TABLE I.—*Cl. tetani* in Samples of Air (690 cubic feet—19.5 cubic metres)

Place	Samples Yielding <i>Cl. tetani</i>	Total Samples	Days
Road	24 (89%)	27	9
Operating theatre (exhaust-ventilated) ..	33 (65%)	50	14
Burns dressing station (plenum-ventilated) ..	0	23	8

TABLE II.—Cumulative Results of Sampling for *Cl. tetani* on Six Days in Road, Operating Theatre, and Dressing Station

Volume of Sampling Medium Tested (ml.)	Corresponding Volume of Air Tested		Proportion of Samples Yielding <i>Cl. tetani</i>		
	c. ft.	Cubic m.	In Road	In Exhaust-ventilated Operating Theatre	In Plenum-ventilated Dressing Station
15.0	345	9.77	11/24	7/24	0/24
7.5	172.5	4.88	10/24	1/24	0/24
3.25	86.25	2.44	6/24	0/24	0/24
1.625	43.125	1.22	0/8	—	—

Small numbers of air-borne *Cl. tetani* were found in the environment of another city hospital and of a hospital in a rural district. The air of an operating theatre in the latter, which was ventilated by open windows, also yielded *Cl. tetani*.

Other Reservoirs of *Cl. tetani*

Cl. tetani was isolated from 6 out of 7 samples of garden soil, 5 out of 5 samples of ward floor dust, 5 out of 6 samples of street dust, 8 out of 11 trouser turn-ups of laboratory staff, and 10 out of 35 specimens of human faeces. It was not found in any of the 273 swabs from burns which we examined.

Discussion

These studies show that very small numbers of *Cl. tetani* could usually be found in the air of a city hospital; since rather more of these organisms were found in the air outside the hospital and none at all in a dressing station ventilated with filtered air, it appears that contamination was introduced from outside, and was drawn into the operating theatre by exhaust ventilation. The same source of *Cl. welchii* and exclusion of that organism by plenum ventilation with filters have been described elsewhere (Lowbury and Lilly, 1958).

In spite of the regular isolation of *Cl. tetani* from air in these studies, tetanus has not occurred in any patient following an operation in this hospital during the past nine years. The risk of clinical infection from the small numbers of *Cl. tetani* which we found in the air must therefore be extremely remote. From the data presented by Robinson and others (1946), it seems that post-operative tetanus may result from an increase in the amount of environmental contamination with *Cl. tetani*. On the other hand, the rarity of tetanus may simply reflect the sparsity of tetanus bacilli in the environment. It would be useful to know what degree of contamination with *Cl. tetani* is found in theatres in which patients are known or thought to have contracted post-operative tetanus. Spores of *Cl. tetani* can germinate and produce toxin in tissues only under special and, perhaps, exceptional conditions. Although tetanus may follow trivial injury (see Press, 1948), it is nevertheless a rare sequel even of severe lacerated wounds in unprotected patients, and tetanus following rectal operations is a rarity in spite of the relatively frequent presence of *Cl. tetani* in human faeces. As in the case of gas gangrene, we may suppose that self-infection by faecal tetanus bacilli is a possible source of post-operative infection (particularly in abdominal surgery), but, as such cases sometimes occur in small outbreaks, infection from the environment is perhaps more important.

The functions of plenum ventilation in operating theatres are (1) to remove staphylococci and other organisms liberated in the theatre, and (2) to exclude dirt and bacteria from air admitted to the theatre. The latter, as our studies

have shown, include *Cl. tetani*, and *Cl. welchii*, which can be effectively kept out by cotton-wool and fibre filters in series.

Summary

Samples of approximately 690 cu. ft. (19.5 cubic m.) of air from an exhaust-ventilated operating theatre, a plenum-ventilated dressing station, and the road outside the hospital were examined for tetanus bacilli. These were sparsely present in 24 out of 27 examples from the road and 33 out of 50 samples from the operating theatre; none were found in 23 samples from the dressing station.

Cl. tetani was found also in all specimens of hospital floor dust, in trouser turn-ups of laboratory staff, and in 10 out of 35 human faecal specimens; it was not found in any of 273 swabs from burns.

These findings are discussed in relation to the occurrence and prevention of post-operative tetanus.

A simple plate technique (the "bench mouse") for the recognition of toxigenic *Cl. tetani* is described and illustrated.

We thank Mr. W. Cater, A.I.O.T.T., for assistance in air sampling; Dr. R. E. O. Williams for suggestions on the collection of samples; the clinical director, surgeons, and nursing staff of this hospital for their co-operation; and Mr. R. Gill for the photographs.

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CLEANSING OF HOSPITAL BLANKETS

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Several investigators have shown that the usual methods of laundering do not effectively reduce the bacterial contamination of blankets (see Blowers and Wallace, 1955). This unsatisfactory state of affairs is tolerated only because of the great practical difficulties in devising a method of laundering which is cheap, effective, and adaptable to normal laundry procedures.

We were recently asked to report on the bacteriological efficiency of laundering blankets at Guy's Hospital. In the course of this work it was noted that the standard of cleanliness achieved was much better than expected as judged by reports in the literature and by previous observations by one of us (C. G. A. T.) in a similar investigation at another hospital.

It has been suggested that our findings may be of interest to others who are concerned with laundry hygiene.

Materials and Methods

Laundry Methods Used for Blankets.—Blankets were washed in a Tullis washing-machine fitted with interrupter gear. The machine was filled with 80–100 gallons (360–450 litres) of soft water (0° H) at a temperature of 100° F. (37.8° C.) to which was added 4 oz. (120 g.) of "Crex" and 8 oz. (240 g.) of "sulphanol T" paste.† Twenty blankets were washed on each occasion. The washing process lasted 10 minutes and was followed by two rinses each of 100 gallons (450 litres). Immediately after the second rinse excess moisture was removed from the blankets by means of a Broadbent 36-in. (90-cm.) hydro-extractor. The blankets were then transferred to another floor of the laundry and dried by air at 180° F. (82° C.) for 45 minutes in a Broadbent heated tumbler. They were then stored in a secluded part of the laundry on wooden racks under cover of clean cotton sheeting.

Source of Blankets.—Samples were taken on eight separate occasions at intervals from October, 1957, to April, 1958. Blankets arriving in the laundry from medical and surgical wards were taken at random and compared with blankets which had been laundered on the previous day and which were awaiting issue to the wards.

Method of Sampling.—The sweep-plate technique was found to be satisfactory. The blanket to be tested was held flat on a horizontal surface and six to-and-fro sweeps were made over a distance of 1 ft. (30 cm.) with an inverted Petri dish. A duplicate sample was then taken from another part of the blanket. The medium employed was nutrient agar containing 0.01% phenolphthalein diphosphate. After incubation at 37° C. for 18–24 hours counts were made of (a) total colonies, and (b) colonies of *Staph. aureus*. Colonies of *Staph. aureus* were recognized when colonies of typical appearance gave a bright red colour when the plate was held over a bottle of strong ammonia (Barber and Kuper, 1951); when necessary the identity was confirmed by means of the slide coagulase test.

Studies on Antibiotic Sensitivities.—These were performed using Evans's "sentesit" tablets.

Studies on Air-borne Contamination.—Settle plates were used to measure the air contamination in different parts of the laundry during normal working conditions. Plates of nutrient agar were exposed for known periods of time, and after incubation for 18–24 hours counts were made of total organisms and *Staph. aureus*. The results were expressed as organisms falling on 1 sq. ft. (0.093 sq. m.) per minute.

For studying the passage of air currents through laundry machinery *Serratia marcescens* was used as a marker organism. Heavy aerosols of this organism were produced from a broth culture by means of an atomizer, and the resulting distribution of the organism was then studied: air contamination was measured by means of settle plates; dry blankets were sampled by the sweep-plate technique; wet blankets were sampled by pressing the blanket directly against the nutrient medium; and various parts of the inside and outside of laundry machinery were sampled by means of swabs moistened with nutrient broth.

Smoke produced by exposure of titanium tetrachloride was used for detecting the predominant air currents under different conditions of ventilation.

Results

Table I shows the results of a series of counts taken over a period of six months for blankets arriving dirty in the laundry compared with counts after the laundry processes were complete.

Evidently the laundering processes greatly reduce the population of both total organisms (95.7% are removed) and *Staph. aureus* (98% are removed). It should be noted,

*A preparation of sodium sesquicarbonate manufactured by Imperial Chemical Industries Ltd., designed to produce mildly alkaline conditions.

†An anionic detergent based on sulphonated fatty alcohols supplied by Skilbeck Bros. Ltd.

TABLE I.—Comparison of Blankets Before and After Cleaning

	Before Cleaning	After Cleaning
No. of blankets sampled	100	100
Total No. of organisms isolated ..	47,818	2,034
Total No. of <i>Staph. aureus</i> isolated ..	1,085	22
<i>Staph. aureus</i> isolated expressed as a percentage of the total organisms ..	2.3	1.1
No. of blankets yielding <i>Staph. aureus</i>	87	15

however, that even with the small number of organisms (2,034) isolated from the laundered blankets in the above experiments no fewer than 22 colonies proved to be *Staph. aureus*, and that 15 out of 100 laundered blankets were contaminated with this organism. In separate experiments in which samples of fluff from freshly laundered blankets were collected on culture plates sown with *Staph. aureus* there was no evidence that the blanket fibres inhibited the growth of this organism.

The sensitivities of 50 colonies of *Staph. aureus* isolated from dirty blankets were compared with those of 50 *Staph. aureus* isolated during the period of this survey from patients in the wards. The results are shown in Table II. It will be seen that the two groups of organisms show a similar sensitivity pattern.

TABLE II.—Comparison of the Sensitivities of *Staph. aureus* Isolated from Blankets and from Patients

Antibiotic	<i>Staph. aureus</i> from blankets % resistant	<i>Staph. aureus</i> from patients % resistant
Penicillin	68	70
Chloramphenicol .. .	6	8
Streptomycin	40	36
Tetracycline	32	36

The results of air studies in this particular laundry were largely negative, in the sense that, although air contamination occurred at various stages in the laundering process, no significant recontamination of blankets could be detected.

Settle plates exposed to the air in the room in which incoming articles were sorted showed, as expected, that the air was heavily contaminated: it was usually found that 300–600 organisms were falling on 1 sq. ft. (0.093 sq. m.) per minute. On the other hand, in the room used for storing the laundered blankets the air was relatively clean, and, at a period of maximum activity when blankets were being issued only 23 organisms were falling on 1 sq. ft. (0.093 sq. m.) per minute.

Experiments with aerosols of *Serratia marcescens* made it possible to study air-borne contamination of blankets during the various laundering processes, but in fact no important contamination was noted. For instance, although large volumes of air were drawn into the hydro-extractors there was no evidence that this caused significant contamination of the blankets inside. Similarly, though the hydro-extractors themselves produced a moderate increase in air contamination, this was of no account, since this contaminated air had no access to that part of the laundry in which the blankets were finally dried and stored.

Discussion

The results of laundering blankets in the way here described compare favourably with the results of many other accepted methods. One factor causing a fall in bacterial counts may be the use of sulphonated fatty alcohols as the cleansing agents, since the other procedures involved are in common use in many large laundries. However, the methods described are not ideal, since large numbers of organisms, including *Staph. aureus*, can still be isolated from the freshly laundered blankets. As suggested by Frisby (1957), the ultimate solution of the problem presented by hospital

blankets may be the replacement of woollen blankets by blankets made of some material which can withstand boiling and other rigorous laundry procedures.

When considering laundry hygiene, attention should not be directed solely to the process of washing. It is clearly important to see that freshly washed articles are not recontaminated.

In sorting dirty articles of clothing in a laundry it is usual for air contamination to reach high levels. Again, large laundries have powerful appliances which by design or accident draw in large volumes of air and then expel dust or aerosols into the environment. Obviously it is important that this contaminated air should not have access to regions of the laundry where freshly laundered articles are exposed.

By very simple methods—exposing plates to the air during normal working conditions, producing artificial contamination with aerosols of an easily recognizable organism, and studying the prevailing air currents with smoke—it is possible to detect these sources of contamination.

We cannot generalize on the steps which should be taken to remove such sources of contamination, since these will largely depend on the layout of individual laundries. However, it seems likely that quite simple alterations in ventilation or the resiting of machinery or sorting-rooms and store-rooms will usually improve the hygiene of laundries where these defects still exist.

Summary

Hospital blankets are often contaminated with pathogenic organisms which are not removed by accepted methods of laundering.

A simple method of laundering blankets is described which, though not ideal, appears to give better results than many of the methods in current use.

In planning methods of laundry procedure it is important to guard against air-borne re-contamination of freshly laundered articles.

We acknowledge the help received in the course of this investigation from Mr. H. Besser, the laundry manager at Guy's Hospital.

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Medical Memorandum

Agranulocytosis with Thrombocytopenia following Chlorothiazide Therapy

Chlorothiazide (6-chloro-7-sulphamyl-1,2,4-benzothiadiazine-1,1-dioxide), an orally effective non-mercurial diuretic agent, has been employed extensively both in hospital and in general practice during the past year. This drug is believed to be free of toxicity, and the only side-effects observed occasionally have been mild gastro-intestinal disturbances. One case with a maculopapular rash and pruritus has been noted by C. K. V. van Dommalen (1958, personal communication) following the use of chlorothiazide, but no other toxic manifestations have been published. It is therefore worth recording a case of fatal bone-marrow dysplasia following treatment with chlorothiazide.

CASE REPORT

A man aged 70 was admitted to hospital with a history of having collapsed in the street four weeks previously. He had been treated with digoxin and chlorothiazide at home for acute congestive cardiac failure due to hypertensive heart disease. The total amount of chlorothiazide administered

was 25 g. over a period of 13 days. He had received no other drugs, and there was no history of occupational exposure to chemicals or radiation. He was transferred to hospital after four weeks' treatment because of the development of delirium and incontinence over the previous two days. On admission he was found to be mildly confused, with a generalized maculopapular and purpuric rash over the face, trunk, and extremities. A pyrexia of 100.4° F. (38° C.), mild congestive cardiac failure, left hydrothorax, and a strongly positive Hess test were noted. There was no enlargement of lymph nodes or spleen. Tendon jerks in the lower limbs were absent and proprioception and deep sensation lost. Next day his condition deteriorated, he became mildly jaundiced, and there was further extension of the rash. He died six days after admission.

Investigations.—On his admission there was a normocytic normochromic anaemia with haemoglobin of 10.1 g. per 100 ml., and 3,000 white cells per c.mm. (lymphocytes 97%, monocytes 3%). Examination of two blood films revealed only a single eosinophil polymorph, and, although a few of the lymphocytes were atypical, no primitive forms were seen. The Paul-Bunnell test and W.R. and Kahn tests were negative. Two days later the white cells numbered 900 per c.mm. (neutrophil polymorphs 14%, lymphocytes 73%, monocytes 10%, atypical cells 3%). The neutrophil polymorphs stained histochemically showed a high alkaline phosphatase content. Platelets were 76,000 per c.mm., and E.S.R. 44 mm. in one hour (Westergren). Blood urea was 140 mg. per 100 ml., serum bilirubin 1.8 mg. per 100 ml., and thymol turbidity 4 units.

The direct Coombs test and Schumm's test were negative. Electrophoresis of the plasma proteins showed an increase in α_2 globulin. Serum electrolytes were: sodium 133 mEq/l., chloride 94 mEq/l., and potassium 3.9 mEq/l. Examination of the pleural fluid showed a simple transudate containing fresh blood.

The cause of the antecedent heart failure was confirmed at the post-mortem examination as being due to dilatation of a hypertrophic left ventricle. There was extensive purpura in the skin, the white matter of the brain, and the intestine. The bone marrow was replaced macroscopically by fibro-gelatinous tissue, and histological examination of that obtained from the sternum, lumbar vertebral body, and shaft of the femur showed it to be very hypoplastic. Myelocytes and some metamyelocytes were seen, but mature granulocytes were scanty. Erythropoiesis was normal or only slightly depressed. There was a relative increase of plasma and reticulum cells and a great increase in free iron. The number of megakaryocytes present in the marrow had also strikingly increased.

COMMENT

It is impossible to avoid the conclusion that the marrow disturbance in this case was due to an idiosyncratic reaction to chlorothiazide. The dosage of chlorothiazide was high but not excessive. The maculopapular element of the rash had the familiar characteristics of a drug eruption, and the purpura was linked with a severe thrombocytopenia. The combination of a low platelet count in the peripheral blood with large numbers of megakaryocytes in the marrow is the antithetical phenomenon that has been noted by Weisfuse *et al.* (1954) in the case of quinidine. The agranulocytosis, which was almost complete at one stage, is a frequent finding in this type of reaction, and the patient had not been exposed to any other potentially toxic material.

We thank Dr. H. E. S. Pearson who was in charge of this case, and Dr. P. Darby for the histological reports.

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