

OXFORD MEDICAL PUBLICATIONS

U R I N E

EXAMINATION AND CLINICAL INTERPRETATION

BY

C. E. DUKES

M.Sc. (LONDON), M.D. (EDIN.), D.P.H. (LONDON)

*Pathologist to St. Peter's Hospital for Stone and
other Diseases of the Urinary Organs, London.*

Pathologist to St. Mark's Hospital, London

'What others treat with levity
Is here treated with gravity.'

A. D.

OXFORD UNIVERSITY PRESS
LONDON NEW YORK TORONTO

1939

OXFORD UNIVERSITY PRESS
AMEN HOUSE, E.C. 4
London Edinburgh Glasgow New York
Toronto Melbourne Capetown Bombay
Calcutta Madras
HUMPHREY MILFORD
PUBLISHER TO THE UNIVERSITY

PRINTED IN GREAT BRITAIN

U R I N E
EXAMINATION AND
CLINICAL INTERPRETATION



‘THE UROLOGIST’

Painting by A. van Ostade, 1665.

PREFACE

THE development of medical science during recent years has added considerably to the value of urine examination. A generation or two ago a close inspection of the urine and a few chemical tests provided all the information that could be gained from this source. Then came the microscope, and the field of urine analysis was extended to examination for cells, casts, and crystals. The advent of bacteriology once more enlarged the scope of urine analysis and led to a much more precise understanding of urinary infections. Meanwhile the simplification of chemical methods of analysis made it possible for urine tests to be used more and more for the measurement of renal function and for the detection of pathological constituents. Lastly, the discovery of the excretion of hormones in the urine has led to biological methods of examination, such as are used in the diagnosis of pregnancy.

In this book on the examination of the urine I have tried to collect together methods for the carrying out of all laboratory investigations on the urine likely to be useful in clinical medicine. Ten years' experience as pathologist to a special hospital for diseases of the urinary organs has given me personal interest in this subject. The methods recommended for the simpler chemical, microscopic, and bacteriological tests are the outcome of this experience. For the more elaborate chemical and biological tests, outside the scope of ordinary routine clinical pathology, I have endeavoured also to select methods which are reliable, and have given references to the original sources.

This book is not only a guide to the performance of urine tests. It sets out also to provide an interpretation of each test. For instance, the tests for albumin in the urine are preceded by a description of the clinical conditions in which albuminuria is known to occur. Similarly the tests for tubercle bacilli are accompanied by a description of tuberculosis of the urogenital system, so that the conditions under which tubercle bacilli are likely to be found in the urine may be made clear.

I hope that this book will be useful to general practitioners, physicians, and surgeons, apart from its function as a guide to the performance of laboratory tests. Every clinical pathologist knows how much more zest comes into his work when he can co-operate with a colleague who is 'pathologically minded' and has some acquaintance, if not with the performance of tests,

at any rate with their precise uses and limitations. It has been my privilege to enjoy associations of this character and I believe it to be the duty of clinical pathologists to try to foster an interest in pathology in those with whom they are destined to work.

C. E. DUKES

May, 1939

ACKNOWLEDGEMENTS

BOOKS

I SHOULD like to express special acknowledgement to certain text books which I have worked with for years and which I have consulted freely in writing this book. The chief amongst these are:

Practical Physiological Chemistry, by S. W. Cole (Heffer & Sons, Cambridge).

Chemical Methods in Clinical Medicine, by G. A. Harrison (J. & A. Churchill, London).

Physiology and Pathology of the Urine, by J. Dixon Mann (C. Griffin & Co., London).

Handbook of Practical Bacteriology, by T. J. Mackie and J. E. McCartney (E. & S. Livingstone, Edinburgh).

Diagnosis and Treatment of Venereal Disease, by D. Lees (E. & S. Livingstone, Edinburgh).

Diseases of the Kidney, by W. Girling Ball and Geoffrey Evans (J. & A. Churchill, London).

Stone and Calculous Disease of the Urinary Organs, by J. Swift Joly (W. Heinemann, London).

Muir and Ritchie's Manual of Bacteriology, revised by C. H. Browning and T. J. Mackie (Oxford University Press).

Forensic Medicine, by Douglas J. A. Kerr, (A. & C. Black, Ltd.).

Manson's Tropical Diseases, by P. H. Manson Bahr (Cassell & Co., Ltd.).

The Practice of Medicine in the Tropics, edited by W. Byam and R. G. Archibald (Oxford University Press).

Medical Research Council Special Reports, No. 9, 19, 179. H.M. Stationery Office.

Several of the methods described for estimation of those chemical constituents of the urine which are rarely examined in routine pathological work have been taken from Cole's *Practical Physiological Chemistry*.

ILLUSTRATIONS

Most of the illustrations of pathological specimens are photographs of operation specimens removed by the surgeons to St. Peter's Hospital and sent to the laboratory for examination. I am much indebted to Professor A. E. Crew for the coloured illustrations of the Ascheim-Zondek and Friedman tests, and to Messrs. Charles Griffin & Co. for permission to reproduce several drawings from *Reider's Atlas of Urinary Sediments* (London, 1899). The Welcome Historical Museum kindly supplied photographs of the pictures reproduced in the ~~Prontispiece~~ ^{frontispiece}.

and Figs. 1, 2, 3, and 74. Plates i and ii are from a set of coloured drawings given to me by the late Sir John Thomson Walker. Dr. Manson Bahr has kindly allowed me to reproduce Plate iii from his book on *Tropical Diseases*. I am grateful to Professor Kerr for permission to make use of the coloured illustration of blood spectra (Plate iv) from his book on *Forensic Medicine* (A. & C. Black, Ltd.). Plate v is reproduced with permission from Byam's and Archibald's *Practice of Medicine in the Tropics* (Oxford University Press), and Plate vii from the Medical Research Council Special Report No. 19. Sir Girling Ball and Dr. Geoffrey Evans have allowed me to make use of the illustration of renal carbuncle in Plate vi. Dr. S. H. Daukes kindly supplied me with the illustrations of bilharzia ova (Fig. 70), and some of the illustrations of bacteria and spirochaetes have been lent by the publishers of Muir and Ritchie's *Manual of Bacteriology*. The illustration of the *Xenopus* pregnancy test (Fig. 75) is from a paper by Dr. Elkan and the picture of *Trichomonas vaginalis* (Fig. 69) from an article by Dr. Assinder, both published in the *British Medical Journal*. Mr. Ogier Ward has kindly allowed me to reproduce the illustration of calculi composed of bacteria (Fig. 92) from the *British Journal of Surgery*. Illustrations of scientific apparatus have been lent by Messrs. Baird & Tatlock and Messrs. Gallenkamp.

PERSONAL

I am under a special obligation to Miss S. H. Douglas, Mr. G. H. Shepherd, and Mr. J. McDonnell. Miss Douglas has carried out a long series of comparisons of blood urea and urine urea estimations with me, using all the methods described in this book, and the views expressed as to the relative advantages of different methods are largely based on her experience. She has also read the manuscript and checked the references. I am grateful to Mr. Shepherd for his willingness to take down notes and to typewrite at any spare moment of the day. Most of all I should like to thank my laboratory technician, Mr. J. McDonnell, for his unfailing patience in preparing reagents and apparatus for new tests and for his loyal co-operation through all the years we have been associated together.

CONTENTS

PREFACE	v
ACKNOWLEDGEMENTS	vii
Books. Illustrations. Personal.	
CHAPTER I. PHYSICAL CHARACTERS	1
Historical introduction. Collection of specimens. Inspection of urine. Volume. Specific gravity. Osmotic pressure. Surface tension. Reaction.	
CHAPTER II. CHEMICAL CONSTITUENTS	28
Average composition of urine— <i>Organic constituents</i> —urea, uric acid and urates, xanthine bases, creatinine and creatine, amino-acids. <i>Inorganic constituents</i> —Sodium and potassium, ammonia, calcium, magnesium, iron, chlorides, sulphates and sulphur, phosphates, nitrates.	
CHAPTER III. ALTERATIONS IN COLOUR	88
Normal pigments. Adventitious pigments. Blood. Haemoglobinuria. Spectroscopic examination of urine. Bile-pigments. Urobilin. Porphyrinuria. Melanin pigment. Alkaptonuria.	
CHAPTER IV. ALBUMINURIA	117
Clinical varieties of albuminuria—1. Functional. 2. Organic. 3. Albuminuria in pregnancy. 4. Accidental and extra-renal albuminuria. 5. Bence Jones albuminuria. Varieties of urinary protein. Detection of albuminuria. Separation and identification of urinary protein. Estimation of urinary protein.	
CHAPTER V. SUGAR AND OTHER REDUCING SUBSTANCES: KETOSIS	130
Normal glycosuria. Alimentary glycosuria. Nervous glycosuria. Renal glycosuria. Glycosuria in diabetes. Tests for the detection of sugar. Tests for distinguishing glucose from other reducing substances. Quantitative estimation of glucose. Fructose. Lactose. Galactose. Pentose. Glycuronates. Salicylates. Alkaptonuria. Uric acid. Ketosis.	
CHAPTER VI. MICROSCOPIC EXAMINATION FOR CELLS AND CASTS	154
Methods of examination of uncentrifuged and centrifuged urine. Extraneous matter in urinary deposit. Epithelium. Spermatozoa. Pus. Red blood corpuscles. Casts. Cylindroids. Urinary crystals and amorphous deposits. Uric acid, urates, calcium oxalate, phosphates, calcium carbonate, cystine, leucin and tyrosin, calcium sulphate, xanthine, hippuric acid, bilirubin, haematin, cholesterin, indigo, melanin. Preservation of urinary deposits. Microscopic examination of stained films from the centrifuged deposit.	
CHAPTER VII. BACTERIA AND OTHER PARASITES	197
Normal bacterial flora. Infections due to staphylococci, streptococci, pneumococci, gonococci, <i>B. coli</i> , <i>B. proteus</i> , <i>B. pyocyaneus</i> , typhoid, and paratyphoid bacilli. Tuberculosis, infections with Ducrey's bacillus, anaerobic infections, actinomycosis, mycotic infections, syphilis, tetanus, fever, Weil's disease, Trichomonas infections, schistosomiasis, malaria, hydatid disease.	

CHAPTER VIII. HORMONE TESTS	283
Pregnancy diagnosis by tests for gonadotropic hormones. Complications of pregnancy. Application of gonadotropic hormone tests to conditions other than pregnancy. Choice of pregnancy diagnosis tests—Asheim-Zondek test, Friedman test, Xenopus test. Oestrogenic hormones. Progesterin or corpus luteum hormone. Androgenic hormones.	
CHAPTER IX. EXCRETION OF VITAMINS AND ENZYMES	302
Vitamin C deficiency. Vitamin B deficiency. Excretion of diastase enzyme.	
CHAPTER X. EXCRETION OF DRUGS AND POISONS	311
Alcohol, arsenic, antipyrine, arsenobenzol, atropin, barbiturates, bismuth, boric acid, bromides, chloral hydrate, chloroform, copaiba, copper, formalin, iodides, lead, mercury, morphine, phenol, phenacetin, phenolphthalein, phenolsulphonphthalein, plasmoquine, quinine, salicylates, sulphanilamide, urotropine, uroselectan.	
CHAPTER XI. URINARY CALCULI	336
History. Factors in the causation of urinary calculi. Formation of urinary calculi. Varieties of urinary calculi—uric acid, calcium oxalate, phosphatic calculi, calcium carbonate, cystine, xanthine, mixed calculi, foreign body calculi. Lesions caused by calculi. Urine analysis in calculous disease. Chemical analysis of urinary calculi.	
CHAPTER XII. RENAL FUNCTION TESTS	361
The elimination of waste products. Regulation of the composition of the blood. General considerations with regard to renal function tests. 1. <i>Urine tests</i> —specific gravity test, urea concentration test, chloride concentration test, dye tests for renal function. 2. <i>Blood tests</i> —blood urea, estimation of alkali reserve, blood cholesterol, creatinine, calcium, and phosphates. 3. <i>Combined blood and urine tests</i> —Urea clearance tests. Choice of renal function tests.	
INDEX	385

COLOUR PLATES

I. Villous papilloma of renal pelvis	.	.	<i>to face page</i>	92
II. Cystoscopic appearances of diseases of bladder			„ „	94
III. Blackwater fever urine	.	.	„ „	96
IV. Blood spectra	.	.	„ „	102
V. Benedict's test for sugar in urine	.	.	„ „	134
VI. Renal carbuncle	.	.	„ „	200
VII. Pus cells, gonococci, and other bacteria from urethra	.	.	„ „	218
VIII. Tubercle bacilli and pus cells in urine deposit	.		„ „	254
Smegma bacilli and pus cells in urine deposit				
Film of pus containing staphylococci and streptococci				
Gonorrhoeal pus				
IX. Negative Ascheim-Zondek test on mouse	.		„ „	286
X. Negative Ascheim-Zondek test on mouse	.		„ „	288
XI. Positive Ascheim-Zondek test on mouse	.		„ „	290
XII. Friedman test in rabbit	.	.	„ „	292

ILLUSTRATIONS

'The Urologist'. Painting by A. van Ostade, 1665	<i>Frontispiece</i>
1. Physician examining urine brought by patients, 15th century.	<i>Page 3</i>
2. Physician examining urine brought by patients, 16th century manuscript	5
3. A bedside diagnosis of urine.	7
4. Urinometer	17
5. Specific gravity bottle	17
6. Table showing acid-base balance of foods	22
7. Lovibond comparator with disks	26
8. Ureometer	34
9. Maclean's urea apparatus	35
10. Van Slyke volumetric gas apparatus	35
11. Apparatus for estimation of urea by urease	42
12. Conway unit	44
13. Van Slyke manometric gas apparatus	47
14. Apparatus for estimation of ammonia	70
15. Renal purpura	92
16. Carcinoma (hypernephroma) of kidney	93
17. Carcinoma of bladder	94
18. Pocket spectroscope.	99
19. Esbach's albuminometer	125
20. Ruling of Fuchs-Rosenthal slide	155
21. Extraneous matter from urinary deposit	157
22. Extraneous matter from urinary deposit	158
23. Extraneous matter from urinary deposit	159
24. Renal epithelium	160
25. Vesical epithelium	161
26. Vaginal epithelium	161
27. Spermatozoa, leucocytes, and amorphous granules	163
28. Hyaline and granular casts	168
29. Colloid casts and fat globules	168
30. Hyaline, blood, and leucocyte casts	169
31. Cylindroids	170
32. Uric acid crystals—prism and whetstone shapes	174
33. Uric acid crystals—hour-glass and barrel-shape forms	174
34. Amorphous urates	176
35. Ammonium urate	176
36. Calcium oxalate. Envelope crystals	178
37. Calcium oxalate. Dumb-bell crystals	178

38. Amorphous phosphates	180
39. Triple phosphate crystals	180
40. Ammonium magnesium phosphate	181
41. Stellar phosphate crystals	181
42. Flakes of calcium phosphate from pellicle on surface of urine .	182
43. Magnesium phosphate crystals	182
44. Calcium carbonate and ammonium urate	183
45. Cystine crystals, leucocytes, and red blood cells	185
46. Leucin and tyrosin	187
47. Calcium sulphate crystals	187
47A. Hippuric acid crystals	189
48. Bilirubin crystals in degenerated cells	189
49. Bilirubin crystals in fragment of bladder tumour	191
50. Cholesterin crystals	191
51. Staphylococcal epididymitis	201
52. Staphylococcal epididymo-orchitis	202
53. Staphylococci	204
54. Streptococci	207
55. Haematogenous <i>B. coli</i> infection of kidney	228
56. <i>B. coli</i> cystitis following post-operative retention of urine .	235
57. <i>B. coli</i> from urine culture	237
58. Tuberculosis of kidney	246
59. Tuberculous kidney with double renal pelvis and double ureter	247
60. Renal tuberculosis	248
61. Tuberculosis of testicle	250
62. Culture of tubercle bacilli from urine	257
63. Ducrey's bacillus in pus from soft chancre	259
64. <i>Spirochaeta pallida</i> under dark-ground illumination	265
65. <i>Sp. pallida</i>	266
66. <i>Sp. refringens</i>	266
67. <i>Sp. gracilis</i>	266
68. <i>Leptospira icterohaemorrhagiae</i>	272
69. <i>Trichomonas vaginalis</i>	274
70. <i>Schistosoma haematobium</i> ova in urinary deposit	275
71. Hydatid cyst of kidney	279
72. Scolices of <i>Taenia echinococcus</i>	280
73. Hydatid hooklets	280
74. Diagnosis of pregnancy from urine inspection	285
75. <i>Xenopus laevis</i> in test jar	294
75A. Diagram	315
76. Hydronephrosis of kidney (pelvic type) with secondary oxalate calculus	337
77. Calculous disease of kidney	340
78. Uric acid calculus	341

ILLUSTRATIONS

xv

79. Crystalline oxalate calculus	342
80. Spiked oxalate calculus	342
81. Two spiked oxalate calculi	343
82. Branched phosphatic calculus	343
83. Pyramidal articulated phosphatic calculi from bladder	344
84. Two phosphatic vesical calculi	345
85. Vesical calculus composed of a mixture of calcium carbonate and phosphate	346
86. Cystine calculi	347
87. Vesical calculus composed of phosphates surrounding calcium oxalate	348
88. Vesical calculus with laminated nucleus of uric acid	348
89. Vesical calculus surrounding wedge of slippery elm	349
90. Vesical calculus surrounding candle wax	349
91. Vesical calculus surrounding head of safety-pin	350
92. Urinary calculi composed of bacteria	350
93. Calculous disease of kidney	354
94. Carcinoma secondary to renal calculus	355
95. Calculi in ureter	356
96. Line chart for calculating standard blood-urea clearance	378
97. Line chart for calculating maximum blood-urea clearance	379

I

GENERAL CHARACTERS

HISTORICAL INTRODUCTION

At the beginning of a book which sets out to show what may be learnt from the examination of the urine it is of interest to recall what was the attitude of physicians in the past. To-day it is agreed that the examination of the urine is an indispensable part of any complete medical survey in health or sickness, but in former times it was not always considered worth while to bestow on the urine bottle the careful scrutiny depicted in van Ostade's famous picture 'The Urologist' (see frontispiece).

The physicians of the Ancient World did not completely neglect urine examination, and there are records to show that Babylonian physicians as early as 4000 B.C. made observations concerning colour and consistency of urine. The Greeks also recognized that the examination of urine might be a valuable aid to diagnosis. Hippocrates (460-377 B.C.) in his *Prognostics* and *Aphorisms* wrote the first organized treatise on diseases of the urinary tract which has been preserved. He drew attention to the importance of the colour, odour, and sediment of urine. He observed the cloud of mucus which may settle from urine on standing, and though the chemical composition of urine was unknown to him he noted that the volume of urine excreted should be in proportion to the fluid intake. Galen (A.D. 130-200) based his teaching on the views of Hippocrates and Aristotle and in his great theoretical system of medicine made no fresh contribution to uroscopy. The views of Galen with regard to the cause of disease and the action of remedies were for thirteen centuries regarded as an infallible creed and their authority began to wane only when the advances of chemical science began to make their deficiencies apparent.

Arabian physicians contributed little towards the subject of urology and were content to accept the conclusions of the Greeks. The works of Avicenna (A.D. 980-1037) comment on the difference in character of urine passed in the morning and at night, and on the influence of age, food, and drugs upon the colour. In the eleventh century Ismail of Jurjani gave a full account of views on urology in Persia and discussed the significance of changes in colour, consistency, transparency, quantity, sediments, odour, and froth.

The physicians of these times were restricted to the evidence afforded by its colour, odour, and quantity, for the detection of changes in the composition of the urine. This evidence was apt to be fallacious because wide difference of composition may produce similar appearances, and differences of appearance do not always denote significant changes of composition. Moreover, accurate medical diagnosis was prevented by the relatively vague conceptions of the bodily functions. For instance, a great many diseased states were ascribed to defective digestive processes, the conception of digestion including not only the assimilation but also the utilization of food. It was common to ascribe abnormalities of the urine to defective digestion and to consider changes in the colour, translucence, or opacity of the urine as evidence of defective digestion. This view is reflected in Avicenna's *Canon of Medicine*, written in the early years of the eleventh century (English translation by O. C. Gruner 1930).

In some medieval schools of medicine urine examination seems to have attained an importance out of proportion to its value. The school of Salerno favoured the view that uroscopy was superior to all other diagnostic methods. The accompanying pictures from fifteenth- and sixteenth-century manuscripts show physicians examining urine brought by patients (Fig. 1, and Fig. 2). Magicians also made a great pretence of examining the urine and claimed to be able to foretell the sex of a child by the examination of the urine of a pregnant woman. In England a book was written by Dr. Fletcher in 1541 entitled, *The Differences, Causes, and Judgements of Urine*, in which the value of urine analysis was certainly not underrated as the following sentence shows: 'Amongst all signs of sickness and health whereby the skilful physician is led into the knowledge of the state of the body two are of most general and certain signification which are taken from the pulse and urine, without which all the knowledge of physicke besides is obscure, doubtful, and uncertain.'

The seventeenth-century woodcut entitled, 'A bedside diagnosis of urine' depicts the physician feeling the patient's pulse with one hand and pointing with the other to the vessel containing urine, which one of the students is holding (Fig. 3).

The methods of examination of the urine advocated by physicians prior to the seventeenth century consisted only in making observations on the colour, odour, sediment, and sometimes even the taste. Chemical tests were altogether unknown. The deductions drawn from inspection of the urine were often