

CARCINOMA OF THE BILHARZIAL BLADDER IN EGYPT

Clinical and Pathological Features

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THE relationship between bilharziasis and carcinoma of the bladder was first reported by Fergusson (1911). Since then many valuable contributions have been added. Makar (1955), El Sebai (1961), and Abdel Tawab (1966), from Egypt emphasised this relationship. Similar conclusions were also reported from Rhodesia (Gelfand *et al.*, 1967), and from Iraq (Halawani *et al.*, 1970).

The aim of this study is to present the particular clinical and pathological aspects of carcinoma of the bilharzial bladder as seen in Egypt. The work is based on data collected from 304 cases with bladder cancer examined at the Department of Urology, Mansoura University Hospital, and the Institute of Cancer, Cairo, during 3 consecutive years (1967-1970).

Age and Sex Distribution.—Figure 1 is a diagrammatic representation of the age and sex distribution of 304 patients with carcinoma of the bladder. The male to female ratio was 4 : 1. The average age was 46.7 years for the males, 44.6 for the females, and 46.3 for the whole group.

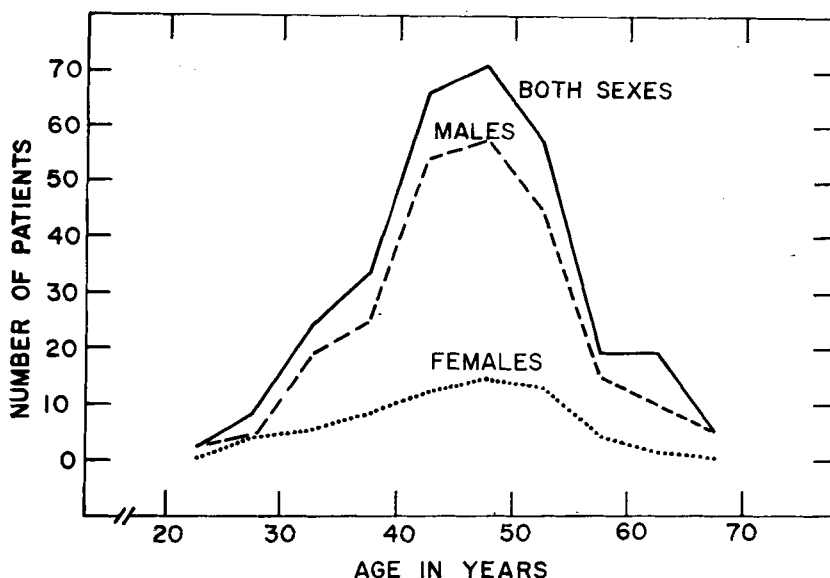


FIG. 1

Age and sex distribution of 304 cases of bladder cancer.

Clinical Presentation.—A summary of the main clinical presentations is given in Table I. Cystitis symptoms, painful micturition, frequency and hæmaturia were the most frequent clinical presentations.

Staging.—The T.N.M. staging system advocated by the U.I.C.C.¹ was applied. Bimanual examination of the empty bladder under anæsthesia, cystoscopy and biopsy were considered

¹ Union International Contre le Cancerum, Geneva, 1967. The sub-committee of clinical stage classification and applied statistics. Malignant tumours of the urinary bladder: clinical stage classification and presentation of results.

mandatory in determining the clinical stage. This was later checked in the course of pathological examination.

Seventy-five cases (24.6 per cent) were considered clinically inoperable. Table II represents the staging of 229 cases as pathologically determined. The majority of cases (68.2 per cent)

TABLE I
Presenting Symptoms in 304 Patients with Carcinoma of the Bladder

| Symptoms | No. of Cases | Percentage |
|-------------------------------|--------------|------------|
| Burning micturition | 140 | 65.1 |
| Frequency | 138 | 64.2 |
| Hæmaturia | 103 | 47.9 |
| Necroturia | 84 | 39.1 |
| Suprapubic pain | 51 | 23.7 |
| Pyuria | 50 | 23.3 |
| Difficulty | 35 | 16.3 |
| Renal pain | 29 | 13.5 |
| Retention | 7 | 3.3 |

TABLE II
Pathological Staging (U.I.C.C.) of Carcinoma of the Bilharzial Bladder

| Stage | Number | Percentage |
|-------|--------|------------|
| P1 | 8 | 3.9 |
| P2 | 35 | 15.1 |
| P3 | 157 | 68.2 |
| P4 | 29 | 12.8 |
| Total | 229 | |

TABLE III
Error in Clinical Staging (T.N.M.) as Verified by
Pathological Staging in 135 Cases

| Clinical Stage | No. of Cases | Pathological | | | |
|----------------|--------------|--------------|-----|-----|-----|
| | | P1 | P2 | P3 | P4 |
| T1 | ... | ... | ... | ... | ... |
| T2 | 37 | 1 | 9 | 27 | ... |
| T3 | 96 | ... | 6 | 74 | 16 |
| T4 | 2 | ... | ... | ... | 2 |

Total clinical error: 50 cases (37.2 per cent)
Error due to understaging: 43 cases (31.8 per cent)

revealed deep infiltration of muscles or perivesical adipose tissue (P3). The pre-operative estimation of the extent of the disease was compared with the pathological one in 135 cases to establish the degree of clinical error (Table III). The over-all error in clinical staging was 37.2 per cent and was highest at the T2 stage (75.6 per cent). In the majority of cases the error was due to clinical under-estimation of the extent of the disease.

TABLE IV
Site of Origin

| Site | Number | Percentage |
|--------------------------|--------|------------|
| Posterior wall | 102 | 44.6 |
| Anterior wall | 36 | 15.7 |
| Lateral walls | 33 | 14.4 |
| Vault | 25 | 10.8 |
| Trigone | 13 | 5.7 |
| Multicentric | 20 | 8.8 |
| Total | 229 | |



FIG. 2



FIG. 3

Fig. 2.—Multicentric bladder tumours.

Fig. 3.—Nodular fungating tumour, lateral wall of bladder.

TABLE V
Gross Type of Carcinoma

| Type | Number | Percentage |
|-----------------------------|--------|------------|
| Nodular fungating | 157 | 68.5 |
| Ulcerative | 58 | 26.5 |
| Papillary | 9 | 3.6 |
| Fibrillary | 5 | 2.3 |
| Total | 229 | |

Table IV presents the site of origin of 229 cases of bladder cancers. The posterior wall was the commonest site of involvement (44.6 per cent), the trigone was the least (5.7 per cent). Multicentric tumours (Fig. 2) with involvement of more than one wall were present in 8.8 per cent of cases.

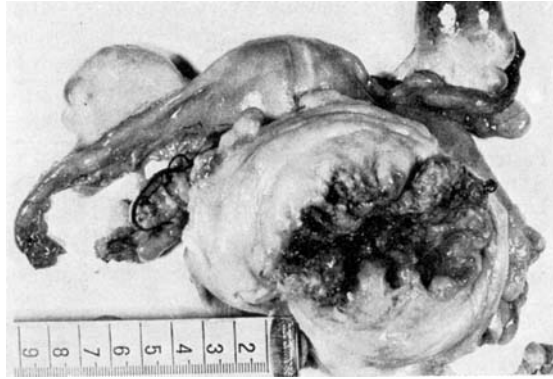


FIG. 4

Malignant ulcer, posterior bladder wall, invading vagina.

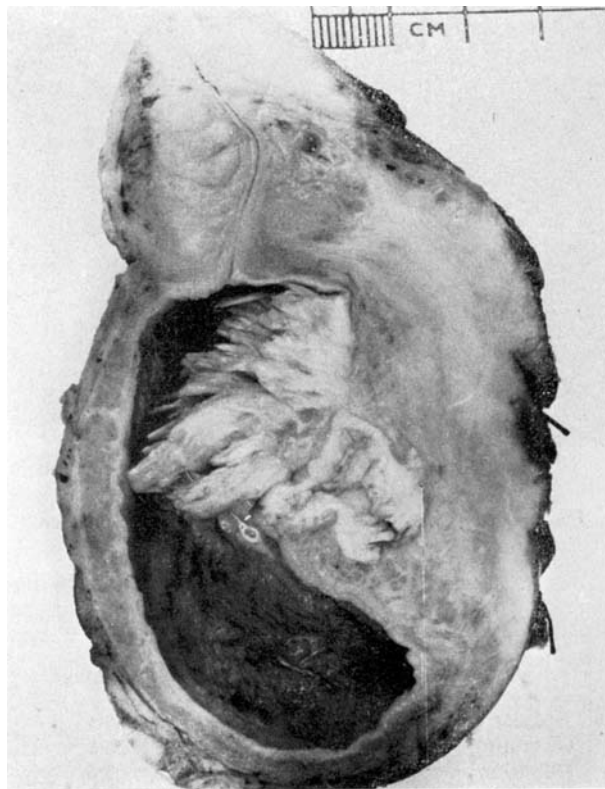


FIG. 5

Fibrillary tumour.

The gross morphological pattern of the tumours examined is given in Table V. Nodular fungating tumours (Fig. 3) are the commonest (68.5 per cent). Malignant ulcers (Fig. 4) constitute 26.5 per cent of cases. Papillary tumours are uncommon (3.6 per cent). A rare form which assumed a fibrillary appearance (Fig. 5) was present in 2.3 per cent of cases. Keratinised white masses were projecting from the surface of the growth like a tuft of hair.

Tumour Histology and Grade (Table VI).—Squamous cell carcinoma accounts for 66·7 per cent of cases. Of these 47 per cent were of the well differentiated variety (Fig. 6), 40 per cent were of Grade II tumours (Fig. 7), and 12 per cent only were of the poorly differentiated type (Fig. 8).

TABLE VI
Tumour Histology and Grade

| Type | Grade | | | | | | Total | |
|----------------|-------|------|-----|------|-----|------|-------|------|
| | I | | II | | III | | No. | % |
| | No. | % | No. | % | No. | % | | |
| Squamous | 72 | 47·2 | 61 | 40·5 | 19 | 12·2 | 152 | 66·7 |
| Transitional | 4 | 7·7 | 17 | 30·7 | 33 | 61·5 | 54 | 23·4 |
| Adenocarcinoma | 3 | 16·7 | 11 | 55·6 | 5 | 27·7 | 19 | 8·1 |
| Unclassified | ... | ... | ... | ... | 4 | 100 | 4 | 1·8 |
| Total | 79 | 34·6 | 89 | 38·7 | 61 | 26·5 | 229 | ... |

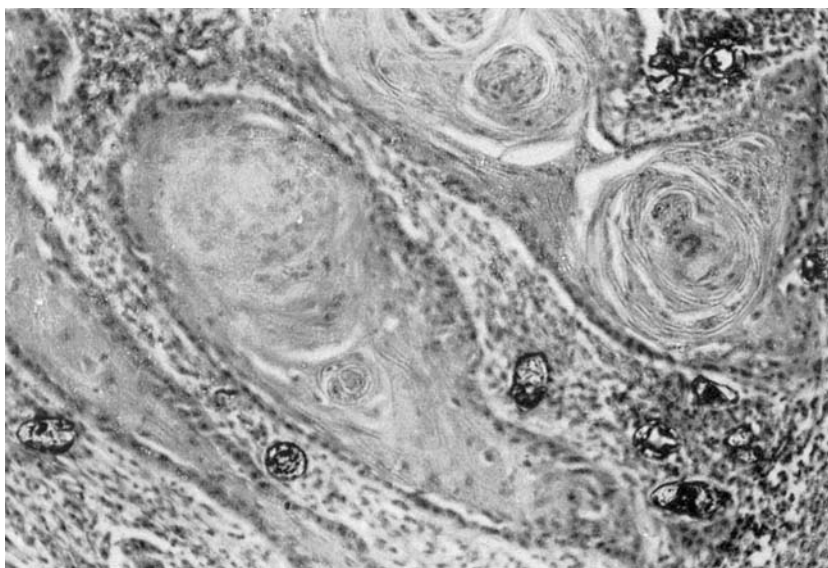


FIG. 6
Squamous cell carcinoma, Grade I. ×100.

Transitional cell carcinoma represents 23·4 per cent of cases only. This type may undergo squamous metaplasia (Fig. 9), a condition which should be distinguished from genuine squamous cell tumours.

Adenocarcinoma (Fig. 10) is uncommon and constitutes 8 per cent of the cases only.

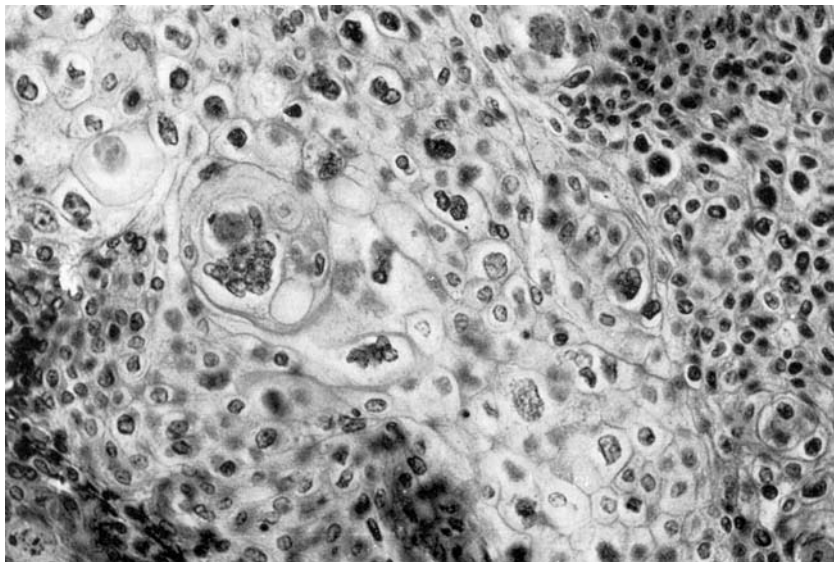


FIG. 7
Squamous cell carcinoma, Grade II. $\times 250$.

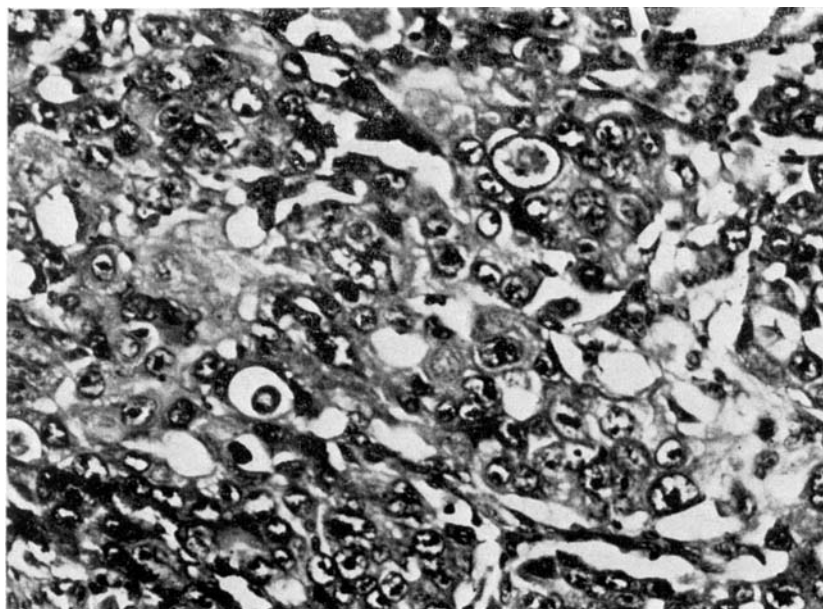


FIG. 8
Squamous cell carcinoma, Grade III. $\times 250$.

Lymph node involvement.—Of the 229 cases examined, the regional lymph nodes were the seat of metastatic deposits in 34, an incidence of 15 per cent. Of these metastases involved one node in 14/34, and more than one in 20/34 of cases. Evidence of capsular infiltration could be demonstrated in 9/34 of the cases.

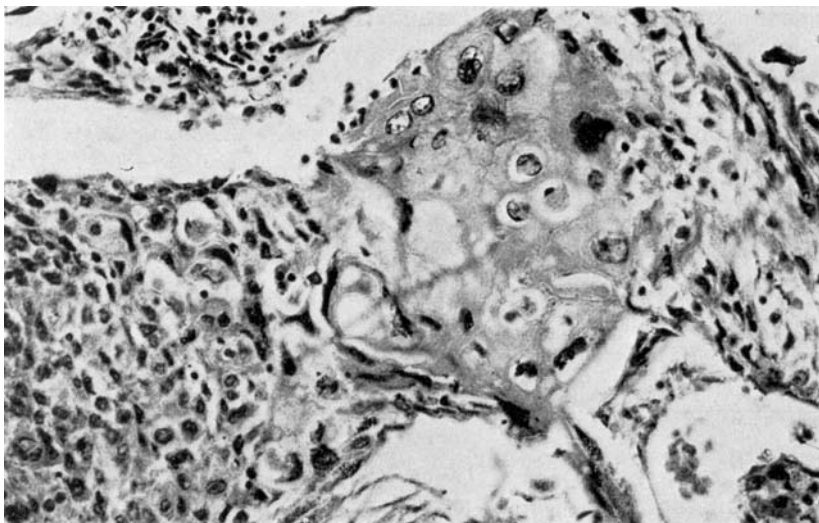


FIG. 9

Transitional cell carcinoma, Grade III, with squamous metaplasia. $\times 250$.

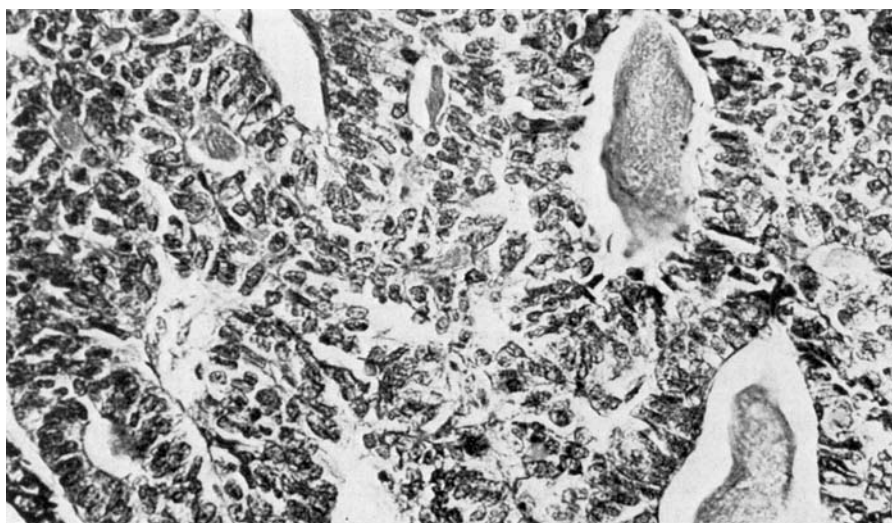


FIG. 10

Adeno-carcinoma. $\times 250$.

The incidence of lymph node involvement was correlated to the tumour stage (Table VII), to the tumour histology (Table VIII) and to the tumour grade (Table IX). A statistically significant relationship could be revealed between the incidence of lymph node involvement and the tumour stage (especially at the P4 stage), and the tumour grade. However, a relationship between lymph node involvement and the histological type of tumour proved to be insignificant.

TABLE VII
Relationship between Lymph Node Involvement and Pathological Stage of the Carcinoma

| Stage | Negative Nodes | | Positive Nodes | | Total | |
|-------|----------------|------|----------------|------|-------|------|
| | No. | % | No. | % | No. | % |
| P1 | 7 | 87.5 | 1 | 12.5 | 8 | 3.6 |
| P2 | 32 | 90.9 | 3 | 9.1 | 35 | 14.8 |
| P3 | 136 | 86.3 | 21 | 13.7 | 157 | 68.7 |
| P4 | 20 | 68.9 | 9 | 31.1 | 29 | 12.9 |
| Total | 195 | 84.8 | 34 | 15.2 | 229 | ... |

TABLE VIII
Relationship between Lymph Node Involvement and Histological Type of Carcinoma

| Histological Type | Negative Nodes | | Positive Nodes | | Total | |
|----------------------|----------------|------|----------------|------|-------|------|
| | No. | % | No. | % | No. | % |
| Squamous . . . | 130 | 85.3 | 22 | 14.7 | 152 | 67.1 |
| Transitional . . . | 47 | 86.6 | 7 | 13.2 | 54 | 22.6 |
| Adenocarcinoma . . . | 15 | 80.9 | 4 | 19.1 | 19 | 8.7 |
| Unclassified . . . | 3 | ... | 1 | ... | 4 | 1.7 |
| Total . . . | 195 | 84.9 | 34 | 15.1 | 229 | ... |

TABLE IX
Relationship between Lymph Node Involvement and Grades of Carcinoma

| Grade | Negative Nodes | | Positive Nodes | | Total | |
|-------|----------------|------|----------------|------|-------|------|
| | No. | % | No. | % | No. | % |
| I | 73 | 92.5 | 6 | 7.5 | 79 | 34.6 |
| II | 73 | 82.0 | 16 | 18.0 | 89 | 38.5 |
| III | 49 | 80.6 | 12 | 19.4 | 61 | 26.9 |
| Total | 195 | 85.3 | 34 | 14.7 | 229 | ... |

DISCUSSION

The average age incidence of 46.7 years is definitely much lower than figures reported for non-bilharzial cases. Payne (1959) gave an average age incidence of 63.5 years, with only 12 per cent of cases under the age of 50. Whitmore's (1962) figure was 58 years for a series of cases

treated by radical cystectomy. Miller, Mitchell and Brown (1969) reported that the maximum incidence was in the seventh decade.

The male to female ratio of 4 : 1 can be explained by the fact that men working in the fields are at a higher risk of repeated infestations by the parasite.

The over-all error in clinical staging in this series was 37.2 per cent, with a tendency to under-estimate the extent of the disease in most cases. Whitmore (1962) gave a lower incidence of clinical error (22.7 per cent). On the other hand, Marshall (1952) and Kenny *et al.* (1970) gave a higher incidence (36.7 and 56 per cent respectively). Various factors could contribute to the tendency towards underestimation in this series:

1. Certain difficult sites for palpation, *e.g.*, tumours of the vault and anterior wall.
2. Inaccessibility of the regional lymph nodes for clinical assessment.
3. Endoscopic biopsy was only taken to establish the diagnosis and not to evaluate the depth of muscular infiltration due to the high risk of bladder perforation when dealing with advanced tumours.

When they were first examined, 25 per cent of the cases were considered inoperable. The late presentation of the majority of cases could be explained by the fact that the symptoms of simple bilharzial cystitis and malignant cystitis are similar. A considerable amount of time is thus lost before the patient can appreciate that qualitative changes in his symptoms warrant seeking serious medical advice.

The majority of tumours in this series were advanced with deep muscle infiltration in 68.2 per cent of cases. Extravesical spread was observed on 42 occasions in 29 cases (12.8 per cent). The prostate was involved in 5.6 per cent of cases only, as compared with the 50 per cent figure in non-bilharzial cancer (Melicow, 1955). This can be attributed to the fact that the trigone is a rare site of origin for tumours in the bilharzial bladder (5.7 per cent). On the other hand the trigone is a common site of involvement in non-bilharzial tumours; Mostofi (1956) gave a figure of 21 per cent. The rarity of involvement of the trigone in the bilharzial bladder corresponds with the finding that squamous metaplasia rarely affects this site (El Sebai, 1961).

The majority of bilharzial bladder cancers are of the nodular fungating variety in contrast to the overwhelming majority of papillary tumours in non-bilharzial cases. However, the preponderance of true squamous cell carcinoma is the most striking feature and stands in contrast to the well known fact that transitional cell tumours constitute most of the cases in non-bilharzial bladder cancers. Payne (1959) records 962 cases of bladder tumours of which 92.5 per cent were transitional.

Most of the squamous cell tumours are of low grade, characterised by the presence of cell nests and excess of keratin formation. As a result these cases are resistant to irradiation, and radical surgery provides the only chances for cure.

Finally, statistical correlations of results in this study revealed that advanced stages and high-grade tumours are associated with a greater chance of lymph node involvement and logically with higher incidence of recurrences. These facts are in agreement with those of Jewett (1946) and Baker (1955) in non-bilharzial bladder tumours.

SUMMARY

Carcinoma of the bilharzial bladder in Egypt is a special entity. The disease represents certain particular, clinical and pathological features. In this series 304 cases with carcinoma of the bilharzial bladder were presented. The average age for the group was 46.7 years, with a male to female ratio of 4 : 1. When first seen 25 per cent of cases were inoperable. Nodular fungating tumours accounted for 68 per cent of cases. Histologically, most of the cases (66.7 per cent) were of the squamous cell type. The regional lymph nodes were involved in 14 per cent of cases.

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