oral administration of 90 mg methylphenidate per day. All EEGs, however, were taken when the patient was off medication for at least one week. As symptoms waxed and waned during all attacks, abnormalities identical with those observed in the first EEG decreased and in-

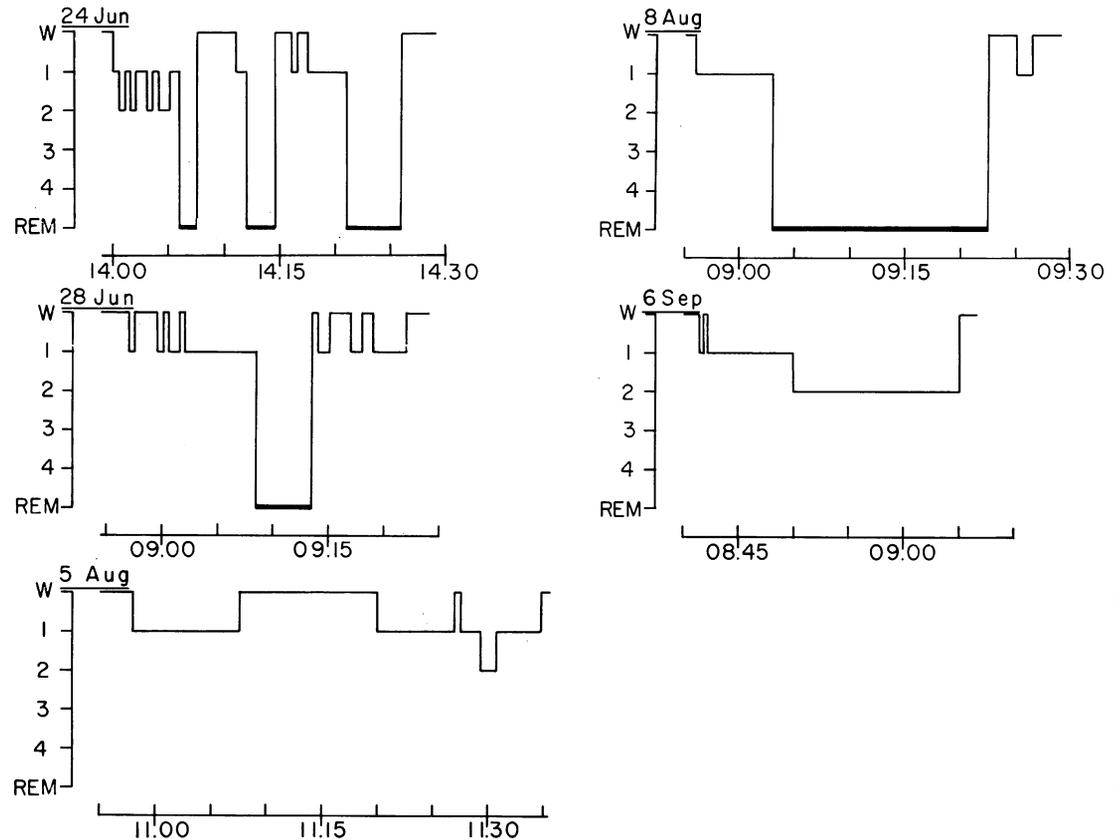


FIG. 4 Diurnal sleep hypnograms during symptomatic (24 and 28 June, 5 and 8 August) and asymptomatic (6 September) periods.

creased respectively. Between attacks, records were normal (Fig. 3).

Figure 4 shows that REM sleep was seen in three diurnal EEGs when the patient was markedly symptomatic (24 and 28 June, 8 August). The remaining recordings were taken when the patient was much improved or asymptomatic and he entered only non-REM sleep.

The result of an overnight sleep polygraphic recording obtained when the patient was markedly hypersomnic is displayed in Fig. 5A and a similar observation made during an asymptomatic interval 11 days later is shown in Fig. 5B. The first overnight recording (Fig. 5A) revealed that the patient was restless and awakened numerous times throughout the night. The patient slept much more soundly during the second session (Fig. 5B). The tracing taken during a clinical attack showed increased wakefulness and stage 1 sleep and decreased amounts

of stages 3, 4, and REM sleep when compared with the other record. The record taken when the patient was symptom free was judged to be essentially normal and stage REM was not seen at sleep onset on either occasion.

#### DISCUSSION

Our 17 year old patient was a 'typical' example of the Kleine-Levin syndrome according to the criteria of Fresco *et al.* (1971). Within 14 months he had experienced, without known cause, four distinct but similar episodes of hypersomnia, hyperphagia, withdrawn agitated behaviour, and outgoing sexual demonstrations. Polygraphic studies of our case revealed two especially interesting findings. Diurnal waking EEG re-

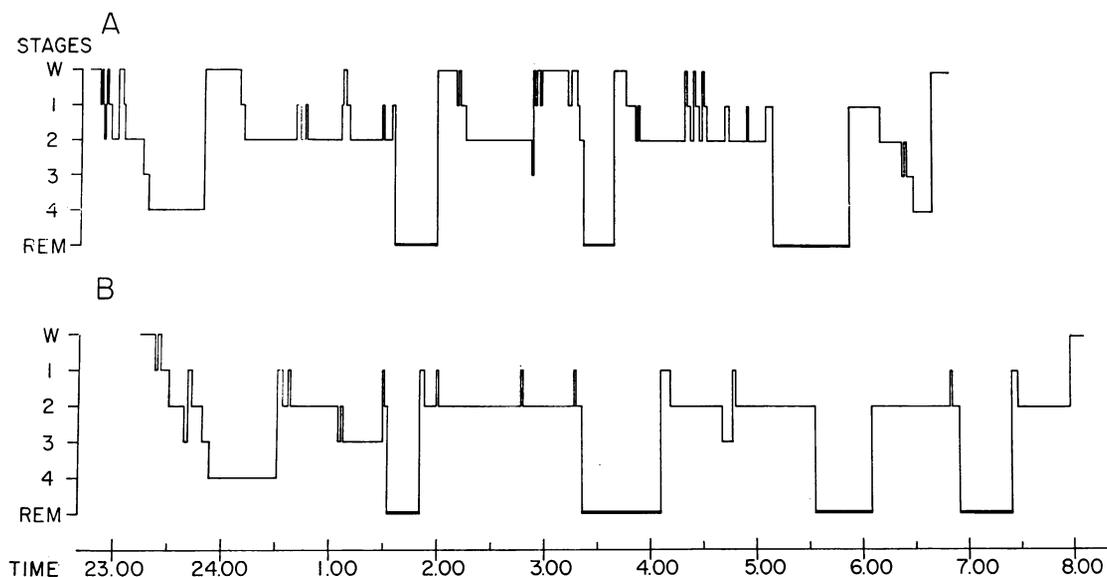


FIG. 5 Nocturnal sleep hypnograms obtained during symptomatic (A) and asymptomatic (B) periods.

cords during three attacks showed moderate diffuse slow wave abnormalities, confined to symptomatic periods, which in severity paralleled changes in his clinical course. Sleep studies during attacks revealed stage REM within the first seven minutes of sleep during diurnal, but not nocturnal, recordings. Otherwise, sleep patterns characteristic of each stage, including spindles, were unremarkable. Sleep during asymptomatic intervals was entirely normal. Because of these polygraphic features we undertook a review of previous reports of similar patients.

**DIURNAL RECORDINGS DURING WAKEFULNESS AND SLEEP** Critchley (1962) drew attention to the presence of abnormalities during attacks in diurnal EEGs of patients with the Kleine-Levin syndrome and to the interesting observation that in some cases the records returned to normal between attacks. Review of the literature has revealed reports of 17 individuals with similar findings (Rossenkötter and Wende, 1955; Critchley, 1962; Garland *et al.*, 1965; Hnayal and Regli, 1967; Messimy *et al.*, 1967; Barontini and Zappoli, 1968; Bonkalo, 1968; Elian and Bornstein, 1969; Suwa and Toru, 1969; Green and

Cracco, 1970; Smirne *et al.*, 1970; Fresco *et al.*, 1971; Popoviciu and Corfariu, 1972; Billiard *et al.*, 1975). In these cases, mild or moderate diffuse, random and occasionally bisynchronous EEG abnormalities, often associated with irregularities and slowing of the alpha rhythm, were stated by the authors to have returned to normal when the patients became asymptomatic.

In most reports of patients with this syndrome, the state of consciousness at the time of taking diurnal EEG records was not clearly defined. Some exceptions are the studies by Rossenkötter and Wende (1955) and Green and Cracco (1970) in which EEG observations during diurnal sleep were specifically described. While the former authors found essentially normal sleep patterns, the latter stated that, in their case, sleep spindles were absent. Neither Barontini and Zappoli (1968) nor Popoviciu and Corfariu (1972) observed stage REM in diurnal sleep. However, the appearance of REM sleep in short diurnal diagnostic EEGs has been reported by Messimy *et al.* (1967) as a characteristic feature of their patient during an attack of the Kleine-Levin syndrome. Billiard *et al.* (1975) studied a young female with periodic hypersomnia linked to menstruation whom they felt was a 'clinical

variant' of the Kleine-Levin syndrome. During three 24-hour recordings during two separate attacks of the illness, the EEG during diurnal sleep showed a mean latency for stage REM of 20 minutes (range nine to 27.5). Although the authors did not emphasize these findings, this last case is likely to be similar to the patients reported here and by Messimy *et al.* (1967).

**NOCTURNAL SLEEP CYCLES** A few authors have directed their attention to nocturnal sleep cycles in patients with the Kleine-Levin syndrome. Four patients with such studies are reported to have shown a decrease in stages 3 and 4 of non-REM and less REM sleep than normal (Messimy *et al.*, 1967; Takahashi, 1967; Barontini and Zappoli, 1968; Suwa and Toru, 1969). In one individual, Smirne *et al.* (1970) were unable to detect REM sleep in an overnight recording, but Billiard *et al.* (1975) reported that their patient had an increase in stages 1 and 2 as well as REM. In no case, including ours, was stage REM seen at nocturnal sleep onset.

**CLINICAL AND PATHOPHYSIOLOGICAL CONSIDERATIONS** In our experience the finding of stage REM during short diagnostic sleep EEGs is exceedingly unusual, except among narcoleptics (Dement *et al.*, 1966), subjects with a history of sleep deprivation (Dement, 1969) or withdrawal of drugs known to inhibit REM sleep (Zarcone, 1973), or in individuals with a disorder which induces disturbed nocturnal sleep, such as the Pickwickian syndrome (Schwartz, 1968). The last three could be ruled out in our case, and neither our patient nor others with the Kleine-Levin syndrome gave a history of paroxysmal sleep episodes, cataplexy, hypnagogic hallucinations, and sleep paralysis seen in narcoleptics. The attacks considered here are of a prolonged nature, usually lasting a few days to several weeks, and associated findings, including hyperphagia, hypersexuality, and personality disturbances, while not always present or prominent, are often seen. However, it is of interest that Ceroni (1968) reported an individual who experienced only one attack of an illness which seemed to represent the Kleine-Levin syndrome and in subsequent years developed a characteristic narcoleptic syndrome accompanied by sleep onset stage REM in diurnal records.

The occurrence of stage REM at diurnal sleep onset in patients with the Kleine-Levin syndrome deserves special attention. One must realize that reports before the description of REM sleep in 1955 by Aserinsky and Kleitman, and most likely all cases reported before Dement *et al.* (1966) drew general attention to the importance of stage REM at sleep onset, must be eliminated when attempting to establish the frequency of occurrence of this finding in such individuals. Also, it is our experience that, without appropriate recording of the electro-oculogram and submental EMG, REM sleep might easily be missed. Hence, this stage of sleep must be actively sought in these patients.

Abnormalities of the waking EEG, the appearance of stage REM at sleep onset during diurnal polygraphic recordings and disturbances in the overnight sleep cycles in our patient and in others previously reported with the Kleine-Levin syndrome, suggest a disturbance of physiological mechanisms controlling electrocortical activity and the state of consciousness. Some authors have considered the associated symptoms of hyperphagia, hypersexuality, and personality disturbances to indicate that a derangement of hypothalamic function is the aetiology (Palmer, 1950; Garland *et al.*, 1965; Gallinek, 1962; Green and Cracco, 1970), but this has not been proved. According to evidence cited in a review by Moruzzi (1972), the development of normal wakefulness and sleep depends upon balanced reciprocal activity of certain centres within the hypothalamus and their interaction with brain-stem structures responsible for activating and deactivating influences on the cerebrum. It is conceivable that alterations of the latter as a consequence of a disturbance in the former could be the cause of all the abnormalities in the EEGs of these patients. Their transient and reversible nature is indicated by the usual spontaneous or drug-induced return of these individuals to normal.

We believe that the prompt recognition of the Kleine-Levin syndrome is of practical importance because these patients are unlikely to respond to therapy other than the administration of cerebral stimulants. The demonstration of altered waking and sleeping patterns in polygraphic records taken during symptomatic

periods should be of assistance in the diagnosis of the condition.

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