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Case study of nodular excrescences in *Arius tenuispinis*, hitherto considered as osteoma

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ABSTRACT: Nodular excrescences in different stages of development were found variously attached to neurocranium, fin ray and skin in 5 out of 132 *Arius tenuispinis* (32 to 40 cm), collected over a period of 1 yr in trawl catches at Visakhapatnam fishing harbour. Chemical analysis of the nodules revealed excessive calcium (26.97 %) as compared to its content in the operculum of affected fish (5.29 %) and unaffected fish (3.53 %), which were used as controls. There was 20 times less phosphorus in the nodules than in the operculum of the affected as well as unaffected fish (8.9 %). Formation of nodules is due to excrescence of excess calcium present in the blood plasma and not a phenomenon of 'osteoma' as hitherto described. In the light of these findings the true genesis of swollen bones reported as 'osteoma' in some deep-bodied fishes appears to be a condition of 'hyperostosis' with hydrostatic function, while the formation of nodules is suggested as due to an impairment of the ultimobranchial glands which control calcium metabolism in fishes.

INTRODUCTION

Selvaraj et al. (1973) observed single and multiple nodular outgrowths in *Tachysurus (= Arius) jella*, collected from the southwest coast of India. The nodules were found on skin, bone and in one case on the inner wall of the body cavity. No histological evidence was produced, although the nodular formations were considered as exostosis and categorised as 'osteoma' and 'osteochondroma'. A chemical analysis of the 'nodules' and neighbouring tissue by these workers revealed that the nodules' phosphorus content was far in excess (8.96 to 16.47 %) of that of neighbouring tissue (2.6 to 5.4 %).

Tumour-like nodules of uncertain pathogenesis, simulating neoplasms in their gross but not in their microscopic appearance, are often conglomerate aggregates of exuded organic and inorganic substances. In the present study, tumour-like nodular outgrowths were encountered in 5 out of 132 specimens of catfish *Arius tenuispinis*, collected from the trawl catches at Visakhapatnam fishing harbour during the period March 1981 to March 1982. A striking feature of their occurrence is that they are confined to *A. tenuispinis*, to the exclusion of other ariids (*A. thalassinus* and *A. dussumieri*) in the same area.

Nodular formations in different species of marine catfishes were reported earlier from different localities along the coastline of India. Menon (1974) observed buccal papilloma in *Tachysurus (= Arius) platysomus* collected from trawl catches at Mandapam (southeast coast of India). Curiously, all the 15 specimens in which the papilloma were observed were females. The affected fish were reported to be otherwise in good health. Neither 'inflammatory reaction' nor 'invasion of the tumour tissue into the deeper layers' was observed. Swamy et al. (1976) reported the occurrence of stony nodules categorised as 'osteoma' in 17 specimens (7 %) of *Arius maculatus* collected at Parangipettai (southeast coast of India). Sections of the nodules were, however, of the form of 'solid bony outgrowth with no space inside'. Microscopic examination of the nodules in *A. tenuispinis* were also found to be devoid of hollow spaces and cellular structures.

Literature on osteoma in fishes is found to include several kinds of bony overgrowths. True osteoma with histological evidence was described by Nigrelli & Gordon (1946) in *Hemichromis bimaculatus*. Wellings (1969) had reservations about the true nature of osteomas and osteochondromas mentioned by Kazama (1924), Sagawa (1925) and Takahashi (1929); and he himself described osteoma with histological evidence in the Pacific halibut *Hippoglossus stenolepis*. Categorisation of every kind of bony outgrowth as

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'osteoma' without histological basis gives scope for doubting their true nature. Thus, the so-called 'osteoma' in the form of swollen bones found in several marine demersal fishes belonging to the families Gadidae, Sciaenidae, Chaetodontidae, Sparidae, Ephippidae, Bothidae and Ballistidae (as reviewed by Mawdesley-Thomas 1974) appear to be non-pathological and related to their habitat and body shape, while the nodular outgrowths found in marine catfishes appear to be pathological, though not necessarily neoplastic in nature. In either case it is a misnomer to name the overgrowths 'osteoma'. Harshbarger (1984) resolved histologically non-neoplastic conditions with features resembling neoplasms, misdiagnosed earlier as neoplasms, and pointed out that the reverse is also true in some cases.

Aetiology of true osteoma in fishes is still left in doubt. Nigrelli & Gordon (1946) attributed traumatic aetiology to the osteoma reported by them. Traumatic aetiology of the 114 sea bream (Takahashi 1929) of which 102 had multiple osteomas, was rejected by Schlumberger & Lucke (1948) for want of convincing evidence of previous fracture. The same consideration leaves in doubt the aetiology of swollen bones in deep-bodied or bream-shaped demersal fishes and marine catfishes. According to Wellings (1969) 'The problem represents a potentially fruitful area for the study of species, genetic and environmental influences in the development of neoplasia'. These considerations may also be applied to explain the swollen bones and nodular outgrowths observed in some fishes. Species-specific sporadic occurrence of nodular excrescences in *Arius tenuispinis* (present study) is explained as an idiosyncratic response to a proximate contaminant in the aquatic environment. We felt that chemical analysis of the nodules and opercular bones (metabolically remote and useful as controls) of the affected and of some unaffected fish would reveal the metabolic process involved in nodule formation, which was hitherto considered as 'osteoma' in some other catfishes.

MATERIAL AND METHODS

Material for the present study was collected from trawl catches at Visakhapatnam fishing harbour, during the period March 1981 to March 1982, in the course of routine examination of *Arius tenuispinis* for osteological studies. The trawl catches consisted of dead fish, which were landed after keeping the fish in a dead condition for several hours. The affected fish were in the size range 32.0 to 40.0 cm. Fish of similar size, without the excrescences, were also collected and used as controls. Nodular excrescences of a large size (Table 1) were removed from the fish for estimating percentage content of calcium, sodium, potassium and phosphorus. Opercular bones removed from the right side of the affected fish as well as of unaffected fish of similar size (controls) were also subjected to the same kind of analysis.

The sample material of nodule and/or bone from each fish, crushed and ground in a steel mortar into pieces that can pass through a 1 mm mesh sieve, was decomposed with 2 aliquots of 5 ml each of 8 N HNO_3, for about a day until the melts disintegrated completely. The solution was stored in polyethylene bottles for later chemical analysis. Sodium and potassium were determined on a Flame Photometer (Corning-EEL, England). Calcium was determined by titration with EDTA using calcein indicator. Phosphorus was determined by ammonium molybdovandate method using a spectrophotometer. The transmittance was measured at 420 nm.

Comparison of sample means of the chemicals, between nodules, affected and unaffected fish, was made by t-test. The sample size of nodules was restricted by their non-availability to 4 only. Due to small sample size and high variability, the variance of the sample means was also high. The sample size of bone was also kept small to make the results comparable with those of the nodules. Despite high variance of the small samples, ratios were calculated to provide an idea of the magnitude of differences, which were, however, tested for significance statistically.

Microscopic examination of thin sections of the nodule was made on a slab of the dried nodule ground very thin and mounted in thick balsam.

Experimental studies or examination of live specimens in the case of marine catfishes were precluded because of their capture far away from the shore and the difficulty of keeping them alive under laboratory conditions.

RESULTS

Description of the nodules

The nodules were observed in several parts on the surface of the body (Table 1), either simple or multiple. Observed occurrence of the nodules among the 5 fish, in different parts of the body, showed that 3 had overgrowths on the fins (Fig. 1), 2 on the neurocranium (Fig. 2), 1 on the midlateral surface of body, 1 at the bases of the 1st and 2nd mandibulary barbels and 1 below the eye. The nodules were of various shapes, sizes, structures and colours. All the nodules except those at the base of the mandibular barbel were covered by a lining of skin which could be peeled off with a pointed needle.

Table 1. *Arius tenuispinis.* Details of nodular excrescences

Date of collection	Length in cm	Sex	Site	Size in mm (length × width × height)	Description
18 Mar 1981	32.0	?	1. 6th pelvic ray (Fig. 1)	10.5×6×5	Attached to 6th pelvic ray, covering adjoining rays also. Solid, oval, creamy, rough surface. Middle of 6th pelvic ray actually embedded in the nodule
			2. Sutural connection between frontal and sphenotic (Fig. 2)	13.5×9×3	Solid, oval, creamy, rough granular surface, fused with the skull
18 Sep 1981	39.4	Male	1. Trilobed situated between the outer mandibulary barbel and lower jaw	– ×5×6	Solid, 1 lobe attached to the base of mandibulary barbel, 2nd to the lower jaw and 3rd to the skin. Round, smooth surface covered by black skin
15 Oct 1981	32.4	Female	1. Tip of the pectoral spine	12×3×2	Little more than the width of the pectoral spine, granulated rough surface, oval, brown
			2. On the middle of the 1st pelvic fin ray	7×3×2.5	Like a hump, raised in the middle, sloping towards edges, rough granulated surface, brown
6 Nov 1981	35.6	Female	1. Situated below the eye attached to skin	– ×5×6.5	Solid, round, rough granulated surface, creamy
9 Feb 1982	36.4	Female	1. Situated on the frontal, fused with the skull	33.5×13×6	Solid, oval, brown, rough globular protruberances
			2. Situated on the mid-lateral surface of the body attached to the skin above the pelvics	26×13×5	Solid, elongated, brown, smooth surface with transverse grooves

Sections of nodules

A slab of the dried nodule was ground very thin and then mounted in thick balsam. Two such nodules were spared for studying the appearance of sections under a microscope while the other nodules were used completely for chemical analysis.

The section of the nodule situated at the bases of the 1st and 2nd mandibular barbels, stained with Haematoxylin-eosin, showed the presence of foamy rectangular bodies, some of which burst open with outflow of the foamy granules (Fig. 3). These granules were found distributed all over the ground substance. The rectangular bodies were more or less loosely scattered inside the nodule but formed a 2 or 3-layered thick rim at the periphery. In the spaces between the rectangular bodies were found faintly stained stellate bodies with radiating thin fibrils. Neither the rectangular bodies nor the fibrillar stellate bodies were related to the chondrocytes or fibrocytes respectively, as they were devoid of nuclei.

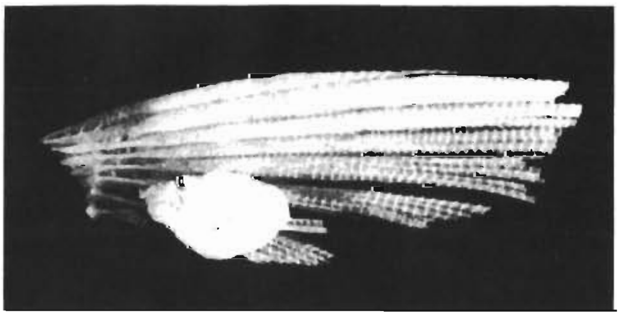

Fig. 1. Nodule on pelvic fin, attached to the 6th ray only. The pelvic ray is surrounded by nodular growth on all sides

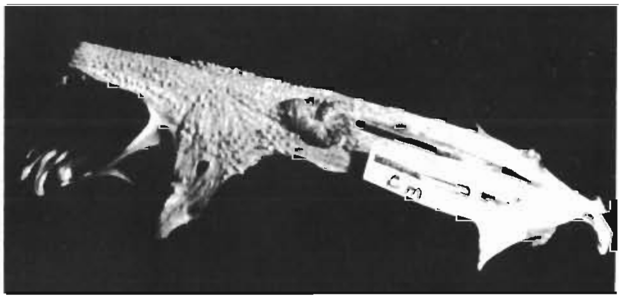

Fig. 2. Nodule on the neurocranium attached to the sutural connection between frontal and sphenotic

Another section representing the nodule from the mid-lateral surface of the body was also ground very thin and mounted on balsam (Fig. 4). This section showed an amorphous ground substance which produced a pink colour when stained with Heidenhan's

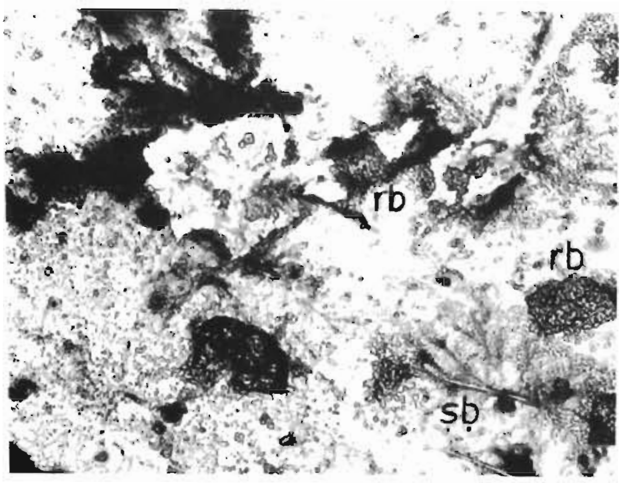

Fig. 3. Section of the nodule from the base of barbels, showing rectangular bodies (rb) and stellate bodies (sb). Stained with Haematoxylin-eosin

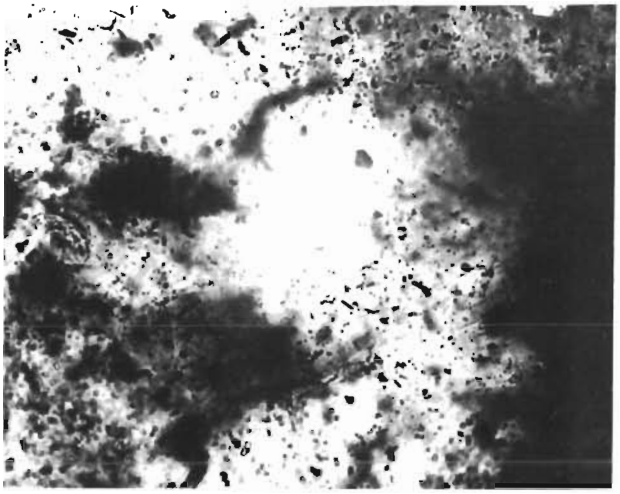

Fig. 4. Section of nodule from the midlateral surface of the body showing amorphous ground substance with black patches. Stained with Heidenhan's Azan

Azan. There were no cellular structures, except patches of black granules and cloudy black patches, distributed with varying intensities in the ground substance. The nature of the ground substance and the nature of the dark patches was not known.

Chemical analysis

Four prominent nodules which developed to a large size were selected. They belonged to 3 different fish and their location on the body varied from fish to fish. In Table 2a, results of the chemical analysis along with lengths of the fish and positions of the nodules are given. Results of the chemical analyses of opercular bones of the affected fish (in parentheses) and average values of chemical composition of opercular bones of 4 unaffected fish are also given in the Table.

Of the 3 cations, calcium varied markedly and abnormally. Average values ranged from 3.53 % in unaffected fish to 26.97 % in the nodules. The higher Ca content of 5.29 % on average in the opercular bones of affected fish, compared to the 3.53 % in those of unaffected fish, was indicative of a disturbance in Ca

Table 2a. Chemical analysis of nodules, operculum of affected fish (given in parentheses) and average of operculum of 4 unaffected fish

Fish length in cm	Position of nodule	Percentage of chemical Ca	Na	K	P
32.0	Pelvic ray	30.06 (5.08)	1.45 (0.28)	1.03 (0.1)	0.55 (9.03)
36.4	Midlateral on body	23.37 (6.55)	0.55 (0.06)	0.54 (0.07)	0.29 (11.58)
	Frontal bone	31.61	0.58	0.16	0.38
39.4	Lower jaw	22.86 (4.25)	0.53 (0.04)	0.17 (0.03)	0.48 (6.11)
	Averages:				
	Nodule *	26.97 ± 4.59	0.78 ± 0.46	0.48 ± 0.42	0.42 ± 0.12
	Affected fish **	5.29 ± 1.61	0.13 ± 0.18	0.07 ± 0.05	8.90 ± 3.77
	Unaffected fish *	3.53 ± 1.21	0.40 ± 0.18	0.105 ± 0.04	8.94 ± 1.09

* Degrees of freedom 3; ** degrees of freedom 2

Table 2b. Comparison of sample means by t-test of Ca, Na, K and P, between nodules (N); and opercular bones of affected (A) and unaffected (U) fish

Material analysed	Ca		Na		K		P	
	A	U	A	U	A	U	A	U
N	••	••	•	NS	NS	NS	••	••
A		NS		•		NS		NS

NS: not significant; • significant at 5 % probability level; •• significant at 1 % probability level

metabolism, promoting accumulation of Ca in the bones of the affected fish. Ca content in the nodules (26.97 %) was far in excess of its content in the bones of the affected as well as unaffected fish. The difference between sample means is significant at the 1 % probability level in the comparison between nodules and bones, while the comparison between bones of affected and unaffected fish shows that the difference is not significant.

In contrast to the accumulation of Ca, there was marked decrease of phosphorus in the nodules compared to its percentage content in the bones (Table 2b, significant at 1 % probability level). P content in the bones does not show a significant difference between the affected and unaffected fish.

While the Ca content in the nodules is about 7.7 times that of bones in unaffected fish, and 5.1 times that of bones in affected fish, there is a 20 times decrease in P content of nodules, compared to that of bones.

Contemporaneous with bioaccumulation of Ca, an increase in sodium and potassium ions was also observed in the nodules. The ratio of Na between bones of unaffected fish and nodules is 1:2 (not significant) while in the case of K, it is 1:4 (not significant). Ratio of the elements between bones of the affected fish and nodules is 1:6 (significant at 5 % probability level) and 1:7 (not significant) respectively. Thus, bones of unaffected fish had a higher content of Na and K than bones of fish with nodules.

DISCUSSION

Formations of bony outgrowths of endoskeleton have often been encountered in fishes. The terms 'osteoma' and 'hyperostoses' were rather commonly applied to describe such outgrowths. There is a third category of these outgrowths in the form of nodular excrescences. Two aspects that need to be considered in the context of their occurrence are how far are they natural phenomena with functional significance or how far are they due to a disturbance in the physiological make-up of the organism. In either case, taxonomic, genetic and environmental factors play an important role. An analysis on these lines of the information available in the literature may serve the purpose of sifting true osteoma from hyperostoses and nodular excrescences. There are extensive reviews on the subject (Schlumberger & Lucke 1948, Wellings 1969, Mawdesley-Thomas 1972, 1974, Hewitt 1983) dealing with osteoma and hyperostoses but not nodular excrescences. Explanations of the 3 different conditions found in the literature from at least the 16th century and the fossils (Hewitt 1983) formed eons before that, are long overdue.

There has been much discussion about the aetiology of osteomata. Initially, the general opinion was that bony outgrowths were associated with a traumatic aetiology (Nigrelli & Gordon 1946). The frequent occurrence of papilloma in Bothidae and Pleuronectidae led Mawdesley-Thomas (1974) to state 'Fish which live at the bottom of the ocean may expose themselves to local trauma by scraping themselves against a rough sea bed', which may be true with papillomata but not with multiple osteomata, as has been substantiated by Schlumberger & Lucke (1948) in the case of sea bream.

From the literature it appears that not all bony overgrowths can be regarded as osteomata. Early reports of osteomata, reviewed by Mawdesley-Thomas (1972, 1974) were all from highly compressed deep-bodied fish (*Chaetodon, Chrysophrys major, Chaetodipterus faber, Alutera schopfi* and *Pagrus unicolor*). The illustrations presented by him correspond to the characteristics of 'hyperostosis' described in *Drepane punctata* (Murthy 1967), another highly compressed deep-bodied fish.

In *Drepane punctata* (Murthy 1967), as a rule, all fish above a certain size developed excess growth of bone in different parts of the skeleton. The earliest deformity to develop was the frontal swelling at the size of 230 mm, followed by swellings of supraoccipital and ribs (>268 mm), lacrymals, neural and haemal spines (>390 mm) and caudals (>370 mm). These swellings increase in size with the growth of the fish. Thus, the swellings appear first in the anterior region, creating a hydrostatic imbalance and later in the posterior region, as if to restore the balance.

Gregory (1933) considered the possibility that the swollen supraoccipital and interorbital ridges tend to depress the frontal region of the fish which perhaps requires correctional movements of pectoral fins or counterbalancing in some other parts as in the swollen epineural and haemal spines. Gopinath (1951) also attributed the extraordinary development of secondary ossification of supraoccipital crest in *Caranx semifas-*

ciatus and *Alectis indica* (deep-bodied fish) to a demand for hydrostatic balance and stability, although the explanation was not acceptable to Hewitt (1983) who regarded that 'prevalence of swollen oil- or fat-filled cancellous bones, in large deep-bodied percoids, is a buoyancy adaptation'. Development of swollen bones, cancellous or not, in the head region, appears to be frequent in deep-bodied fish, which have to maintain a hovering posture while nibbling at sedentary benthic organisms or on coral fronds. In such cases, the argument of hydrostatic function of hyperostosis can be upheld. Consequent growth of excess bone on epineural and haemal spines appears to be a counterbalancing mechanism developed to nullify the hydrostatic imbalance created by bony swellings in the head region. Thus, the formation of excess bone in the head region as well as in the postabdominal region appears to be a species-specific natural process serving a hydrostatic function. This appears to be less energy-consuming than the correctional movements of paired and median fins to keep the bottom feeders in a hovering position or to restore the fish to the normal horizontal position. Since hyperostosis in deep-bodied fish is a natural phenomenon and not a disease manifestation, the question of aetiology does not arise.

Hyperostosis in non-deep-bodied fish, e.g. formation of stones in an elongated fish like *Trichiurus lepturus* (James 1960) and also nodular excrescences with or without connections with bone as in *Arius* spp., calls for other kinds of explanations. A striking feature in these fishes is that, of all the species of a genus present in a given locality, only 1 species developed nodular excrescences. Formation of nodules appears to be species-specific in each locality, arising probably from endogenous factors in some individuals only or in response to contaminants in the aquatic environment.

Selvaraj et al. (1973) suspected impaired ionic metabolism as the possible cause for the formation of 'stones' and went to the extent of suggesting the involvement of genetic predisposition as an additional factor, although they described the 'stones' as 'osteochondroma' and 'osteoma' in *Arius jella*, without histological evidence. Mehrle & Mayer (1975) determined the effect of Toxaphene on calcification and mineralisation and found that bone quality of Toxaphene-exposed fish showed a significant increase of calcium and decreasing trend of phosphorus during development. Chemical quality of the nodules in *A. tenuispinis* (present study) shows the same trend. Diffuse or focal vertebral hyperostosis and other displastic vertebral changes were induced in *Cyprinodon variegatus* exposed to 1 to 5 $\mu g\ l^{-1}$ trifluralin (Couch 1984).

It is well known that species-specific enzyme systems, sometimes mediated by hormones, control metabolic pathways (Mawdesley-Thomas 1974). Gillespie & Evans (1979) attributed the formation of ceroid coating on Ca granules, removed from trout with Nephrocalcinosis, to the breakdown of cells due to necrosis, which possibly destroys a biochemical mechanism that prevents auto-oxidation of the unsaturated fatty acids, allowing the formation of ceroid. Harrison & Richards (1979) and Smart et al. (1979) pointed out the importance of increased CO_2 concentrations as a possible cause of Nephrocalcinosis. Unsuitable feeding as a possible cause (Cowey et al. 1977) was refuted by Schlotfeldt (1980) who thought that Nephrocalcinosis in intensive culture is due to a multiplicity of factors, in which the complex of environmental conditions is of crucial importance. It was shown experimentally by Couch (1984) that exposure of *Cyprinodon variegatus* to trifluralin caused enlargement of the pituitary and vertebral hyperostosis. Thus, there is growing evidence to show that adverse environmental conditions bring about hormonal changes which control metabolic pathways. In human pathology, hyperparathyroidism is known to cause Nephrocalcinosis, attendant renal damage, and significant serum chemical alterations, particularly persistent hypercalcemia and increased serum alkaline phosphate activity, as well as significantly altered renal tubular reabsorption of phosphate (Lichtenstein 1977, p. 422). In rainbow trout nephrocalcinosis, half of the stones were found to contain phosphates of 5 different types similar to some human urinary stones (Gillespie & Evans 1979). Evidence regarding control of Ca metabolism in fishes is related to the hormonal secretions of ultimobranchial glands (counterpart of parathyroid in higher vertebrates) and corpuscles of Stannius (Copp 1969). Removal of the latter in *Anguilla anguilla* in sea water increased plasma Na, K, Ca and Mg and decreased plasma inorganic phosphate concentrations, as transient phenomena (Chester Jones et al. 1969).

Chemical analysis of the nodules and operculum of affected and unaffected *Arius tenuispinis* showed a very high content of Ca in nodules accompanied by marked decrease of P (both statistically significant), with a significant decrease in Na ion also in the affected fish. It appears as though excess accumulation of Ca in the body fluids of the affected fish culminated in the formation of nodules, after the Ca content in their bones reached the saturation point. It also shows that whatever metabolic disturbance was responsible for the accumulation of Ca in the nodules was also responsible for the elimination of P at a faster rate than Ca at the body fluid level. Since P is found to be more or less the same in the metabolically remote opercular bones of the affected as well as unaffected fish, its elimination appears to be taking place through the kidney, even before entry into the metabolically active body fluids, from where the mineral content of the nodules seems to be drawn. It also shows that the process of calcification and mineralisation of bones is such that excess Ca in body fluids may be absorbed to some extent by the bones, but the reverse process of withdrawal of P from bones to body fluids, to make up their deficiency in the body fluids, cannot take place. Since bones of unaffected fish had a higher content of Na and K than bones of fish with nodules, the excess ions in the nodules were also perhaps drawn from the body fluids, and as a corollary their content in the bones of the affected fish was reduced.

Although at this stage it is speculative, there seems to be a clear possibility of impairment of one or both of the endocrine glands mentioned above, mainly ultimobranchial glands, as the cause for the increase in plasma Ca, followed by development of nodular excrescences in *Arius tenuispinis*, with a spectacularly high Ca content and marginal increase of Na and K in the nodules, as compared to their content in the bones of the fish. Simultaneously, a decline in plasma inorganic phosphate also appears to take place. Sections of the nodules have not revealed any cellular structures or hollow spaces. Since the nodules had accretionary surfaces, the mineral substance of which they are composed appears to be continually added. The composition and nature of the nodular excrescences seems to depend on the particular metabolic pathway that is disturbed. If it is Ca metabolism in *A. tenuispinis* it appears to be P metabolism in *A. jella* (Selvaraj et al. 1973), in which the high P content of nodular excrescences may be attributed to phosphate reabsorption at the renal tubular level, perhaps being deposited in the nodules through serum transportation. Such differences appear to be species-specific.

Each affected individual seems to be hypersensitive to a proximate inimical contaminant in the aquatic environment. In the context of the high degree of pollution of Visakhapatnam harbour waters (Ganapati & Raman 1973), it is easy to envisage contamination of the aquatic environment in the vicinity of Visakhapatnam harbour. Hydrocarbons and heavy metallic ions discharged into the harbour waters from the neighbouring industrial installations could be causative factors of neoplasia in fishes (Srinivasa Rao & Janardhana Rao 1979, Srinivasa Rao & Sultana 1983) and nodular excrescences in *Arius tenuispinis*. In *A. platysomus* (Menon 1974), buccal papilloma were observed in females only, limiting the effect specifically to one sex, perhaps associated with sexual differences also in their response to changes in aquatic environment.

Confirmation and precise formulation of the factors involved requires experimental studies, which are a rather difficult proposition in the case of marine catfishes. The inference about the involvement of ultimobranchial glands and corpuscles of Stannius in the formation of calcareous nodules is necessarily based on circumstantial evidence only.

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