

Clinical features of 53 cases with pustulotic arthro-osteitis

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SUMMARY We have described clinical features of 53 cases with pustulotic arthro-osteitis. Anterior chest wall symptoms such as intersterno-costoclavicular or manubriosternal lesions were observed in all of 53 cases. Spondylitis or spondylodiscitis was found in 18 cases. Sacroiliitis resembling ankylosing spondylitis was seen in 7 cases. Peripheral inflammatory arthritis was seen in 14 cases, which were of nonerosive, of oligoarthritis type, and cured within 1 to 2 months, leaving no residue. HLA B27 was never found, and RA factor was negative. Histological examinations revealed non-specific chronic inflammation of bone and soft tissue. Pustulotic arthro-osteitis is apparently distinct from known rheumatic diseases such as rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, and Reiter's disease. We have proposed that this condition should be classified as a member of the 'seronegative spondylo-arthritis' group as designated by Wright and Moll.

We have shown in a previous article that unique arthro-osteitis often appears together with pustulosis palmaris et plantaris (PPP).¹ Here we shall describe in detail the clinical features of 53 cases with pustulotic arthro-osteitis, and show that this is a new rheumatic disease belonging to the 'seronegative spondylo-arthritis' group of Wright and Moll.

Patients and methods

The patients fell into 2 groups. One consisted of 12 patients found through epidemiological surveys on PPP patients as described previously.¹ The other consisted of 41 patients who had been seen in our orthopedic or dermatology clinics since 1970. Both groups are hereinafter dealt with as one because they showed no statistically significant differences in sex, age of disease onset, duration of the disease, or clinical patterns of skin and arthro-osteitis symptoms. Seventeen were men aged 25 to 64 years, average 45, and 37 were women aged 27 to 74 years, average 50. The age of disease onset is shown in Fig. 1.

Results

CLINICAL SYMPTOMS AND SIGNS

Manifestations of pustulotic arthro-osteitis were observed in the anterior chest wall, the spine, the sacroiliac joint, and peripheral joints.

Anterior chest wall symptoms. This is the most characteristic feature of the condition. The most frequently involved site was the region of the costoclavicular ligament, which was observed in as many as 50 cases. As shown in Fig. 2, painful swelling was visible bilaterally in the costoclavicular area. It was often accompanied by local heat and redness. Mobility of the clavicle was more or less limited, and the shoulder girdle was fixed in a so called square-shouldered position. Patients felt difficulty in shrugging their shoulders. Definite myogelosis was commonly noticed in the trapezius or the levator scapulae muscles. Abduction (lateral elevation) of the arm was slightly limited in most of the cases.

X-ray findings were negative in early phases, but with progress of the disease abnormal ossifications or erosions at the costoclavicular ligament became apparent.¹ In most advanced cases the clavicle and the first rib were completely united with abnormal ossifications (Fig. 3). Osteomyelitis-like hypertrophy

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of the clavicle was also observed in severely affected cases (Fig. 4). The manubriosternal joint was the next most frequently involved site. Painful swelling and tenderness on pressure at this site were observed in 41 cases (77%). The costal cartilage adjacent to the joint was also commonly involved. X-rays showed widening or erosion of the joint space and syndesmophyte formations. More advanced cases had bony ankylosis. These findings are best demonstrated by a lateral tomography of the sternum.¹

In addition to the above mentioned 2 sites,

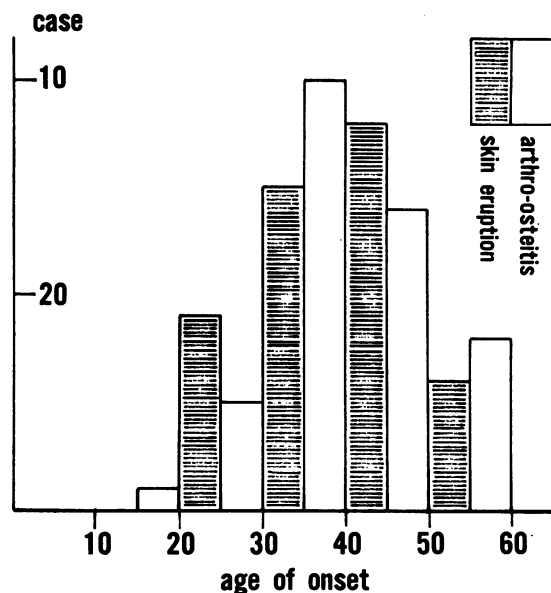


Fig. 1 Age distribution of disease onset.

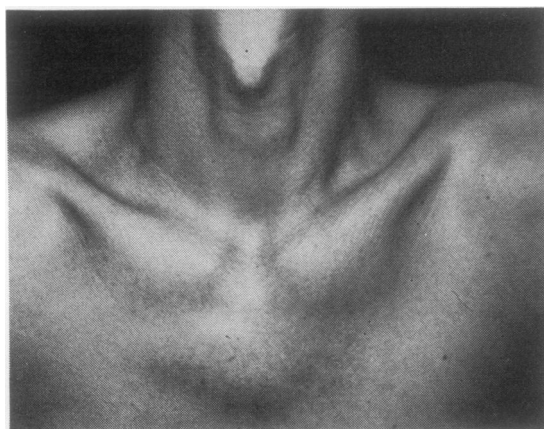


Fig. 2 Anteriorchest wall symptoms. Swelling at the bilateral costoclavicular and the manubriosternal regions are visible.

painful swelling was sometimes noticed at the costal cartilage of lower levels, but x-ray findings were negative and the symptoms were much less severe than those of the costoclavicular or the manubriosternal lesions.

Spinal symptoms. These were recorded in 18 cases (34%). Cervical, thoracic, and lumbar lesions were seen in 10, 10, and 14 cases respectively. The mobility of the spine was highly restricted by pain, which was not completely relieved by rest.

X-ray findings revealed 2 types of lesion. One was of spondylitis type, observed in 12 cases, showing syndesmophyte formation extending over several levels of the spine (Fig. 5). The other was of spondylodiscitis type, seen in 10 cases, where a distinct intervertebral level was involved as in suppurative spondylodiscitis (Fig. 6). However, this difference is made mainly for convenience, because both types of lesions were often seen in the same patient. Spondylitis was observed in 12 cases. As shown in Fig. 5, syndesmophytes were of peripheral type according

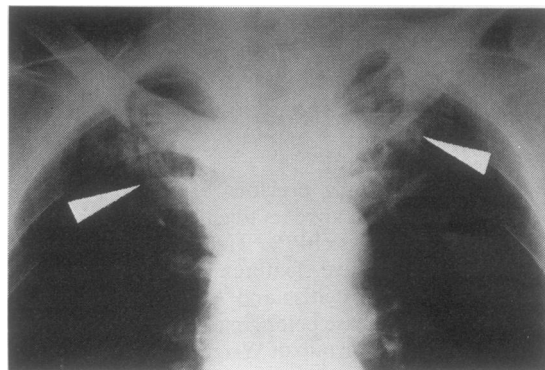


Fig. 3 Interspace between the clavicle and the first rib is completely fused with abnormal ossifications.

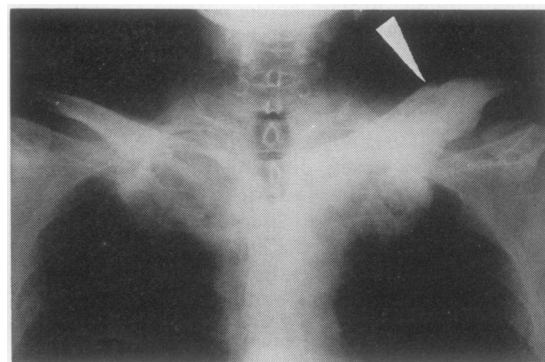


Fig. 4 Osteomyelitis-like hypertrophy of the clavicle.

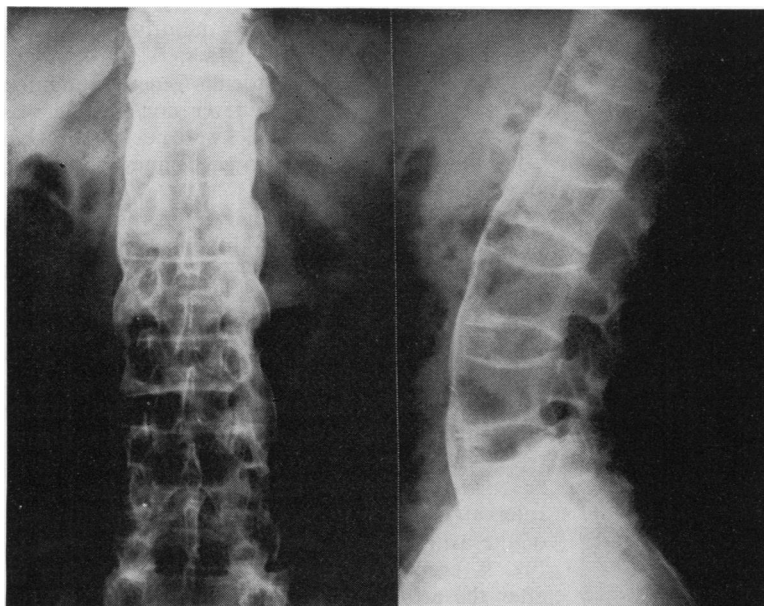


Fig. 5 Ankylosing-spondylitis-like spondylitis.

to McEwen *et al.* classification.² In 3 cases they resembled ankylosing spinal hyperostosis (Fig. 7). In these cases active uptake of the radioisotope ^{99m}Tc established the diagnosis of spondylitis. Spondylo-

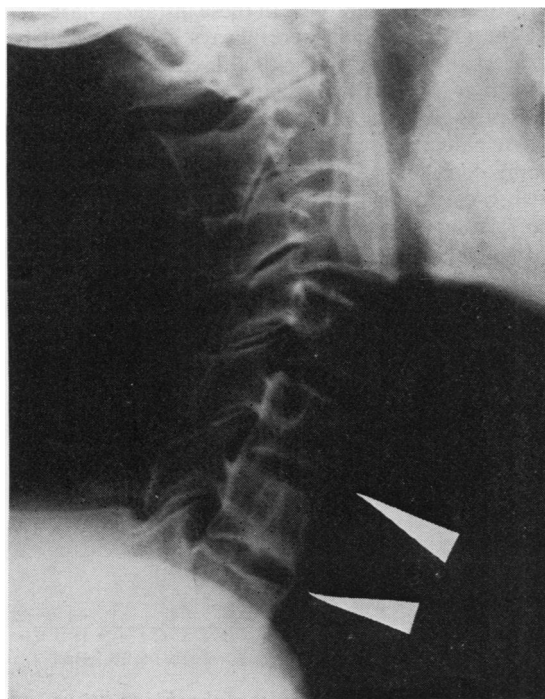


Fig. 6 Spondylo-discitis at the C5 to C7 level.

discitis was found in 10 cases, mostly at the cervical and lumbar levels. In a few cases 2 or more foci of discitis were observed at separate sites (Fig. 6), though it was usually at a single intervertebral site.

Sacro-iliitis. This was seen in 7 cases (13%). All but one were bilateral. Clinical and radiological findings were very close to those of ankylosing spondylitis (Fig. 8).

Erosions and sclerosis of the joint were seen in early cases, and bony ankylosis was observed in advanced cases.

Peripheral arthritis. Inflammatory arthritis of peripheral joints was seen in 17 cases (32%). The most frequently involved site was the acromioclavicular joint, noted in 6 cases. The next most commonly affected joints were the metacarpophalangeal and proximal interphalangeal of the fingers, and the elbow and knee joints. Other joints such as the hip, the ankle, and the wrist joint were also involved, though rarely, but distal interphalangeal joints of fingers were involved in only 1 case. This latter finding formed a relatively striking contrast to psoriatic arthritis.

The affected joints showed swelling, tenderness, and pain on motion. Redness and local heat were sometimes observed. In the majority of the cases arthritis was of mono- or oligoarthritic type. In a few exceptional cases polyarthritides like rheumatoid arthritis developed, but even in these the individual arthritis was of nonerosive type and showed monocyclic patterns. Peripheral arthritis was always cured within 1 to 2 months, leaving no residue.

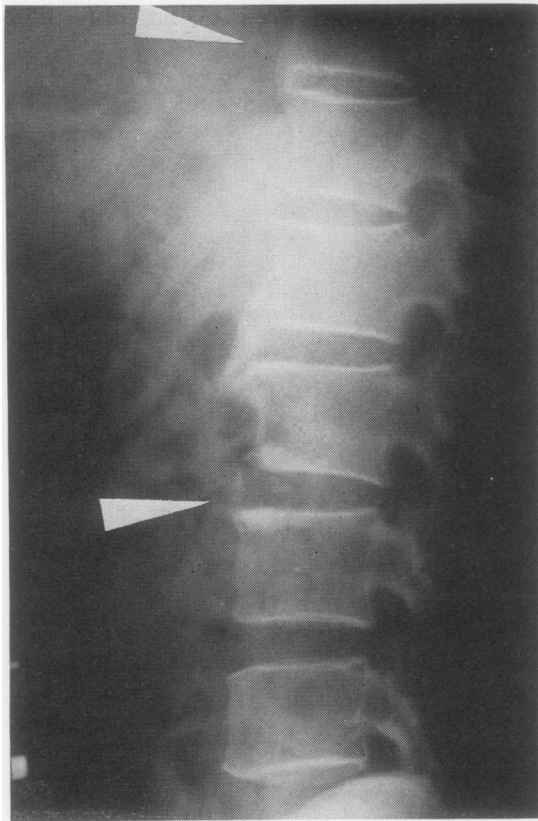


Fig. 7 Ankylosing spinal hyperostosis-like ossifications at the anterior longitudinal ligament of the spine from T12 to L4.



Fig. 8 Sacroiliitis.

X-ray findings were always negative except for soft-tissue swellings in acute phases.

Other symptoms. The patient's general condition was not impaired. Neither fever nor wasting was observed. Rheumatoid nodules were never found. No abnormality was detected in gastrointestinal, optic, or genito-urinary systems.

Although their aetiological relationships to arthro-osteitis are not clear, the following complications have been noticed: chronic tonsilitis in 5 cases, chronic inflammation of salivary glands in 4, hyperthyroidism in 2, chronic bronchitis in 1, and pulmonary tuberculosis in 2. Among these complications chronic inflammation of salivary glands is noteworthy, because its exacerbations were closely associated with flare-ups of arthro-osteitis symptoms.

SKIN AND ARTHRO-OSTEITIS SYMPTOMS

Intervals from the onset of skin eruptions to the onset of the arthro-osteitis were examined. As shown in Fig. 9, eruptions began within 2 years before or after the arthro-osteitis in more than 70% of the cases, the mean being at about 0. But in 1 case arthro-osteitis occurred 12 years after the occurrence of skin disease, and in another 2 it developed 12 years earlier.

Fifteen of the patients had the impression that their skin diseases were closely related to their arthro-osteitis symptoms. In these instances flare-ups of the arthro-osteitis were always accompanied by exacerbations of the skin disease, or surgical resection of the arthro-osteitic lesions brought about complete remissions of the skin eruptions. Many other patients also had a less distinct impression of some correlation between their skin eruptions and arthro-osteitis symptoms. But in 14 cases no such correlation was observed, that is, arthro-osteitis continued, and there were repeated remissions and

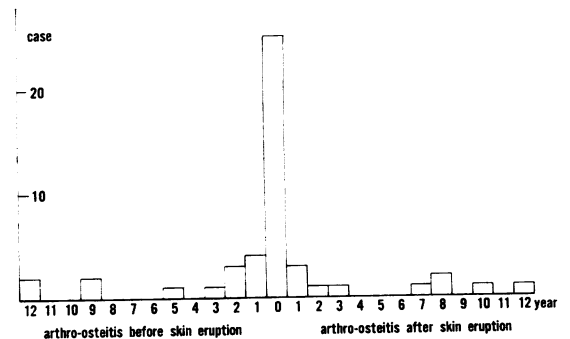


Fig. 9 Intervals from the onset of the skin eruptions to the onset of arthro-osteitis.

exacerbations for many years after complete healing of skin disease.

LABORATORY FINDINGS

Elevation of ESR and positive CRP was seen in most of the cases. A mild degree of leucocytosis ranging up to $13 \times 10^9/l$ was observed in 20 cases. Other blood examinations were within normal limits except slightly increased alkaline phosphatase activity, which was seen in 14 cases. Urine analysis was normal. Serological tests for syphilis and Hb antigen/antibody tests were negative. RA factor was negative except in 3 cases. None of the 3 cases showed clinical signs of rheumatoid arthritis. Human leucocyte antigens (HLA) of A and B locus were examined in 36 cases. No particular deviations from normal controls were found. B27 was never found, and B5, B13, and B17 had not increased. In this connection it should be noted that the frequency of B27 in the normal Japanese population is less than 1.0%.³

PATHOLOGY AND BACTERIOLOGY

Tissue specimens were taken mainly from anterior chest wall lesions of 20 cases. All showed essentially the same histological findings (Fig. 10), namely, nonspecific chronic inflammations of bone and enthesis with marked fibrosis, and mild to moderate degree of infiltrations of mononuclear cells and neutrophils. New bone formation in soft tissues or around bones was seen; bone absorption also was observed. Granulation tissue was commonly seen at the costoclavicular ligament, but abscess formation was seen in only 1 case.

No micro-organism grew from these specimens on culture.

TREATMENT AND PROGNOSIS

This disease shows a chronic course with exacerbations and remissions for many years. There is no radical treatment at the present time, but anti-inflammatory drugs such as phenylbutazone and indomethacin are effective for alleviation of pain. Predonisonone, 10 to 20 mg a day, was less effective than these agents and was seldom prescribed. In some special cases, in which anterior chest wall symptoms were so severe as to interfere with the patient's daily activities, partial resection of the clavicle or the first rib was indicated. However, it seems most important for patients to learn that the disease is essentially benign in nature, and that their functional prognosis is generally good in comparison with that of rheumatoid arthritis.

DIFFERENTIAL DIAGNOSIS

Pustulotic arthro-osteitis has to be distinguished from some other rheumatic diseases.

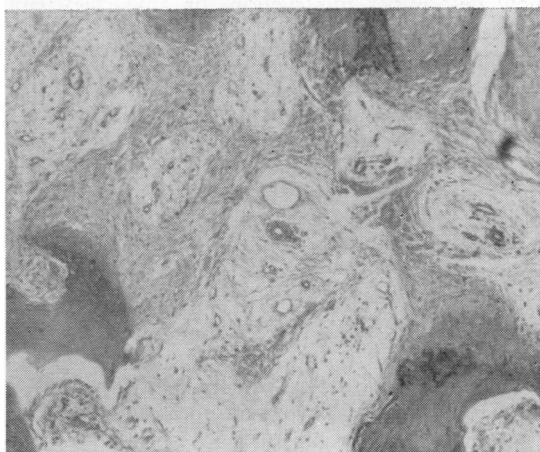


Fig. 10 Histology shows chronic inflammation of bone and soft tissue.

Rheumatoid arthritis. Pustulotic arthro-osteitis differs from rheumatoid arthritis in many ways. Firstly, peripheral arthritis is clearly distinct, that is, much milder and shorter in duration. No abnormal findings are seen on x-ray examination. A high frequency of anterior chest wall symptoms and absence of rheumatoid factor are additional distinctions.

Ankylosing spondylitis. Spondylitis in pustulotic arthro-osteitis is sometimes very close to that of ankylosing spondylitis and is difficult to differentiate. But high frequency of anterior chest wall symptoms and relatively low frequency of sacroiliitis form a contrast to ankylosing spondylitis. Another distinction is the sex distribution, for more than 90% of ankylosing spondylitis patients are male, whereas about 70% of our pustulotic arthro-osteitis patients were female. We have already reported that 74% of

Japanese patients with ankylosing spondylitis carry HLA B27 phenotype,³ but no such association was seen among pustulotic arthro-osteitis patients.

Reiter's disease. This is very rare among Japanese, but must be differentiated from pustulotic arthro-osteitis because it shows a spondylitis or sacroiliitis similar to ankylosing spondylitis. Reiter's disease is differentiated from pustulotic arthro-osteitis by predominance of males and high frequency of HLA B27 again. Extra-articular symptoms such as urethritis and conjunctivitis also help in the differential diagnosis.

Psoriatic arthritis. This accompanies spondylitis or sacroiliitis. Its sex distribution is similar to that of pustulotic arthro-osteitis. The most definite distinction between the 2 diseases is seen in peripheral arthritis. In psoriatic arthritis peripheral joints often show deformities, destruction, or ankylosis, with apparent abnormalities in x-ray findings. Distal interphalangeal (DIP) joints of fingers are especially commonly involved. In contrast, peripheral arthritis seen in pustulotic arthro-osteitis is much less severe and DIP joint involvement is rare. It has been reported that HLA B13 and B17 are increased among psoriatic patients,⁴ and HLA B27 has an intimate relation to psoriatic spondylitis.⁵ No such findings were obtained among pustulotic arthro-osteitis patients.

Discussion

Associations of arthro-osteitis with pustulosis palmaris et plantaris have been sporadically reported by Japanese orthopedic surgeons since 1967.¹ We have clarified in a previous report that this association is not incidental, and proposed the term 'pustulotic arthro-osteitis' to describe this condition. We have also suggested that pustulotic arthro-osteitis is not a rare disease, like ankylosing spondylitis or psoriatic arthritis, among the Japanese population.¹

As stated above under 'Differential diagnosis,'

pustulotic arthro-osteitis is apparently distinct from rheumatoid arthritis, ankylosing spondylitis, Reiter's disease, and psoriatic arthritis. Nevertheless, we have to realise that it is very close to ankylosing spondylitis or psoriatic arthritis, because spondylitis and sacroiliitis seen in these disease groups are similar and almost indistinguishable from each other.

In 1976 Wright and Moll introduced a new concept of 'seronegative spondylo-arthritis,' putting the following diseases into this group: ankylosing spondylitis, psoriatic arthritis, Reiter's disease, Behçet's disease, ulcerative colitis, Crohn's disease, and Whipple's disease.⁶ According to these authors diseases belonging to this group share many properties, such as the following: absence of rheumatoid factor; absence of subcutaneous nodules; peripheral inflammatory arthritis; radiological sacroiliitis, with or without ankylosing spondylitis; miscellaneous clinical features including psoriasiform skin and/or nail lesions, ocular, genital, or bowel ulceration, erythema nodosum, pyoderma gangrenosum, and thrombophlebitis; a tendency to show clinical overlap; and familial aggregation and familial interrelationship.

There is no doubt that pustulotic arthro-osteitis has all these features except the last. We have no data yet to support the possibility that pustulotic arthro-osteitis shows familial aggregation or familial interrelationship, but a family case, consisting of 4 brothers and 2 sisters, has been reported.⁷ Two brothers and 2 sisters among them developed PPP, and these 2 brothers showed also such disorders bilaterally in the clavicles as described here. Although further clinical and epidemiological investigations are necessary to clarify this point, we would like to propose a concept to classify pustulotic arthro-osteitis as one member of the 'seronegative spondylo-arthritis' group. Fig. 11 shows our modification of Wright and Moll's proposal. Overlap between PPP and psoriasis is well known.⁸

To understand pustulotic arthro-osteitis as a

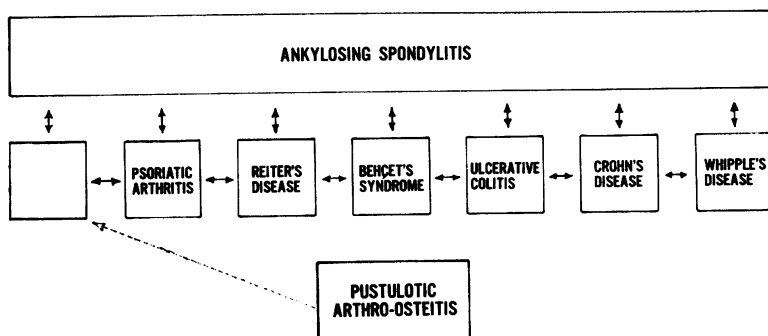


Fig. 11 Scheme proposed by Wright and Moll. Arrows indicate overlaps. Broken line shows our modification.

member of the seronegative spondylo-arthritis group is important not only from the academic but also from the practical point of view. As Wright and Moll state, it will enable a more optimistic prognosis to be given so far as the rheumatic part of the syndrome is concerned, or it will allow earlier diagnosis of any associated disease, or earlier detection of any related disease in family members of patients. Diagnosis of this disease is easy only if physicians are aware of its existence.

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