of vitamin B₁₂. Moreover, if some vitamin B₁₂ is destroyed in the gastro-intestinal tract with the liberation of free ions of cobalt, it is possible that some of the latter might be absorbed as such.

Some of our patients with pernicious anaemia seem to have absorbed a fraction of the radioactive vitamin B₁₂, and this may indicate, as Goldhamer (1936) first suggested, that some patients with pernicious anaemia secrete traces of intrinsic factor. The significance of our figures depends chiefly on the accuracy of the stool collections. Experience in this department with radioactive iron (Fe⁵⁹), which was given by mouth and recovered from the red blood corpuscles and from the faeces, supports the view that incompleteness of stool collection is unlikely to account for all the radioactivity which was not recovered.

It appears that this technique offers a simple measure of intrinsic factor activity in the patient, and that it may also be used to assay preparations for their content of intrinsic factor. It has many advantages over the clinical assay, which requires patients with pernicious anaemia in relapse, but it has the disadvantage that it is an indirect test which depends on the absorptive power of the gastro-intestinal tract at the time at which the test dose is given. Preliminary evidence of the effect of infections suggests that the absorption of vitamin B₁₂ is easily interfered with in the normal subject. Further investigation of this point is in progress.

Summary

The absorption of vitamin B₁₂ has been assessed by measuring the radioactivity in the faeces after an oral dose of 0.5 µg. of vitamin B₁₂ labelled with Co⁶⁰.

In 10 patients with normal haematological findings a mean of 31.0% (standard deviation, 6.9%) of the radioactivity in the test dose was recovered from the faeces. In 13 patients with pernicious anaemia a mean of 88.7% (standard deviation, 6.8%) was recovered.

Sources of intrinsic factor given with radioactive vitamin B₁₂ to patients with pernicious anaemia reduced greatly the percentage of the test dose recovered.

It is a pleasure to express our thanks to Professor L. J. Witts for allowing us to study patients under his care and for his constant help and encouragement; Dr. L. Z. Cosin for allowing us to study patients under his care in the Cowley Road Hospital; Dr. Lester Smith, of Glaxo, Ltd., for supplies of radioactive vitamin B₁₂; Dr. Arnold Welch for the "fraction B"; Dr. W. B. Taylor for the gastric mucosal extracts; Mr. Ray Oliver for advice and assistance in the radioactivity measurements; Dr. John Badenoch for help and advice; and Miss Barbara Hunt for technical assistance. This work was in part supported by a grant to Professor L. J. Witts from the Medical Research Council.

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RESEARCHES IN AETIOLOGY OF NON-SPECIFIC URETHRITIS*

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General Observations

Non-specific urethritis (N.S.U.) is one of the most perplexing conditions encountered in the British venereal diseases clinic to-day. When complicated by Reiter's syndrome its disabling powers are considerable. In the clinics of England and Wales in 1951 there were 10,794 cases of non-specific urethritis, as compared with 14,975 male cases of gonorrhoea.

Although the condition is usually acquired venereally in the male, it is possible that the female may on occasion be infected non-venereally, which would explain the slight non-venereal bias. Thus in 100 cases of gonorrhoea the last sexual risk had been a casual exposure in 60%, whereas in 100 cases of non-specific urethritis the comparable figure was only 40%. Also, of 640 subjects of non-specific urethritis studied 35.3% were married, whereas of 603 male subjects of gonorrhoea only 25% were married. Persons suffering from non-specific urethritis were of slightly older age groups than those with gonorrhoea, and more likely to be in a "white collar" occupation—both observations perhaps being reflections of the marital status.

Some observers (for example, Coutts of Chile) have suggested that the practice of oral and/or anal coitus may frequently be responsible for the transmission of non-specific urethritis. This would not appear to be the case in Great Britain, for such practices were admitted by only 6% of 50 patients with non-specific urethritis so questioned, as against 9% of 100 other patients attending the venereal diseases clinic during the same period.

The incubation period of non-specific urethritis is often longer than that of gonorrhoea. Of two groups, each of 150 cases, 52% of patients with non-specific urethritis had incubation periods of over seven days, as compared with only 32% (in itself a high figure) in the case of patients with gonorrhoea.

Ignoring established rare causes, the following have variously been regarded as possibly responsible for the bulk of cases: (1) bacteria; (2) pleuropneumonia-like organisms; (3) trichomonads; (4) spirochaetes; and (5) a virus. This study was limited mainly to a consideration of bacterial and viral causes.

Bacterial Urethritis

It has for some time been fashionable to divide non-specific urethritis into bacterial and abacterial urethritis, depending on whether bacteria are seen in the urethral smears. Some 301 urethral cultures were made at King Edward VII Hospital, Windsor (pathologist, E. Sayle), on consecutive patients with non-specific urethritis, before and after treatment with the orally administered antibiotics, and on controls. As a result it is considered that "bacterial urethritis" is not a common entity and that the bacteria found are usually commensals (Table I).

*Being a summary of the report presented to the British Medical Association at the conclusion of the term of office as Insole Research Scholar.

The World Health Organization has recently issued the report of the discussion at the third European Seminar for Sanitary Engineers which was held in London from October 27 to November 1, 1952. The book is entitled *Design and Operation of Septic Tanks*, and among topics discussed are the treatment of small sewage plants, the design of small sewage works, and comparative studies of septic tanks. It is published in the Monograph Series (No. 18), price 7s. 6d., and is obtainable through H.M. Stationery Office, London, or direct from the Sales Section, Palais des Nations, Geneva.

TABLE I.—*Urethral Cultures*

Organisms	Controls (105 Cultures)		Non-specific Urethritis Cases			
			Before Treatment (81 Cultures)		After Treatment (69 Cultures)	
	No.	%	No.	%	No.	%
<i>S. albus</i> ..	72	68.6	66	81.4	55	79.7
<i>Bact. coli</i> ..	22	21.0	16	19.7	9	13.0
Diphtheroids ..	19	18.1	26	32.1	27	39.1
Saprophytes ..	8	7.6	4	4.9	9	13.0
<i>S. aureus</i> ..	4	3.8	1	1.2	—	—
Monilia ..	3	2.8	1	1.2	1	1.4
<i>B. proteus</i> ..	—	—	—	—	1	1.4
Enterococci ..	—	—	2	2.5	—	—
Streptococci ..	—	—	1	1.2	2	2.9
Sterile ..	2	1.9	1	1.2	3	4.3

Viral Urethritis

Attempts were made, by different means, to ascertain whether there was any cross-reaction in the skin or blood of patients with non-specific urethritis to antigens of various viruses of the psittacosis/lymphogranuloma venereum/trachoma group. A study was also made of Giemsa-stained urethral scrapings, and animal and egg studies were undertaken.

Skin Tests

In all, some 234 tests were performed—175 for lymphogranuloma venereum, 28 for psittacosis, and 31 for cat-scratch fever. Omitting the later tests, the results of the first tests are shown in Table II.

TABLE II.—*Skin Tests*

	Tested	Negative	Doubtful	Positive	% Positive
Lymphogranuloma venereum (1):					
N.S.U. cases ..	84	63	10	11	13.1
Controls ..	62	53	6	3	4.8
Psittacosis (2):					
N.S.U. cases ..	17	15	2	—	—
Controls ..	11	11	—	—	—
Cat-scratch fever (3):					
N.S.U. cases ..	16	12	2	2	12.5
Controls ..	12	12	—	—	—

Antigens kindly supplied by: (1) E. R. Squibb and Sons, International Corporation, New York ("lygranum") and Virus Reference Laboratory, Colindale; (2) Virus Reference Laboratory, Colindale (courtesy of Dr. A. D. Macrae); and (3) Professor P. Mollaret, Hôpital St. Bernhard, Paris, and Virus Reference Laboratory, Colindale (courtesy of Dr. H. J. Bensted).

Thus the skin tests for psittacosis gave negative results. In the series tested, however, some positive readings were obtained with cat-scratch antigen in patients with non-specific urethritis, but not in controls. Also a somewhat higher incidence of positive readings to the skin test for lymphogranuloma venereum was noted in patients with non-specific urethritis than in controls. This aspect of the problem, therefore, would merit further attention.

Serum Tests

A total of 412 complement-fixation tests for lymphogranuloma venereum (L.G.V.), on sera from 275 persons, were made by Dr. A. D. Macrae, of the Virus Reference Laboratory, Colindale. A further 323 complement-fixation tests for enzootic abortion in ewes (E.A.E.), on sera from 250 persons, were performed by Dr. J. T. Stamp, of the Edinburgh and East Scotland College of Agriculture, Edinburgh. The latter veterinary disease is considered to be caused by a virus of the lymphogranuloma venereum/psittacosis/trachoma group.

The results of these tests are being recorded fully elsewhere, but are summarized in Table III.

In view of these findings and the results of serial tests performed on some cases, it was not thought that there was any relationship between the results of either test with non-

TABLE III.—*Serum Tests (First Tests Only)*

	Tested	Negative	Doubtful	Positive	% Positive
Lymphogranuloma venereum:					
N.S.U. cases ..	141	122	13	6	4.3
Controls ..	132	120	9	3	2.3
Enzootic abortion in ewes:					
N.S.U. cases ..	123	113	6	4	3.2
Controls ..	127	118	4	5	3.9

TABLE IV.—*Comparison of L.G.V. and E.A.E. Tests*

Titres	1/10 or Below	1/20	1/4 or Over	Total E.A.E. Tests
1/4 or below ..	218	15	—	233
1/8 ..	1	10	8	19
1/16 or over ..	1	3	7	11
Total L.G.V. tests	220	28	15	263

specific urethritis sera. There was, however, close agreement between the results of the two tests on 263 parallel specimens of sera (Table IV).

Giemsa-stained Urethral Scrapings

As the so-called virus of non-specific urethritis has not yet been successfully passaged in animals or eggs, the evidence for or against its existence has had to depend upon the presence or absence of inclusion bodies in Giemsa-stained urethral scrapings.

Some 1,463 Giemsa-stained urethral scrapings, taken from patients with non-specific urethritis, their female consorts, or from controls, were examined at the laboratories of the School of Pharmacy, London, under the supervision of Dr. G. M. Findlay until his death in March, 1952, his technician being Miss E. M. Howard. Through the courtesy of Professor G. A. H. Buttle, Miss Howard's services were made available after that date so that the work could be completed.

In order to determine the significance, or otherwise, of the various bodies seen, in due course the findings were classified as blue or red "colonies" (being granular bodies varying from 1-6 μ in diameter) and blue or red granules. The incidence of these various bodies in urethral scrapings was compared in male patients with non-specific urethritis before treatment, after successful treatment with one of the orally administered antibiotics, and after unsuccessful treatment (Table V).

TABLE V.—*Incidence of Various Bodies in Giemsa-stained Urethral Scrapings from Male Patients with Non-specific Urethritis*

	Before Treatment (206 Cases)		After Successful Treatment (182 Scrapings)		After Unsuccessful Treatment (103 Scrapings)	
	No.	%	No.	%	No.	%
Blue colonies ..	71	34.5	18	9.9	23	22.3
Red ..	17	8.3	15	8.2	6	5.8
Blue granules ..	36	17.5	15	8.2	17	16.5
Red ..	38	18.4	42	23.1	24	23.3
Nil ..	78	37.9	115	63.2	50	48.5

The fact that the incidence of red colonies and red granules was unaffected by treatment, successful or unsuccessful, appeared at once to exclude these as possessing no significance. On the other hand, the incidence of both the blue colonies and blue granules fell markedly after successful treatment with the orally administered antibiotics, but remained high when the treatment was unsuccessful. Moreover, at the time of actual re-treatment given to 42 cases the incidence of blue colonies was 30.9% and of blue granules 23.8%.

A group of 80 controls was also studied. These consisted of 12 specimens of non-urethral pus, urethral scrapings from 18 normal males, from 13 patients attending the clinic on account of fear of venereal disease, from 17 patients with syphilis, and from 20 patients with non-syphilitic genital lesions (for example, warts, genital herpes, etc.). In only two (2.5%) were blue colonies, and in only one (1.25%) were blue granules discovered. Up to this point, therefore, the material showed promise so far as correlation between the blue colonies and blue granules and the activity of non-specific urethritis was concerned.

However, it was appreciated that the control scrapings so far studied were in the main taken from dry urethrae, whereas those from non-specific urethritis cases were from wet urethrae. A further control series, this time of 108 cases of gonorrhoea treated at varying periods of time previously with penicillin, was therefore taken. In these, 15 (13.9%) showed blue granules and, as this incidence was almost as high as in the untreated non-specific urethritis cases, these, too, had to be discounted. The incidence of blue colonies, however, was 14.8%, still very substantially below the 34.5% found in the patients with untreated non-specific urethritis.

But when the gonorrhoea cases were arranged according to the length of time which had elapsed from the giving of the penicillin until the taking of the scraping it was noted that at one to three days after injection the incidence of blue colonies was 21.7%. This figure was not far removed from the 27.6% incidence of these bodies two to seven days after the beginning of the treatment of non-specific urethritis with one of the orally administered antibiotics (Table VI).

TABLE VI.—Incidence of Blue Colonies in Gonorrhoea Cases

Time Since Treatment	Cases	Blue Colonies	%
Untreated	23	2	8.7
1-3 days	46	10	21.7
4-7	24	4	16.6
Over 7 days	15	—	—
Total	108	16	14.8

It would seem that the blue colonies were but products of inflammation, since in both gonorrhoea and non-specific urethritis their incidence decreased as the urethra became drier. That they were seen relatively seldom in the discharges of untreated gonorrhoea was probably connected with the essentially high leucocytic and low epithelial count of the specimens at this stage. It was therefore regretfully concluded that none of the bodies studied in this investigation were involved in the causation of non-specific urethritis.

[A consideration of smears from female cases is omitted from this summary and will appear in the paper being prepared with Miss E. M. Howard.]

Animal Experiments

Attempts to transmit the virus of non-specific urethritis into baboons, guinea-pigs, mice, and eggs were made in the laboratories of the School of Pharmacy.

A sustained attempt to pass the virus into the lungs of mice was a failure. The haemorrhagic lesions which were seen in a number of the 1,735 mice used in these experiments proved not to be related to the disease. Limited attempts at intracerebral inoculation into mice, subcutaneous inoculation into guinea-pigs, and conjunctival instillation, urethral inoculations, and inoculation into the knee-joints of baboons, likewise failed to give any clear-cut evidence of transmission. Attempts to transmit the virus in the chorio-allantoic membranes of eggs also failed: these latter experiments, which involved about 100 eggs, were confused by the presence of other bodies which bore a resemblance to those seen in the urethral scrapings of patients suffering from non-specific urethritis.

Summary and Conclusions

When compared with gonorrhoea, non-specific urethritis was apparently more frequently contracted from regular consorts, indicating a possible non-venereal bias in its aetiology.

In the urethritis group more patients were married, they tended to be older in age, and they were more likely to have achieved "white-collar" status than those of the gonorrhoea group.

There was no evidence to suggest that the practice of buccal or anal coitus was commonly responsible for the transmission of non-specific urethritis.

The disease tended to have a longer incubation period than gonorrhoea.

A study of 301 urethral cultures taken from patients with non-specific urethritis before and after treatment, and from controls, suggested that the so-called "bacterial urethritis" was uncommon.

The results of 412 complement-fixation tests for lymphogranuloma venereum and 323 complement-fixation tests for enzootic abortion in ewes showed nothing distinctive between sera from patients with non-specific urethritis and from controls.

A study of 234 skin tests for lymphogranuloma venereum, psittacosis, and cat-scratch fever, on the other hand, showed more positive readings in non-specific urethritis cases than in controls, and this aspect of the problem therefore merits further attention.

From the examination of 1,463 Giemsa-stained urethral scrapings it was considered that the bodies seen were products of inflammation and unconnected with the virus of non-specific urethritis. Thus, if inclusion bodies sometimes seen in these scrapings are responsible for the isolated case, the causative organism cannot be seen in the majority.

Attempts to pass the virus into the lungs of mice (1,735 mice being used in these experiments), mouse-brains, guinea-pigs, and into the conjunctiva, knee-joint, and urethra of baboons were also unsuccessful.

The "virus" of non-specific urethritis has not been isolated, and remains to be discovered.

The World Health Organization has recently published in pamphlet form a survey of modern legislation relating to nursing. The aim of the survey, it is stated, was to examine the extent to which legislation has established a system of control over the organization and practice of nursing and to indicate the new problems caused by the introduction of the auxiliary and specialized nurse. The survey reviews the laws of 22 countries. It notes the dichotomy of nursing laws: on the one hand, permissive laws which do not restrict the practice of nursing, but which give official recognition in the form of legislation to trained nurses, and thereby differentiate the qualified from the unqualified; and, on the other hand, mandatory laws which safeguard the health of the community by prohibiting the unqualified from practising, and which consequently need to define nursing. There is a general lack of precision in the definition of nursing functions, and the survey remarks that nursing, unlike midwifery and dentistry, defies precise legal definition, and consequently the professional nurse is not always provided with sufficient protection in the exercise of her calling. In recent years the shortage of nurses has become acute all over the world, and is mirrored to-day in the increasing number of laws being enacted in relation to auxiliary nursing staff and male nurses.