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OBSERVATIONS ON THE ENZYMATIC ACTIVITIES IN RELATION TO TRAUMA AND DISEASES IN THE MAXILLO-FACIAL REGION A PRELIMINARY REPORT

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INTRODUCTION

The serum transaminase (glutamic oxalacetic transaminase and glutamic pyruvic transaminase) concentrations in various kinds of tissue necrosis have been the subject of study for over 10 years (*LaDue et al.*, 1954, *Wroblewski & LaDue*, 1956). The majority of these investigations relate to the diagnosis of cardiac infarction and hepatobiliary diseases. Changes in the transaminase activities in the blood have also been observed, however, after acute trauma and surgical procedures carried out on various organs (*Lawrence & Schulkins*, 1956, *Chinsky & Sherry*, 1957, *Lieberman et al.*, 1957, *Nickell & Allbritten*, 1957, *Fisk et al.*, 1958, *Person & Judge*, 1958, *Snyder et al.*, 1958, *Björnesjö et al.*, 1959, *Weisberg & Sampson*, 1959, *Ayres & Williard*, 1960, *Jensen*, 1961, *Hoch-Ligeti*, 1962, *Korn et al.*, 1962, *Nissen & Bohn*, 1964, *Dragon & Pataki*, 1966, *Hollmen & Saukkonen*, 1967). Some of the series reported include patients with injuries of the jaw, face or head (*Chinsky & Sherry*, 1957, *Lieberman et al.*, 1957, *Hoch-Ligeti*, 1962).

It has been shown that under normal conditions the human blood serum contains a specific enzyme capable of hydrolyzing polypeptides, i.e. γ -glutamyl transpeptidase (GT), the activity of which has been found to increase in certain pathological conditions (*Szewczuk & Orlowski*, 1960). Elevated serum GT values have mainly been noted in diseases of the liver (*Szczeklik et al.*, 1961, *Kokot et al.*, 1963). The highest enzyme concentrations have

been observed in patients showing obstructive icterus and liver metastases, in which conditions GT has been found to respond more sensitively than the transaminases (GOT, GPT) or alkaline phosphatase (*Aronsen et al.*, 1965, 1967, *Nosslin et al.*, 1966).

Since individual variations were observed in the serum enzyme activities of patients surgically treated for pathological conditions in the maxillo-facial region, the determination of γ -glutamyl transpeptidase, in addition to the transaminases, has since autumn 1967 been included in the clinical routine laboratory determinations. These observations are presented and discussed in this preliminary report.

MATERIAL AND METHODS

The series consisted of 50 patients treated at the Department of Maxillo-Facial Surgery (Table I). Fracture of the jaw was present in 27 cases, acute or subacute abscess of the maxillary region in 7, chronic osteomyelitis in 7, a malignant tumour in the lower jaw in 3, and a cyst in the maxillary bone in 3, while 3 patients showed prognathism, on account of which vertical osteotomy was performed. In a total of 37 cases some surgical procedure was carried out in the maxillo-facial region, while 13 patients were conservatively treated. In some cases both GT, GOT and GPT were determined, while in others only one of these variables was studied. In addition, alkaline phosphatase was determined in most cases. If the enzyme values were within the normal range at the first determination, repeat assays were as a rule not made. For practical reasons it was not possible to make systematic determinations every day for a certain length of time. Therefore, the series was not uniform, and the individual cases were not directly comparable.

Table I
Distribution of patient material

Group	Number of patients	Median age (range)	Female	Male
A Fracture of the jaw	27	33 (8—63)	1	26
B Abscess	7	29 (14—59)	2	5
C Osteomyelitis	7	34 (11—60)	4	3
D Miscellaneous	9	36 (17—69)	4	5
Total	50		11	39

The method employed in the assay of γ -glytamyl transpeptidase was based on the technique described by *Orlowski & Szcwczuk* (1961). As substrate was first used α -(N- γ -DL-glytamyl) aminopropionitrile (GAP), later γ -L-glutamyl- α -naphthylamine (GANA) (synthesized by AB Ferrosan, Sweden), which in this work has been used. The normal values were 1—40 units, and the mean value was 16 units, with the former substrate. With the latter substrate the normal values were 10—80 units and the mean value was about 25 units.

Serum GOT and GPT were determined by the method described by *Reitman & Frankel* (1957) (AB Kabi, Sweden). The normal values were 0—40 units for GOT, 5—35 units for GPT.

For the determination of alkaline phosphatase the method described by *Bessey et al.* (1946) was used. The normal values were 1.2—2.9 B-L units (C. H. Boehringer Sohn, Ingelheim am Rhein).

RESULTS

The changes in enzymatic activity in the various disease groups are shown in Table II. The maximal values in the individual cases are presented in Fig. 1.

Table II
*Frequency of GT, GOT, GPT, APh elevation in various oral surgical disorders**

Operation or disorder	Total	Enzyme activity							
		GT		GOT		GPT		APh	
		Total	Elev.	Total	Elev.	Total	Elev.	Total	Elev.
A Fracture of the jaw	27	21	8	24	10	23	6	23	1
Conserv. treatment	11	8	4	9	4	8	2	9	1
Osteosynthesis	16	13	4	15	6	15	4	14	0
B Abscess	7	4	2	7	2	5	2	7	2
C Osteomyelitis	7	6	2	7	2	7	1	7	1
D Miscellaneous	9	6	3	9	0	8	3	7	1
Mandibular prognathism	3	2	0	3	0	3	0	2	0
Cyst of the jaw	3	2	1	3	0	2	0	2	0
Malignant tumours	3	2	2	3	0	3	3	3	1
	50	37	15	47	14	43	12	44	5

*If the unit value in an assay was higher than normal, the level was regarded as elevated. The following values were regarded as normal:

GT < 80 units

GOT < 40 units

GPT < 35 units

APh < 2.9 B-L units

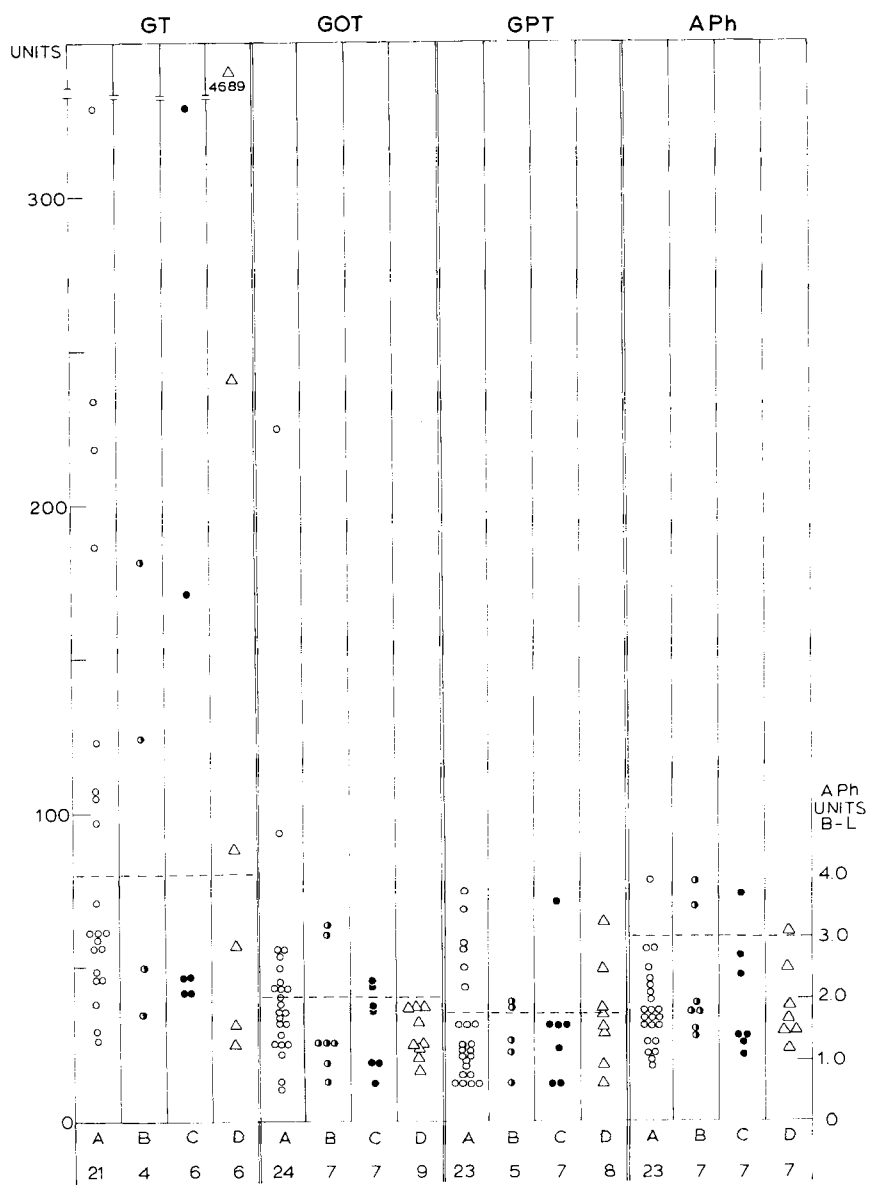


Fig. 1. Serum GT, GOT, GPT and APh levels in patients with oral surgical disorders. The dots represent the highest level observed in the individual cases. The number under each bar refers to the total number of patients in the group. A. Fractures of the jaw. B. Abscesses. C. Osteomyelitis, osteitis. D. Miscellaneous.

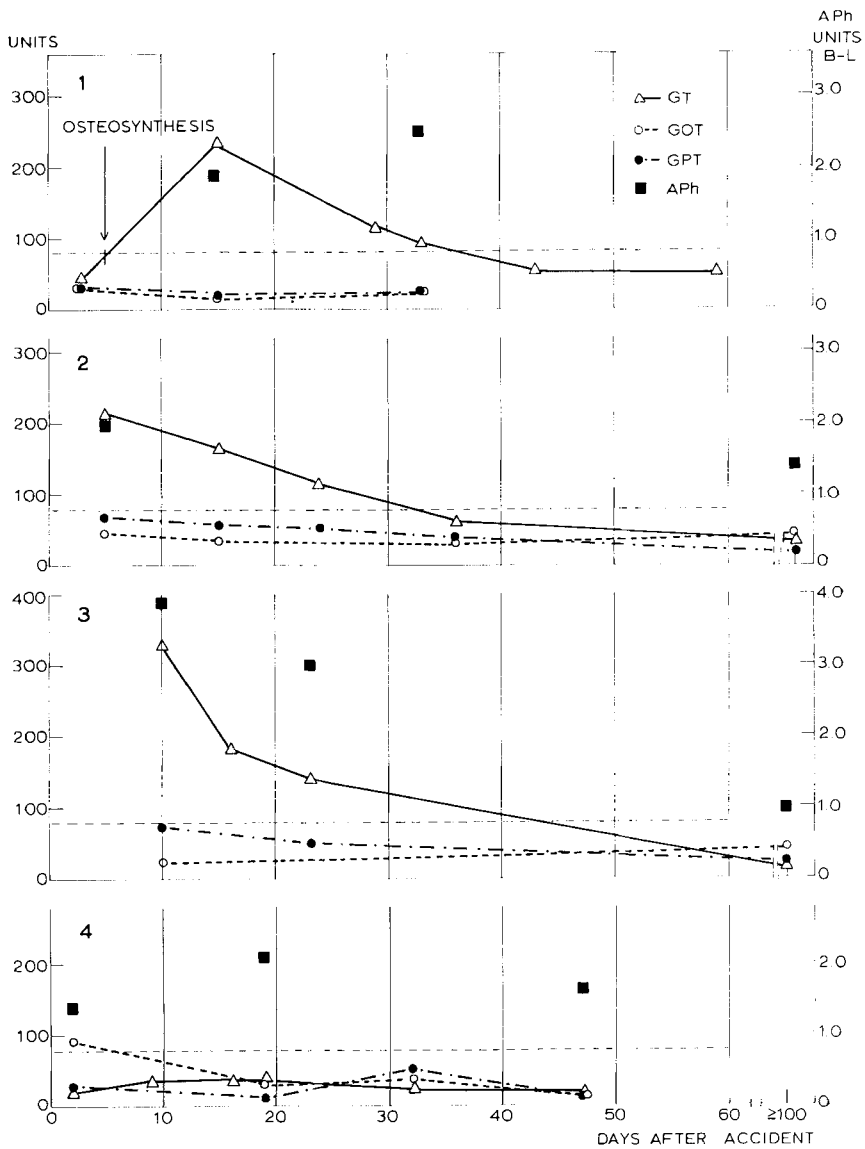


Fig. 2 a. The course of the GT, GOT, GPT and APh activities in three patients with severe maxillary fractures (I male, 54; II male, 26; III male, 63). For the sake of comparison a case with fractures of the upper jaw and right tibia is shown in which no elevated GT values were noted in the serum (IV male, 19).

Maxillary fractures

Of the 27 patients with maxillary fractures, 11 were conservatively treated by intermaxillary fixation and extraoral plaster. In addition, extraoral osteosynthesis was performed in 16 cases. In a case of incomplete fracture free bone was transplanted from the iliac crest. Two surgically treated patients with fractures of the jaw had also sustained fractures of the limb, which were conservatively treated by a plaster cast.

Of the *conservatively treated patients with maxillary fractures* four out of eight had elevated serum GT values, the maximum being 239.0 units. This value was obtained 10 days after the trauma, when the patient was transferred from another hospital to the Department of Maxillo-Facial Surgery. In this case, as well as in the remaining three cases, the GT values remained higher than normal for many weeks after the trauma (Fig. 2). Elevated GOT values were observed in four patients out of nine, and elevated GPT values in two out of eight patients. Alkaline phosphatase was clearly increased in the blood in only one case.

Of the *surgically treated patients with maxillary fractures* four out of 13 showed increased GT activity in the serum post-operatively, the maximum being 292.0 units. Elevated GOT values were noted in six out of 15 cases, elevated GPT values in four out of 15. After osteosynthesis the alkaline phosphatase concentration in the serum did not in any case exceed the upper limit of the normal range. Two patients still exhibited elevated GT values three weeks after operation. In one case the GT activity rose above the normal level one month after operation and remained elevated for over a month. This patient contracted mild viral pneumonia during the period of treatment.

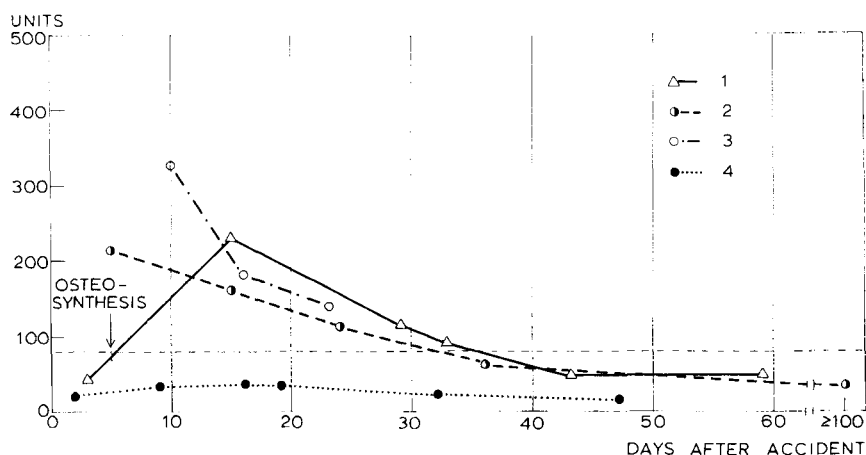


Fig. 2 b. GT values from the a) graph superimposed.

Abscesses

GT was determined in only four of the seven patients who showed abscesses of the maxillary region. In two cases the GT activity was clearly increased (Fig. 3), but the GOT and GPT values were not elevated. The abscess was submandibular in all of these cases. Of the remaining three patients with maxillary abscesses two showed a definite increase in both GOT and alkaline phosphatase; GT and GPT were not determined. These two patients were both under 20 years of age.

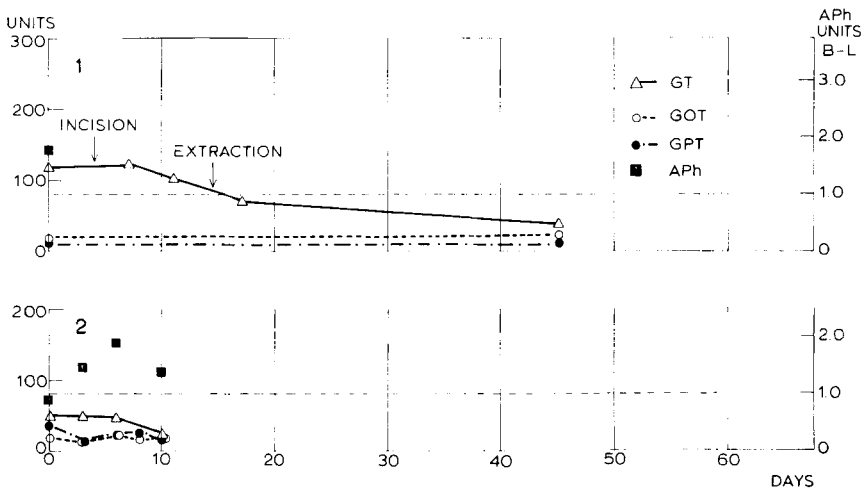


Fig. 3. Changes in serum GT activity during the period of treatment in a patient with a submandibular abscess. For the sake of comparison the results of GOT and GPT assays performed in this case at the initiation and termination of treatment are shown (male, 31). In addition, the diagram shows a case of submandibular abscess in which the enzyme values were within the normal range (male, 59).

Osteomyelitis, osteitis

In all cases in this group the mandible was the site of the pathological process. Two patients showed subacute inflammation of the bone, and these were the only ones in which definitely elevated GT values were noted (Fig. 4). Five patients had had chronic osteomyelitis for several years and been treated with penicillin for some months prior to operation. In two of these cases a slightly elevated GOT value was once noted. Serum GPT was elevated in one case and alkaline phosphatase in one. In both, the values returned

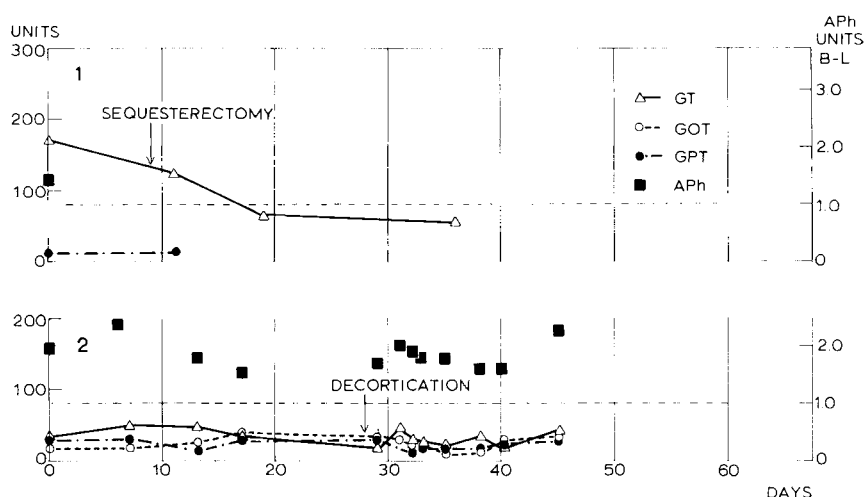


Fig. 4. Serum GT activity after the institution of treatment in two cases of osteomyelitis in the maxilla. At the initial stage of antibiotic treatment patient no. I showed abundant exudation of pus containing *Staphylococcus aureus* from a cutaneous fistula (female, 36). Patient no. II had chronic, non-exudative osteomyelitis in the mandible.

to normal during the period of hospitalization. After surgical decortication the patients became clinically completely asymptomatic, and no progression of the disease was observed in either roentgenograms of the jaw or orthopantomograms. At follow-up investigation, too, the serum GT, GOT, GPT and alkaline phosphatase were within the normal range.

Miscellaneous

Only two patients in this group had elevated GT values in the blood. In one of these cases resection of the mandible was performed on account of fibrosarcoma. The GT values of this patient were still elevated a month after operation (Fig. 5). The other patient exhibited inoperable carcinoma of the mandible and oral fundus and, in addition, severe liver cirrhosis as a result of alcohol abuse. Because of uncontrollable haemorrhage from the neoplastic area caused by irradiation therapy, both external carotids had to be ligated. In association with cytostatic medication (cyclophosphamid) after the irradiation therapy, the already high GT concentration showed a further rise by many hundred units. By contrast, the GOT and GPT values remained within the normal range (Fig. 6). Radioisotope and ultra-sound investigations revealed no liver metastases.

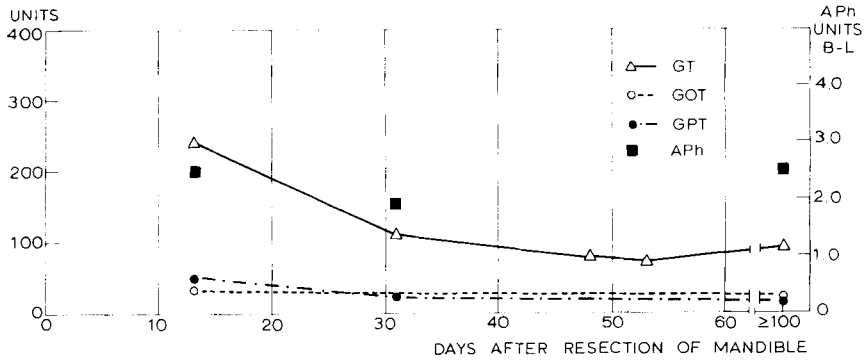


Fig. 5. Postoperative GT, GOT, GPT and APh activity in a patient on whom resection of more than half of the mandible was performed on account of fibrosarcoma (female, 69).

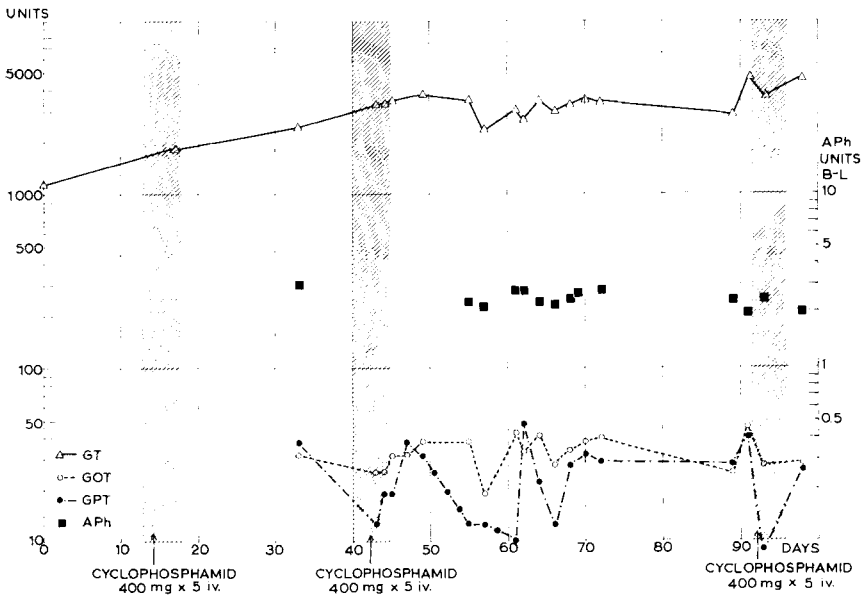


Fig. 6. Serum GT, GOT, GPT and APh activity during cytostatic treatment (cyclophosphamid) in a patient showing inoperable carcinoma of the soft tissues of the mandible and oral fundus. Prior to the enzyme assays the maxillo-mandibular region was treated with 6000 r telecobalt and both external carotids were ligated (male, 56).

DISCUSSION

The transaminase values in the serum are elevated in surgical disorders involving tissue necrosis, severe inflammation or muscular injury. Elevation of the transaminase level can be detected in all cases of injury to metabolically active cells (*Dragon & Pataki*, 1966). A clear correlation has been observed between the extent of tissue damage and the serum transaminase activity (*Nickell & Allbritten*, 1957). The highest transaminase (GOT, GPT) and also glutamyl transpeptidase (GT) concentrations in the serum have been noted in association with liver lesions. On the other hand, surgical procedures carried out on other organs have caused no changes of the same order in the serum transaminase activity (*Chinsky & Sherry*, 1957, *Nickell & Allbritten*, 1957, *Fisk et al.*, 1958, *Weisberg & Sampson*, 1958, *Ayres & Williard*, 1960, *Hollmen & Saukkonen*, 1967, *Widholm & Tarjanne*, 1967). The presence or absence of postoperative complications and the relative degree of inflammation and oedema at the time of surgery seem to bear little relation to the rise (*Fisk et al.*, 1958). Likewise, general anaesthesia seems to have no effect on the transaminase activity in the serum (*Lawrence & Schulkins*, 1956, *Nickell & Allbritten*, 1957, *Stark & Claude*, 1964, *Hollmen & Saukkonen*, 1967).

The enzymatic changes caused by lesions in the maxillary region do not seem to have been the particular object of any investigation. However, in various reports occasional cases are found which are of interest from the standpoint of the present study. *Nickell & Allbritten* (1957) mentioned that severe, acute injuries in the head, trunk and limbs were associated with a significant increase in the serum GOT values were not elevated although the patient had sustained several fractures of the jaw. Another patient with multiple fractures of the skull had a maximum GOT value of 75 units. *Lieberman et al.* (1957) studied a series of 51 victims of traffic accidents. In 27 per cent of the cases the GOT values were not elevated. In this group there were three patients with skull fractures. In 72.5 per cent (37 cases) an increased GOT activity in the serum was observed after the trauma. Two of these patients had fractures of the jaw. One was a 31-year-old man, whose maximum GOT value was 101 units (108 hours after the trauma), the other was a 50-year-old man, whose maximum GOT value was 49 units (11 hours after he had sustained a fracture of the jaw).

In connection with the extraction of teeth (*Bisch et al.*, 1965) in parodontal diseases (*Honjo et al.*, 1964) no elevation of the serum transaminase values (GOT, GPT) was observed.

It seems that no previous report on glutamyl transpeptidase determinations (GT) has been published on patients with diseases of the oral cavity and jaw.

The present results were not consistent, and in most cases the assays were made several days after the damage had been sustained. The low frequency of elevated serum transaminase values in the present series might be due to the fact that the rise begins an hour or two from the trauma and the maximum concentration will be attained in 24–48 hours, after which normalization will occur on the third to seventh day (*Chinsky & Sherry*, 1957, *Fisk et al.*, 1958, *Person & Judge*, 1958, *Björnesjö et al.*, 1959, *Nissen & Bohn*, 1964, *Batsakis & Briere*, 1967, *Hollmen & Saukkonen*, 1967). On the other hand, the definite rise in glutamyl transpeptidase activity observed after very severe injury to the jaw and in some cases postoperatively, and in association with acute infection, is noteworthy and merits further investigation. Another interesting finding was the rise of the GT values in connection with cyclophosphamide medication in a patient who previously had received a therapeutic dose of telecobalt (6000 r) in a carcinomatous area of the mandible. No simultaneous increase in GOT and GPT activity was observed in this case. A corresponding rise in transaminase activity caused by cytostatic treatment has been reported, e.g., by *Gault et al.* (1967).

Among the present patients with maxillary fractures only one showed elevated alkaline phosphatase values. This is in agreement with the observation reported by *Hess & Henly* (1963) that the activity of alkaline phosphatase is usually unchanged during the regeneration of fractures. On the other hand, in patients with multiple injuries an increase in alkaline phosphatase occurs some two to three weeks after the trauma. This increase is mainly associated with healing of the fractures, since the enzymes reflecting a tissue damage and the liverspecific enzymes are already normalized at this stage (*Kataja* 1968). Likewise, a clear increase in GT is observed in these patients some 4 to 20 days from the trauma (*Kataja & Gordin*, 1968).

SUMMARY

In a series of 50 patients treated at the Department of Maxillo-Facial Surgery, routine laboratory studies included the determination of serum transaminases (GOT, GPT) and/or γ -glutamyl transpeptidase (GT) and alkaline phosphatase (Aph). The series consisted of patients with fractures of the jaw (27 cases), maxillary abscesses (7 cases) and osteomyelitis (7 cases), and a so-called miscellaneous group (9 cases) including three patients with malignant tumours of the maxilla.

In all the above-mentioned groups some patients exhibited elevated GT values and an increase in GOT or GPT activity. By contrast, alkaline phosphatase was increased only in a few patients at some stage of the treatment.

Owing to the shortness of the series and the irregularity of the assays no attempt has been made to analyse the results systematically or to draw any final conclusions. However, the observations so far made are interesting enough to justify further studies, which may be expected to yield additional information concerning the changes in enzymatic activity in the serum caused by oral surgical disorders. It may be anticipated, moreover, that these enzyme reactions will prove to be significant indices of the course of the disease.

RÉSUMÉ

OBSERVATIONS SUR LES ACTIVITÉS ENZYMATIQUES DANS LES TRAUMATISMES ET LES AFFECTIONS DE LA RÉGION MAXILLO-FACIALE.

Dans une série de 50 patients traités dans le service de chirurgie maxillo-faciale, les études de laboratoire systématiques comprenaient la détermination des transaminases du sérum (GOT, GPT) ou de la transpeptidase α -glutamyl (GT) et de la phosphatase alcaline (Aph), et éventuellement toutes ces déterminations. La série se composait de patients présentant des fractures de la mâchoire (27 cas), des abcès du maxillaire supérieur (7 cas) et des ostéomyélites (7 cas), et d'un groupe «varié» (9 cas) comprenant 3 patients présentant des tumeurs malignes de la mâchoire.

Dans tous les groupes ci-dessus, quelques patients présentaient une augmentation des valeurs GT et une augmentation de l'activité GOT ou GPT. Par contre, la phosphatase alcaline n'était augmentée que chez quelques patients, à un moment du traitement.

En raison du caractère limité de cette série et de l'irrégularité des tests, les auteurs n'ont pas cherché à faire l'analyse systématique des résultats ni à tirer des conclusions définitives. Les observations réalisées jusqu'à présent sont cependant suffisamment intéressantes pour justifier des études ultérieures, dont on peut espérer qu'elles apporteront des informations complémentaires sur les modifications de l'activité enzymatique provoquées dans le sérum par les affections chirurgicales de la région buccale. De plus, on peut s'attendre à ce que les réactions enzymatiques se révèlent comme des indices significatifs de l'évolution de la maladie.

ZUSAMMENFASSUNG

BEOBACHTUNGEN ÜBER DIE ENZYMATISCHEN AKTIVITÄTEN IN BEZIEHUNG ZUR TRAUMATA UND KRANKHEITEN IM MAXILLO-FAZIALISCHEN BEREICH

Bei 45 Patienten der kieferchirurgischen Station wurde während der Behandlung im Krankenhaus im Anschluss an Routineuntersuchungen die

Aktivität der Serum- Transaminasen (GOT, GPT) und/oder der der γ -Glutamyl Transpeptidase (GT) wie auch die der alkalischen Phosphatase (APh) gemessen.

Die Patientengruppen entstanden aus Kieferfrakturfällen, die mehr als die Hälfte des gesamten Materials bildeten (25), aus Kieferabszessen (6), aus Osteomyeliten (6) und aus einer sog. Mischgruppe, zu der u.a. drei Fälle mit bösartigem Unterkiefertumor zählten.

An allen Gruppen konnten bei einem Teil der Patienten erhöhte GT-Werte und auch gesteigerte GOT- oder GPT-Aktivität festgestellt werden. Der alkalische Phosphatasegehalt dagegen war nur bei einigen Patienten während irgendeines Behandlungsstadiums erhöht.

Aufgrund des geringen Materials und der zeitlich uneinheitlichen Messungen wurde auf ein systematisches Analysieren der Resultate verzichtet. Die zu ziehenden Schlussfolgerungen sind aus demselben Grund auch nicht endgültig formuliert. Die schon gesammelten Ergebnisse geben jedoch Anlass zu weiteren Forschungen, von denen man sich versprechen kann, dass sie die Bedeutung der Enzymreaktionen für die Kontrolle der Weiterentwicklung im Krankheitsbilde beweisen und wertvolle zusätzliche Information über die durch mund- und kieferchirurgischen Krankheiten bedingte Veränderungen in der Enzymaktivität geben werden.

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