TABLE III—Summarized Details of Patients who stated that they did Not want to Disturb their Doctor

	Patient No.						
	1	2	3	4	5	6	7
Age in years (mean 55.9 years)	60	57	65	54	33	61	61
Sex	M.	F.	F.	M.	M.	F.	M.
Social class	II	III	II	III	III	II	III
Years with G.P.	15+	10-15	1-2	15+	13	15+	1
Do you like your G.P. ?	"Yes"	"Not very much"	"Very nice"	"Yes"	"All right"	"Very well"	"Quite nice"
Do you have confidence in your G.P. ?	"Yes"	"Not much"	"O.K."	"Yes"	"Yes"	"Every confidence"	"Every confidence"
Past history	M.I. and angina	None	M.I.	None	None	None	M.I. and angina
Time of onset	21.00 hours	16.30 hours	02.30 hours	18.00 hours	04.30 hours	02.00 hours	08.00 hours
Delay before calling doctor	3 hours	1 hour	5 hours	2½ hours	4½ hours	2 hours	24 hours
(mean 6 hours, median 3 hours)							
Severity of symptoms	Moderate	Moderate	Mild	Moderate	Mild	Severe	Moderate

The difference between the number of patients delaying for longer than 1 hour in this group compared with all the other patients who did not state that they had not wanted to disturb their doctor is statistically significant at $P < 0.05$ ($\chi^2 = 3.93$, D.F. = 1). In other details of age, sex, social class, past history, and severity of symptoms there is no statistically significant difference.

M.I. = Myocardial infarction.

night before calling their doctor it can be postulated that most patients were inhibited from calling their doctor, and this was later volunteered by some patients.

Education of patients to overcome this psychological barrier could be directed along two lines. One would be to educate people about the symptoms of myocardial infarction. It is unlikely that this could be done without creating cardiac neurosis but it might be worth while to attempt to educate "high-risk" patients—for example, those with angina—and attempt to evaluate the benefits of earlier treatment of a subsequent myocardial infarction against the possible harmful effects of the education.

The second line of education would be to correct the impression that the general practitioner works such long hours that he should be disturbed only after severe symptoms of a serious illness have been present for some hours. The average length of time spent by British general practitioners in clinical work is around 40 hours a week.^{16 17} There is the danger, of course, that if patients were encouraged to call the doctor sooner, as has been suggested,⁷ then general practitioners and hospital coronary care units might be overwhelmed by patients who have not suffered a myocardial infarction to the detriment of those who have.

One hopes that there may be a middle course, where doctors are not overworked nor patients inhibited from seeking medical attention when necessary, and individual doctors might wish to try to prevent this inhibition in their patients.

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A New Look at Infectious Diseases

Leptospirosis

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Numerous combinations of symptoms and signs can occur during infections with pathogenic strains of *Leptospira*. The diagnosis of leptospirosis on clinical grounds is apt to be unreliable;

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thus in the United Kingdom at present jaundice occurs in only one-half of all diagnosed cases. However, reliable serological tests are now available which can be carried out in any general-duty laboratory. Suitable treatment—antibiotics and supportive measures—have reduced the mortality from severe infections; in mild infections the patient will recover without special treatment. The epidemiology of leptospiral infections is essentially simple, but many animals other than rats and dogs can act as reservoir hosts. The notion that leptospirosis is a matter only of Weil's "disease" and rats is no longer tenable. The

situation in the United Kingdom has not altered during the last three years or so.¹

Course

The clinical manifestations, the treatment, the epidemiology, and the requirements for laboratory diagnosis—all these aspects of leptospirosis are best understood by considering the course of infection (see fig. 1). The course is basically composed of two overlapping phases: leptospiraemia followed by increasing concentrations of antibodies and leptospiruria.

FIG. 1—Leptospirosis: phases and relevant diagnostic procedures. (Reproduced with slight modifications from Turner, L. H., *Trans. roy. Soc. trop. Med. Hyg.*, 1967, 61, 842.

Leptospire quickly penetrate a surface epithelium and reach the blood stream. There is no local lesion at the site of entry and no obvious regional lymphadenitis. After an incubation period of 7 to 12 days (reported range, 2 to 20 days or more) the patient develops a fever. The leptospire multiplies in the blood stream (a septicaemia); they can be carried to, and may affect, any tissue or organ. The ultimate distribution and concentration of leptospire must therefore account for the various combinations of symptoms and signs which may be evoked. The lesions produced are focal and microscopic; but the number of such lesions in a particular organ or tissue presumably influences the clinical manifestations.

The leptospire are removed from the blood and tissues by non-specific defence mechanisms helped by increasing concentrations of specific antibodies. In the very severely ill patients the titres of agglutinins tend to be low and the pattern of cross-reactions too indefinite to indicate even the serogroup to which the infecting strain belongs. Hence the course of an infection may be adversely affected by some pre-existing defect in such patients, or by some oddity in the antigenic composition of such strains of *Leptospira*. (We do not clearly understand the factors which account for virulence and pathogenicity of leptospire.)

PERSISTENCE IN KIDNEYS

Leptospire tend to persist in the convoluted tubules in the renal cortex where, it seems, they are less affected by specific antibodies. Leptospire may settle and multiply—even forming

colonies—on the epithelium of the tubules. They tend to be shed into the urinary filtrate and are then excreted, thus contaminating the environment. This urinary carrier/shedder state may be transient (incidental hosts) or it may persist, even for the remainder of the host's life (maintenance or reservoir hosts) when a particular strain of *Leptospira* reaches the tubules of a host species in which conditions favour its survival.

In untreated infections in man the urinary phase seldom persists for longer than a month. This phase is, however, of paramount importance in the enzootiology and epidemiology of leptospirosis. Without urinary excretors there could be no leptospirosis: the chain of infection could not be maintained in nature by transmission during the phase of leptospiraemia—by means of agents such as blood-sucking arthropods.

Natural History

This heading embraces topics which are conventionally treated under "epidemiology," it is preferred because leptospiral infections in nature are essentially enzootic and only occasionally epizootic. Human infections are usually sporadic and only rarely occur in outbreaks. The subject is conveniently considered under three subheadings: survival of leptospire outside the bodies of their hosts; modes of transmission; and the vertebrate hosts.

SURVIVAL OF LEPTOSPIRES

Environmental conditions which favour the survival of pathogenic leptospire are moisture, warmth, and pH values of soil and surface waters around neutrality. The case incidence in temperate climates tends to rise during the summer and autumn. Adverse factors include salinity and chemical pollution—for example, hypochlorites and detergents—as well as desiccation and pH values outside the range of about 6.2-8.0 units.

MODES OF TRANSMISSION

Transmission occurs by contact with infected blood, tissues, organs (especially the kidney), or urine. Such contacts are often indirect, occasionally direct.

Indirect contact with an environment which has been contaminated with urine from a carrier/shedder host is the commonest mode overall. Such environments include soil, mud, fresh waters (ponds, streams), vegetation, foodstuffs, stables and stalls, working places infested with rodents, and so forth. The sites of entry for the leptospire are the skin, nose or muzzle (important in grazing animals and dogs), the mouth, and conjunctiva.

Direct contact occurs in handling hosts or their fresh carcasses and organs (especially the kidney). Two other modes of direct contact are important in animals and have been recorded in man: coitus, and transplacental infection of the fetus.

RESERVOIR HOSTS

The principal reservoir hosts in the United Kingdom are mentioned in fig. 2, which also indicates their interrelationships. Livestock can maintain enzootic leptospirosis in the herd or flock, as can laboratory animals in their colony. Seven serogroups of pathogenic leptospire are known to be represented in the United Kingdom: *Icterohaemorrhagiae*, *Javanica*, *Canicola*, *Ballum*, *Autumnalis*, *Australis*, and *Hebdomadis*.¹

Principal Hazards for Man

Some occupational groups formerly associated with leptospiral infections are now seldom affected: sewer workers, fish cleaners, and miners. Farmers, however, still account for a high proportion

FIG. 2—Relationships of the principal reservoir hosts of *Leptospira*. (Reproduced with slight modifications from Turner, L. H., *Trans. roy. Soc. trop. Med. Hyg.*, 1967, 61, 842.)

of cases, especially of *Hebdomadis* infections. As people can now easily reach the countryside—the habitats of reservoir hosts, where control is practically impossible—recreations may expose them to risk of infection (camping, bathing, boating, and so forth). The annual incidence is now less than 60 cases which occur sporadically throughout the country. One gets the impression that, though leptospires are being excreted by various hosts over much of the country, it is just bad luck for man to become infected. There is no justification, at present, for the production of a vaccine, which in any case should be prepared from local strains.

Clinical Manifestations

Leptospirosis is essentially a septicaemic infection. Clinical symptoms and signs occur in a wide variety of combinations. The severity of the effects depends partly on the virulence of the strain of *Leptospira*, partly on the condition of the host in general or of any particular organ or system—which may determine a dominant localization of effects—and perhaps on luck, which may influence the localization and the number of leptospires which gain entry (that is, the size of the inoculum). The degree of severity ranges from subclinical to fatal.

The patterns of clinical symptoms and signs which are evoked in leptospiral infections cannot be regarded as pathognomonic. The manifestations recorded by Weil in 1886—and Landouzy in 1883 and by Vassiliyev in 1888—were so regarded after Japanese and German investigators first isolated leptospires from patients with such symptoms. Nevertheless, the complete or “classical” syndrome may occur in patients in whom attempts to demonstrate leptospiral infection (by isolation or serology) are unsuccessful. Probably such patients have an infectious jaundice, as the original authors surmised; but *Leptospira* is not the only microbial agent which is responsible, even outside the tropics. The same remarks apply also to the so-called “incomplete” forms of Weils’s so-called “disease.”

The diagnosis of leptospirosis on clinical grounds is therefore unreliable. Confirmation and exclusion of leptospirosis are matters for the laboratory, and in practice this is usually by means of serological reactions.

The commoner symptoms and signs are listed below:

Onset.—often sudden, with fever which may be biphasic in untreated patients.

Malaise.—prostration is often more severe than the clinical signs would seem to warrant; chills or rigor; joint pains.

Alimentary system.—anorexia; sore throat; occasionally diarrhoea; abdominal tenderness (diffuse or localized to the right hypochondrium).

Muscles.—pain, tenderness (sometimes acute)—affecting legs, pectorals, back, or abdomen, not only the calves.

Meninges.—headache (sometimes intractably severe), neck stiffness.

Cerebrospinal Fluid.—increased pressure; pleocytosis (neutrophils at first, lymphocytes later); increased protein, variable chloride concentration, normal glucose values.

Eyes.—photophobia; engorgement of the episcleral vessels (i.e. conjunctival injection); subconjunctival haemorrhages; uveitis and optic neuritis are uncommon sequelae.

Skin.—macular rash, often morbilliform (localized rather than generalized), petechiae.

Lymph nodes.—enlargement of superficial groups, cervical or general; mesenteric nodes are also affected. Not unduly tender.

Lungs.—oedema; congestion; occasionally consolidation with radiological evidence of pneumonitis; sputum may be blood-tinged.

Vascular system.—haemorrhages are usually slight when they occur, but may be gross and fatal. Epistaxis may occur at the onset; later bleeding may affect the skin (petechiae, ecchymoses), eye, kidney (cells in the centrifuged deposit of urine), lung, stomach, and intestines.

Heart.—hypertension; arrhythmias; defects of conduction.

Blood.—the erythrocyte sedimentation rate is usually raised, often appreciably. The total white cell count varies—often within the normal range, or raised; but occasionally subnormal. In all cases there is a preponderance of neutrophils.

Kidneys.—albuminuria with cells and granular casts are common but may occur only transiently in the early stage. The concentration of blood urea is often raised without oliguria.

Liver.—involvement may be detected only by revealing abnormal biochemical reactions. Liver function tests when abnormal are indicative of hepatocellular rather than obstructive dysfunction. The serum transaminase concentrations are rarely markedly increased. Jaundice, when it occurs, appears 2–5 days after the onset of fever while the patient’s condition is deteriorating rather than improving.

Leptospirosis should therefore be considered in the differential diagnosis of the following conditions: aseptic meningitis; other febrile illnesses associated with involvement of the central nervous system (encephalitis, non-paralytic poliomyelitis); influenza-like illness (and dengue, in the tropics); jaundice complicating a febrile illness, especially when associated with renal involvement, haemorrhages, and meningism—or any of these; enteric-like illnesses; brucellosis and other relapsing fevers; “glandular fever” when infectious mononucleosis has been excluded; rickettsioses (Q fever, tropical typhuses); pneumonitis (undiagnosed); pyrexia of undetermined origin in which the duration of fever is three weeks or less and irrespective of the clinical symptoms and signs; and acute abdominal emergencies in which laparotomy fails to show any cause for the symptoms.

Treatment

Patients with mild infections recover without treatment. The principles of treatment are the same irrespective of the identity of the strain of *Leptospira*—antibiotics, supportive measures, and the relief of symptoms.

ANTIBIOTICS

Crystalline penicillins are preferred, but other antibiotics—except chloramphenicol, which is of little effect—may be used. The dosage of penicillin is at least 2 mega units in 24 hours; higher dosages are indicated if treatment is started later than day 3 of the illness or in the more severely ill. The earlier treatment is started the better the effects: the fever is terminated within 24 hours (sometimes after a Herxheimer reaction) and complications are prevented. The course of antibiotic should continue for 7 days.

SUPPORTIVE MEASURES

Supportive measures are conventional. Because renal failure is responsible for most fatalities the condition of the kidneys must be carefully supervised; peritoneal dialysis or the artificial kidney should be used without delay—they have saved lives. Cardiac stimulants should be withheld: they may precipitate a fatal failure.

Diagnosis

A compound screening antigen (C.S.A.) for use in a complement-fixation test is prepared in (and distributed by) the Reference

Laboratory (assisted by Dr A. F. Mohun, Whittington Hospital, London N.19). This antigen is used by more than 40 of the laboratories in the Public Health Laboratory Service and by some group laboratories. It distinguishes leptospirosis from other causes of febrile illnesses (and from other causes of jaundice). Sera are then referred to the Reference Laboratory for agglutination tests which usually indicate the agglutinogenic serogroup to which the infecting strain belongs.

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- ¹ Turner, L. H., *British Medical Journal*, 1969, 1, 231.

Contemporary Themes

Drug Taking Among Medical Students at Glasgow University

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Summary

A survey of medical students was conducted at Glasgow University during two successive academic sessions. In 1971, out of 786 students matriculating in the first to fourth years, 749 present at lectures (95.3%) returned properly completed questionnaires. These showed that 100 (13%) had at one time or another taken drugs and that 27 (3.6%) had continued to do so. In 1972, out of 604 students matriculating in the first, second, and fifth years 487 (80.6%) returned questionnaires indicating that 79 (16%) had taken drugs at least once and that 19 (3.9%) had continued.

Marijuana and hashish were by far the most commonly used drugs, the use of "harder" drugs being limited. About half of the students acknowledged the regular use of alcohol, and approximately a fifth were regular tobacco smokers. Those who took drugs were predominantly males who tended to smoke and drink more than other students. They also came from homes where the parents no longer lived together and tended to live away from home more than the other students. Exposure to drugs increased between 1971 and 1972, but the number accepting drugs did not. Appraisal of this problem is needed, since though still small it has the potential for rapid growth.

Introduction

"Drug taking in the teenage community" was one of the topics set for dissertation by medical students as part of their fourth professional examination in 1971, and as relevant data

were not available it was felt that information on drug taking among Glasgow University medical students might at least provide some indication of the local situation. To examine the repeatability of data derived from the first survey and observe any change after the interval of a year it was decided to repeat part of the survey in the next session. Accordingly a questionnaire (see Appendix) was designed for distribution at selected lectures to students in the first four years of their medical training in 1971 and in the first, second, and fifth years in 1972.

Method and Results

The questionnaires were distributed and collected with the co-operation of lecturers before the lecture began. Distribution was preceded by a short explanation of the reasons for the survey, and the students were then allowed 10 minutes to complete and return the questionnaire.

TABLE 1—Exposure to Drugs

Session and Year of Study	Males			Females		
	Total	Offered Drugs		Total	Offered Drugs	
		No.	%		No.	%
1970-1:						
1st year	158	49	31.0	86	15	17.4
2nd "	112	39	34.8	44	13	29.5
3rd "	119	46	38.7	62	14	22.6
4th "	126	48	38.1	42	11	26.2
1971-2:						
1st year	126	52	41.3	92	29	31.5
2nd "	86	41	47.7	50	13	26.0
5th "	95	47	49.5	38	12	31.6

In 1971, 752 questionnaires were distributed among 786 students in the first four medical student year groups matriculating in that year; 749 (99.6%) were returned properly completed, a response rate of 95.3%. Similar rates of return and

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