SYMPOSIUM ON CANCER OF THE URINARY BLADDER

SYMPOSIUM ON CANCER OF THE URINARY BLADDER

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We extend our thanks to all members of their staff, and to the members of the Research Institute of tropical Diseases, the Faculty of Medicine of the University of Cairo, and Qualiub Training Centre, together with our Colleagues in Research and Clinical Medicine.

We appreciate particularly the generosity with which the National Research Centre, the Egyptian Cancer Society, and the Faculty of Medecine of the Alexandria University have put their facilities at our disposal and through their hospitality made it possible to the meeting to achieve its purposes.

SYMPOSIUM ON THE GEOGRAPHICAL PATHOLOGY OF NEOPLASMS OF THE URINARY BLADDER

The Symposium on the Geographical Pathology of Neoplasms of the Urinary Bladder was convened by the International Union against Cancer with support from the Government of the United Arab Republic and from the Anna Fuller Fund.

Sessions were held at the National Research Centre, Cairo, from March 26th to 31st, 1961 under the chairmanship of Dr. Harold Stewart. The scientific secretary during the preparatory stages of the Symposium and its sessions was Dr. Johannes Clemmesen.

The following members were present :

- Professor A. El Katib, President Egyptian Cancer Society. Dar-El Hekmah, 42 Kasr el Aini, Cairo.
- Professor V. R. Khanolkar, President U.I.C.C. Tata Memorial Hospital, Parel, Bombay.
- Dr. Harold L. Stewart, Chairman, Laboratory of Pathology, Nat. Cancer Institute, Nat. Institutes of Health, Bethesda 14, Maryland.
- Dr. Johannes Clemmesen, Vice-Chairman, Secretary, Dept. of Pathology & Cancerregisteret, Finsen Institute, 49 Strandboulevarden, København, Ø.
- Professor A. L. Aboul Nasr, General Secr. Egyptian Cancer Society, 42 Soliman Pascha Street, Cairo.
- Dr. N. Ansari, Chief Endemo-Epidemic Diseases, World Health Organisation, Palais des Nations, Geneve.
- Dr. Georgiana Bonser, Dept. of Experimental Pathology & Cancer Research, School of Medicine, University of Leeds, Leeds 2.
- Professor E. BOYLAND, Chester Beatty Research Institute, Royal Cancer Hospital, Fulham Road, London, S.W. 3.
- Dr. E. Cowart, Namru 3, Cairo.
- Dr. O. G. Dodge, Makerere College, The University College of East Africa Dept. of Pathology, P.O. Box 2072, Kampala, Uganda.
- Dr. Harold F. Dorn, General Secr. U.I.C.C., National Institutes of Health, Bethesda 14, Maryland.
- Professor R. M. Fawzy, Dept. of Urology, Manial Hospital, Cairo.
- Professor M. El Gazayerli, Director, Dept. of Pathology, Faculty of Medicine, Alexandria University, Alexandria.
- Professor J. GILLMAN, Johannesburg, now: Medical Research Council P.O. Box M. 32, Acera, Ghana.
- Professor J. Higginson, Department of Pathology and Oncology, University of Kansas Medical Center, Kansas City 12, Kansas.

- Dr. W. C. Hueper, National Cancer Institute, National Institutes of Health, Bethesda 14, Maryland.
- Professor C. Jackson, Kampala, now: National Research Council P.O. Box M. 32, Acera, Ghana.
- Dr. K. Lockwood, Cancerregisteret, Strandboulevarden 49, København, Ø.
- Professor N. Makar, Hunterian Professor of the R.C.S. (ENG), Emeritus Professor Cairo University, 12 Hassan Sabry Street, Zamalek, Cairo.
- Dr. F. K. Mostofi, Armed Forces Institute of Pathology, 6865 16th Street, N.W. Washington 25, D.C.
- Professor A. H. Moussa, Department of Endemic Diseases, Manial Hospital, Cairo.
- Professor H. F. NAGATY, Department of Parasitology, Ein Shams Univ., Faculty of Medicine, Abbassia, Cairo.
- Professor A. M. Pamukcu, University of Ankara, Ankara.
- Professor M. Payet, Institut des Hautes Etudes, Dakar, Senegal.
- Dr. M. Prates, Chief of Pathology, Hospital de Lourenço Marques, Lourenço Marques Mozambique.
- Dr. J. Price, University of Wisconsin, Madison 6, Wisconsin.
- Dr. I. Sibai, Faculty of Medicine, Kasr el Aini, Cairo.
- Professor Ichiro Tsujii, Professor of Genito-Urinary Department Hokkaido University, Medical School, Sapporo, Hokkaido.
- Professor E. V. VIGLIANI, Clinica del lavoro della Universita di Milano, Milano.
- Dr. M. H. C. Williams, Imperial Chemical Industries Ltd., Dyestuffs Division, Hexagon House, Blackley, Manchester.

The purpose of the Symposium was to review present knowledge of the Occurrence and Behaviour of Cancer of the Urinary Bladder and Allied Diseases and to make proposals for the amplification of this knowledge, with a view to treatment and prevention.

As a result the Symposium passed the following recommendations:

1.0. GENERAL

Tumours of the urinary bladder may conveniently be grouped under the following three main categories:

1. So-called spontaneous tumours, generally ascribed to unknown etiological factors, either intrinsic or extrinsic, possibly of biological character. (An unknown part of these tumours may actually belong under the succeeding categories).

- 2. Tumours conditioned by occupational exposure to chemical carcinogens and various other well-defined, etiological factors in the environment of patients.
- 3. Tumours associated with a parasitic infection, viz. bilharziasis.

1.1. Statistical Studies

- 1.1. Statistics on the incidence of all neoplasms of the urinary bladder are essential to assess the importance of various etiological factors such as occupational and industrial carcinogens, food additives, smoking of tobacco, and factors now unknown. Such statistics should be worked out in as many countries as possible, particularly where accurate information is available on the distribution of cases by sex and age as well as on the methods and results of treatment.
 - 1.1.2. Statistics on the frequency of bladder

neoplasms should include all cases of epithelial tumours of the urinary bladder whether malignant or benign, in view of the difficulties involved in the histological distinction between these categories. In the presentation of data other major histological categories should be specified, to permit international comparisons which may suggest differences in etiological pattern.

1.1.3. Morbidity rates for Denmark and mortality rates for England both show an increase for bladder neoplasms. In the United States a real increase in frequency may also be developing. Further studies are urgently needed to verify whether a similar increase is occurring in other countries, and to define the causal factors involved.

1.2. Pathological Studies

- 1.2.1. To facilitate comparisons between different regions further steps should be taken to standardize clinical and pathological criteria and nomenclature for tumours of the urinary bladder.
- 1.2.2. Groups of pathologists should be established for consultation on diagnosis, training and research in bladder tumours.
- 1.2.3. Research into the pathology of bladder tumours should include studies of the reaction patterns of the bladder mucosa and the developmental stages of papillomas and carcinomas and various other lesions in all parts of the urinary tract. Special attention should be paid to histochemical and histophysical properties and their significance to prognosis.
- 1.2.4. Factors influencing the development, recurrence and spread of bladder neoplasms should be investigated.

1.2.5. The incidence of various coincidental lesions should be investigated to determine the presence of common etiological factors.

1.2.6. Methods for early diagnosis of bladder

neoplasms, including cytological technique,

should be further developed.

1.2.7. Methods for fixation and sectioning of specimens should be standardized to permit the collection of accurate and comparable information on histology, pattern of growth, mode and extent of infiltration of bladder neoplasms.

1.3. Animal Research

The study of spontaneous cancer of the urinary tract in animals offers a useful subject :

- 1.3.1. A registry for animal tumours should be established.
- 1.3.2. A comparative atlas of animal tumours should be compiled.
- 1.3.3. Material from zoological gardens and from abbatoirs should be used more extensively.
- 1.3.4. More information should be collected on bladder tumours occurring in the cat and other carnivores, in herbivores, (especially ruminants), and in rabbits, hamsters and guineapigs.

2.0. OCCUPATIONAL AND OTHER ENVIRONMENTAL FACTORS

2.1. All authorities concerned with public health governmental and non-governmental, as well as all chemical manufacturers, should be told that since the beginning of the manufacture of aromatic amines in various countries more than two thousand workers producing and using chemicals capable of causing cancer of the urinary bladder are known to have contracted this disease. At suitable intervals the chemical and medical experts of industry should meet to prevent the continuation of this hazard.

The following steps should be considered:

- 2.2.1. Statistical data on the incidence of tumours, based on the populations at risk to special chemicals or groups of chemicals, should be collected and exchanged.
- 2.2.2. Research work on biological testing of suspect chemicals should be coordinated by consultation between all the available experts interested in this field.
- 2.2.3. Alternative processes and products should be developed to provide substitutes for established carcinogenic chemicals as has already been found possible in the case of 2-napthylamine, xenylamine, and 2-acetylaminofluorene.

2.2.4. A universal code of practice for the medical and technical prevention of occupational bladder tumours should be agreed upon.

2.2.5. The most effective methods of early diagnosis should be made available for all populations at risk in the past, present and future.

2.3. The extent to which occupational and other environmental exposure to bladder carcinogens has influenced the increases in incidence of bladder tumours found in some countries, should be explored.

Experimental Research.

2.4. Studies on the relationship between

chemical structure and the biological effect of carcinogens on the urinary bladder should be continued and extended.

2.4.1. Further study of the mode of administration of the chemical carginogens should be made.

2.4.2. Extension of metabolic studies, including the development of chemical methods, should take place.

2.4.3. The effect of nutritional status on the induction of cancer should be studied.

2.4.4. The role of urinary stasis in chemical

carcinogenesis of the bladder deserves further

2.4.5. Further studies of differences in effect of chemicals on different species of animals are required.

3.0. BILHARZIASIS

In the search for an understanding of the relation between bilharziasis and cancer of the urinary bladder the members of the symposium accepted the following facts:

3.0.1. That bladder cancer occurs relative to all forms of malignant disease with greater frequency in Egypt and certain other regions of Africa than in European countries or North America.

3.0.2. That this relative increase occurs in a

young population.

3.0.3. That an unusually high proportion of these cancers are of squamous type in comparison with those found in Europe or North Ame-

3.0.4. That in Egypt and other parts of Africa where bladder cancer is reported to occur frequently bilharzial infection is endemic, and

3.0.5. that bilharzial cystitis occurs at an early age and is associated with an intense inflammatory reaction in the bladder wall and with marked epithelial hyperplasia and metaplasia.

An association between bilharziasis and cancer of the urinary bladder is thus accepted by the members of the conference, but they conclude that further investigation is urgently needed in

order to prove a causal relationship.

Further, they are aware that infestation of the human with the parasite bilharzia is widespread and severe. It is estimated that some 150 million human beings throughout the world suffer at present from bilharziasis in Africa, Eastern Mediterranean region, China, Japan, the Philipines, Celebes and parts of South America.

Thus the study and control of bilharziasis is

a problem of far wider importance than the neoplastic disease of the urinary bladder which may ensue and with which the symposium is mainly concerned.

The symposium therefore recommended the

following methods of approach:

3.1. Statistical studies

3.2. Field studies

3.3. Experimental research

- 3.4. Research into and application of methods of control
- 3.5. Training of research workers
- 3.6. Interchange of information.

Statistical Study.

- 3.1.1. Frequency and degree of infestation with bilharziasis should be determined within welldefined geographical areas, such as highly infested Qualioub in lower Egypt and moderately infested areas in upper Egypt where perennial irrigation has not yet been established. Other areas of particular suitability are found in Mozambique around Lourenço Marques, in Uganda, Northern and Southern Rhodesia, in Ghana, and in Nigeria.
- 3.1.2. Comparative studies of regions infested with different species of parasites should be carried out, with a view to the type of parasite and the lesions it produces.

3.1.3. In the areas under study all tumours of the bladder should be registered according to sex and age, and examined both clinically and post mortem, together with other neoplasms.

- 3.1.4. Post-mortem examinations in the areas studied should cover all deaths, or an unselected part. Medico-legal autopsies applying adequate preparation should be used as a comparable indicator of bilharziasis in the general population.
- 3.1.5. Foreign personnel who have contracted bilharziasis in infested areas and later repatriated, as well as populations migrated from areas of high infestation to less infested regions, should be made the subject of follow-up study.
- 3.1.6. Reviews of existing records from hospitals and pathology laboratories giving data on current admissions for bladder cancer and suitable control groups may give valuable information, on the development in the area concerned.

Field Studies.

3.2.1. The significance of bilharziasis to Public

Health and Public Economy of infested areas should be made clear.

- 3.2.2. Studies into snail taxonomy and snail ecology should be encouraged.
- 3.2.3. Standardization is required of procedures for epidemiological investigation and of measures for the evaluation of control measures. This includes e.g. examination of urine and stools, sero-immunological methods, and intradermal tests.

Experimental Research in Bilharziasis.

- 3.3.1. Studies on problems of immunity and acquired resistance including the influence of nutritional status are required.
- 3.3.2. In vitro and in vivo studies of various types and strains of parasite in several animal species should be undertaken, particularly with regard to physio-pathology and patho-anatomy.

3.3.3. The effect of chemotherapeutic agents on metabolic and other functions of the parasite and its host will deserve special studies.

3.3.4. A study of carcinogens in the experimentally infected animals is required.

3.3.5. Further research for methods of infecting strains or species of animals to produce lesions comparable to the human disease is needed.

Research into and Application of Methods of Control.

The Symposium agreed that intensive application of known hygienic methods for the control of bilharziasis would rapidly reduce the rate of infection if applied over large areas, but the search for new methods of control is nonetheless needed.

Such new methods would include :

3.4.1. Snail control through modification and

improvement of agricultural and irrigation methods.

- 3.4.2. Chemical methods for killing snails and rendering them unable to mature the parasite.
- 3.4.3. Early and close co-operation between engineers and Health Authorities in the planning of irrigation.

Training of Research Workers.

- 3.5.1. Many more workers, both medical and scientific, are needed in laboratories and in field work.
- 3.5.2. The establishment of scientific institutes and more active support of existing institutes, especially in areas where these diseases occur, should be undertaken.
- 3.5.3. In view of the special circumstances prevailing in Egypt, a research institute particularly concerned with bilharziasis should be established as soon as possible.

Interchange of Information.

3.6.1. Free exchange of information between scientific institutes is to be encouraged.

3.6.2. Frequent personal contact and exchange of scientists should be facilitated between various fields of research and between countries. This applies particularly to physicians, physiologists, biochemists, pathologists, and workers in fresh water ecology, parasitology, sanitary engineering and related disciplines.

These recommendations should be carried out in conformity with the practices of the World Heath Organization *).

^{*)} It is to be noted that this Organization has already published a Report on «Second African Conference on Bilharziasis » (WHO/CCYA), World Hlth. Org. techn. Rep. Ser., 1960, 204.

A PROBLEM IN GEOGRAPHIC PATHOLOGY

A. L. AURORA and V. RAMALINGASWAMI *

presented by V. KHANOLKAR

(Abstract)

The occurrence of calculi in the urinary bladder in growing children in some parts of India, Pakistan and the district of Ubol in Thailand constitutes a paediatric problem of interest. Careful clinico-pathological study of some cases of primary bladder stone among children of Delhi was undertaken with a view to investigate the etiology of the disease.

The present study brings out the probable role of mucopolysaccharides in the urinary tract in initiating and continuing mineral deposition. The role of the dead and dying epithelial cells of the urinary tract has also been raised and it is thought that these might aid in attracting calcium salts and thus initiating or aggravating an established process. The presence of microorganisms raises the question of urinary tract infection leading to cellular exudation and mucoprotein excess in the urinary tract.

The changes in the urinary bladder might be primary or secondary to the presence of the stones. It is for the future to unravel the part played by these and other factors in their interrelationship.

Calcium balances indicate that the children with bladder stone often are in positive calcium balance which reflects the unsaturated state of their body for calcium. This is a pattern seen in the children of poor economic status without stone in the bladder. These and studies on serum chemistry show that children with bladder stone exhibit no metabolic defects of calcium.

Chemical analysis of the stones reveals that they are of mixed character containing calcium, oxalates and phosphates.

The relationship of bladder stone disease in childhood to tumours of the bladder in later life is not known. The investigation has not revealed any single specific cause for the development of bladder stones. There is probably a constellation of factors involved.

La présence de calculs dans la vessie d'enfants en croissance, signalée dans certaines régions de l'Inde, du Pakistan et dans le district de Ubol, Thailande, constitue un problème pédiatrique intéressant. Une étude clinico-pathologique approfondie d'un nombre de cas de calculose vésicale primaire chez les enfants de Delhi a été entreprise en vue de rechercher l'étiologie de l'affection.

L'étude révèle le rôle probable des mucopolysaccharides dans le tractus urinaire dans le déclenchement et l'entretien de la déposition de minéraux. Le rôle des cellules épithéliales mortes ou mourantes du tractus urinaire est également envisagé, et l'on pense que les cellules pourraient contribuer à attirer les sels de calcium, initiant ou aggravant ainsi le processus en cours. La présence de micro-organismes pose la question du rôle de l'infection urinaire qui provoquerait la diapédèse de cellules et un excès de muco-protéines dans l'appareil urinaire.

Les altérations de la vessie peuvent être primaire ou secondaire à la présence des calculs. L'avenir nous apprendra la part de ces facteurs, ainsi que d'autres facteurs et leurs rapports mutuels.

Le bilan calcique montre que les enfants porteurs de calculs ont souvent une balance positive reflètant l'état de désaturation en calcium de leur organisme. Cet état se rencontre également chez les enfants de condition modeste sans calculs vésicaux. Ces études et la chimie du sérum montrent que les enfants porteurs de calculs vésicaux n'ont pas de déficience dans leur métabolisme calcique.

L'analyse chimique des calculs montre une composition mixte, contenant du calcium des oxalates et des phosphates.

Le rapport entre l'affection calculeuse vésicale dans l'enfance et l'apparition de tumeurs vésicales plus tard dans la vie est inconnu. L'étude n'a montré aucune cause spécifique au développement de calculs de la vessie.

Il y a probablement un ensemble de facteurs en cause.

^{*} All India Institute of Medical Sciences, New Delhi - 16.

EPIDEMIOLOGY AND PATHOLOGY OF CANCER OF THE BLADDER IN EGYPT

A. L. ABOUL NASR, M. E. GAZAYERLI, R. M. FAWZI and I. EL-SIBAI

I) EPIDEMIOLOGY OF BLADDER CANCER

In the early part of this century Ferguson (1907 and 1911) reported the high frequency of cancer of the bladder in Egypt and linked this to bilharziasis of the urinary tract. Since then most authors writing on the subject agreed that cancer of the bladder is a common type of cancer in Egypt but there was a great divergence in the opinions about the actual frequency of cancer of the bladder in our country.

It can be noticed that in all the published reports the main concern was to find the relative frequency of cancer of the bladder to other malignant diseases in the series under study. The figures given varied from 43% by Makar to 4.1% by Barsoum.

If these reports are carefully scrutinized it can be easily observed that all the series analysed show a great deal of selection as will be referred to later.

It is very difficult even now to give the exact figures about the morbidity and mortality rates of cancer of the bladder in Egypt. The death certificates cannot be relied on as in many of them the immediate cause of death and not the underlying disease is mentioned.

In this contribution it is tried to present an approximate picture of the relative incidence of cancer of the bladder to the total malignant diseases in Egypt. Last year a series of consecutive new cancer cases seen by one of the authors was analysed to find the ratio incidence of the different types of cancer. The series comprised 734 cases: 371 males and 353 females. Out of these cases there were 55 cases of cancer of the bladder forming a ratio of 7.5%. In male patients cancer of the bladder formed 11.0% while in females only 3.9%. Cancer of the bladder was the most frequent solid malignant tumour in males while in females the most frequent was cancer of the breast.

Looking at Makar's figures (Table I) it can be noticed at once that the percentage of bladder cancers given (43%) is marked out against cancer of five other organs only, viz: the tongue, stomach, colon and rectum, breast and uterus. It can be noticed that the relative incidence of

TABLE I

Incidence of Cancer of the Bladder in 3 Cairo Hospitals during 9 years (1932-1940) compared with that of other cancers

Site	Kasr el Ainy Hospitals	Italian Hospital	Greek Hospital	
Cancer of				
Tongue	210	2	1	
Cancer of				
Stomach	131	37	8	
Cancer of Co- lon and Rec-		*	*	
tum	463	26	3	
Cancer of				
Breast	720	88	47	
Cancer of				
Uterus	652	45	15	
Cancer of			1.90	
Bladder	1696 (43%) Bilharzial	6 (3%) Non-Bilhar- zial	10 (11 %) Non-Bilhar- zial	

non-bilharzial cancer of bladder in the series from the Greek Hospital (11%) is much higher than should be expected due to this selection.

In the present series the six sites mentioned in Makar's table comprised 303 cases out of the total of 734 cases; forming about 40% of the total. If Makar's figure is corrected on this basis it will be found that ratio of cancer of the bladder to the total malignancy will drop to 17% only. It also appears that the diagnosis of malignancy was not confirmed in all the cases included as cancer of the bladder. The author states that cases of «cystitis glandularis» and incrusted «vegetative cystitis» might have been included under the heading of cancer. It can thus be seen that figure will be lower than 17% and not 43%.

The figure quoted after Dolbey and Mooro as 23% is also a miscalculation. They found in the autopsy and biopsy material in Kasr-el-Ainy Hospital (1920-23) 671 cases of malignant diseases out of which there were 51 cases of cancer of the bladder. Thus the ratio will be 7.7% of all malignant diseases. As many of the

figures and impressions quoted came from surgeons analysing their «surgical» series of cancer it was thought advisable to find the ratio of cancer of the bladder to similar cases in the present series (Table II).

TABLE II

Site	Total	Males	Females	
Oral Cavity	52	39	13	
Alimentary Tract	70	44	26	
Breast	131	7	124	
Genitals	119	28	91	
Bones	17	10	- 7	
Sarcomas	29	21	8	
Kidney and arohes	11	7	4	
Bladder	55 (11.3%)	41 (21%)	14 (5%)	
Total	484	197	287	

It can be noticed that cancer of bladder forms 11.3% of these «surgical» cases in the total and 21% in males and 5% in females. This corresponds closely to what has been mentioned in such series.

In the annual report (1951) of Alexandria University Hospitals it was found that out of 1850 cases of malignant diseases admitted 100 cases had cancer in the bladder forming 5.4%. Cancer of the bladder formed 5.8% of all cancer in the biopsies during ten years in the department of pathology in Alexandria Universities and 8% in the autopsy material.

Evidence of Bilharziasis.

The total number of cases collected by the four authors comprises 652 cases of cancer of the bladder. Of these 20 cases i.e. 3% were non-bilharzial while in 632 cases (97%) there was evidence of bilharziasis in the urinary bladder.

Sex Incidence.

Of the total series 543 cases were males and 109 cases females forming a M:F ratio of 5:1. Thus females form only 16.6% of the cases of cancer of the bladder. Payne found 19.6% females in 1400 cases of bladder cancer while the Registrar General's Reviews (1950-56) show a M:F ratio of 2.32:1.

Age Incidence.

Table III shows the distribution of the cases on the decades of age.

It can be noticed that the largest number of cases, about 40% of the whole series, fall in the fifth decade. About 3/4 of the cases (73%) were below 50 years ago, while in Payne's report only 12.4% were under the age of fifty.

The average age in these patients is nearly 44 years which is about 20 years younger than the average age reported by Payne: as 63.5 years.

II. PATHOLOGY OF URINARY BILHARZIASIS

From the liver coupled bilharzial worms travel against the venous current to reach the urinary bladder. There, the female leaves the male worm and continues until it reaches a small venule usually in the submucous coat where it lays its eggs. Around the eggs a bilharzial reaction is set up which may be localized « bilharzioma » or diffuse.

TABLE III

Age Distribution in Present Series

Decades	п	m	IV	v	VI	VII	VIII	Total
Cases	3	53	163	257	120	50	6	652
Percentage	0.46	8.13	25	39.41	18.41	7.67	0.92	100 %

A fresh bilharzioma reveals a centrally placed egg surrounded by a radiating zone of epithelioid cells amongst which eosinophils, lymphocytes and plasma cells are found. Outside this there is a peripheral zone of proliferating but concentrically arranged fibroblasts destined to lay down collagen. In the diffuse variety the eggs are more numerous and the granuloma is more massive. As time passes on maturation of the granuloma takes place. This is characterized by formation of giant cells which attack the eggs, calcification of the eggs, disappearance of the leucocytes and histiocytis and the laying down of collagen.

The lesions in the submucous coat often lift up the mucosa into the cavity of the bladder producing elevations which differ in size and shape. These are the bilharzial tubercles, nodules and papillomas. Microscopically the epithelium covering the last is either atrophic or completely lost but in some cases the covering epithelium may show squamous metaplasia.

In old lesions where calcified eggs and dense collagen are found and the overlying mucosa is atrophic we get areas which look like sand under water. These are called «sandy patches». They

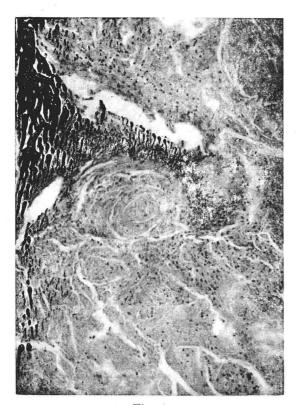


Fig. 1.

Diffuse cellular lesions in the muscle coat.

occur anywhere in the bladder but are commonest in the region of the trigonum.

Bilharzial lesions in the muscle coat cause fibrosis and atrophy of the muscle bundles (Figs. 1, 2).

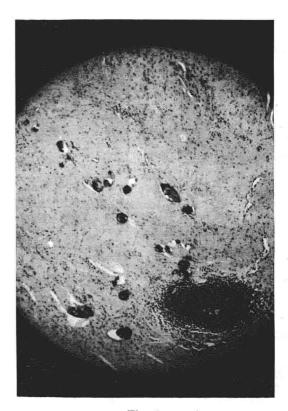


Fig. 2.
Internal meatus.

In heavy infections bilharziasis of the outer coat may cause marked thickening and fibrosis.

The observation of J. GILLMAN and PRATES on infiltration of lymphocytes, plasma cells and eosinophils, frequently out of proportion to the number of eggs in the affected region, was confirmed and substantiated by the following observations. The lymph nodes which drain active ulcers or fresh bilharzial lesions in the urinary bladder show congestion and marked reticulum cell proliferation of the germinal centres as well as proliferation of the members of the R.E.S. in the sinusoids. In addition the sinusoids contain numerous eosinophils and extravasated red blood corpuscles. This remarkable reticulum cell stimulation was also observed in the enlarged hilar lymph nodes draining active bilharzial lesions in the liver. The lymph nodes