Occasionally it is worth introducing a biguanide in modest doses to insulin-dependent diabetics to reduce their tendency to unpredictable hypoglycaemic attacks. The biguanide may partly replace insulin by a drug which in itself causes no risk of hypoglycaemia. This is seldom necessary if insulin is used intelligently by the patient and his adviser.

The therapeutic dose of biguanides is often near to the dose which will start to produce side effects, which occur in the following order: anorexia, nausea, and then vomiting or diarrhoea, or both, with associated malaise. Susceptibility to such side effects varies greatly between individuals and they occur more often if the dosage of the drug is increased too quickly. With-

drawal of the biguanide produces an improvement within eight hours. Rashes are less often associated with the biguanides than with the sulphonylureas.

The biguanides are no better than sulphonylureas in relation to long-term vascular effects. In the University Group Diabetes Programme study, in which phenformin was used in a dose of 100 mg/day, the cardiovascular mortality was over two and a half times that in the diet-treated group, despite the fact that phenformin's potential to lower cholesterol and triglyceride levels in the plasma and produce fibrinolysis might have been expected to exert a favourable effect. The comparative features of the two biguanides are given in table II.

Hospital Topics

Pseudomonas aeruginosa in hospital pharmacies

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Summary

The environments of hospital pharmacies and the preparations made in these pharmacies were examined for *Pseudomonas aeruginosa*. This organism was widely distributed in the pharmacies and was isolated from 9% of preparations. In 11 instances strains of *Ps aeruginosa* from the preparations bore a close resemblance to strains previously found in the pharmacy environments.

Reports of the microbial contamination of pharmaceutical products date from the beginning of the century. A wide range of products may be contaminated, including intravenous fluids, injections, vaccines, antibiotics, creams, hand creams, powders, tablets, mixtures, ophthalmic preparations, and disinfectants. In 1971 the Public Health Laboratory Service reported on the examination of 1220 samples of hospital medicaments intended for oral or topical application.¹ Of these 32% were contaminated and 2.7% contained *Pseudomonas aeruginosa*. We present the results of a search for *Ps aeruginosa* in eight hospital pharmacies and in the preparations made in five of these hospitals.

Examinations

The investigation was carried out in this hospital and seven others (pharmacies A-G), four of which were teaching hospitals.

The environment in the pharmacies was examined using moistened serum-coated swabs. These were incubated overnight at 37° in nutrient broth and then subcultured on to 0.03% cetrimide agar.

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Liquids and non-oily medicaments were examined by adding 1 ml or 1 g to 20 ml of nutrient broth. We added 1 g or 1 ml of oily medicaments to 20 ml of 4% Lubrol W in nutrient broth and this was homogenised in a Stomacher 80 blender (Seward). All broths were incubated overnight and subcultured on to cetrimide agar. Antibacterial agents were neutralised as follows: phenols and alcohols by dilution (1 g or 1 ml in 100 ml of nutrient broth); hexachlorophane or quaternary ammonium compounds by 3% Tween 80 in nutrient broth; formaldehyde and other aldehydes by 2% sodium sulphite broth; halogen compounds by 1% sodium thiosulphate broth.

Gram-negative oxidase-positive bacilli were identified as *Ps aeruginosa* by pyocyanin production or methods previously described.² Typing of strains of *Ps aeruginosa* was by both serological and phage typing methods. *Pseudomonas* spp were identified as Gram-negative oxidase-positive bacilli which grew on 0.03% cetrimide agar and gave an oxidative reaction in Hugh and Leifson's medium.

Results

The pharmacy in this hospital and that of hospital D were examined at intervals over two and a half years (November 1971 to May 1974). Pharmacies in the other hospitals were examined once only. Table I shows the isolation of *Ps aeruginosa* from these departments. The distribution of the organism appeared fairly predictable, as, in addition to being present in moist sites such as sinks, drains, draining boards and taps, it was invariably isolated from cleaning equipment which had been stored wet. It was rarely found where attention was paid to the correct storage and use of the equipment.

TABLE I—Isolation of *Ps aeruginosa* and *Pseudomonas* spp from all hospital pharmacies (1971-4)

Hospital	No of sites examined	No with <i>Pseudomonas</i> spp	No (%) with <i>Ps aeruginosa</i>	No of different types <i>Ps aeruginosa</i> *
Barts	332	84	60 (18)	10
A	61	7	11 (18)	5
B	50	8	21 (42)	7
C	77	18	16 (21)	5
D	249	64	52 (21)	5
E	46	2	3 (6)	NT
F	49	12	8 (16)	NT
G	39	2	1 (3)	NT

*Excluding non-typable strains.
NT = Not typed.

TABLE II—Medicaments contaminated with *Ps aeruginosa* in St Bartholomew's pharmacy and pharmacies A, B, C, and D

	Disinfectant	Cream	Lotion or application	Mixture	Ointment	Mucilage or emulsion	Soap	Total
No examined . . .	149	162	34	86	38	22	8	499
No contaminated . . .	15*	30†	1	0	0	0	0	46

**Ps aeruginosa* recovered from three different types of disinfectant.

†*Ps aeruginosa* recovered from 10 different types of cream.

In this hospital and in hospitals A, C, D, and F, *Ps aeruginosa* was isolated from about a fifth of all the sites examined. We do not know why isolations were more frequent in hospital B but a partially blocked open floor gutter in the manufacturing unit may have been partly responsible. The low recovery from pharmacies in hospitals E and G may have been because the manufacturing units were rarely used and therefore many of the environmental sites where *Ps aeruginosa* might usually be found were dry.

In the two hospitals in which repeated surveys were done the recovery of *Ps aeruginosa* appeared fairly consistent. Typing of the strains showed that in one pharmacy only a few different types were likely to be found and some of these persisted; one strain was regularly recovered. In hospital D one strain was found in the first survey. A year later an identical strain was still present, in addition to others.

Table II shows the range of pharmaceutical products examined in this hospital and in hospitals A, B, C, and D and that 46 of the 499 preparations examined were contaminated with *Ps aeruginosa*. With two exceptions, all the contaminated preparations had been made in the pharmacies. Despite the fact that many of the bacterial counts were in the region of 10^6 organisms per g or ml, none of the contaminated preparations showed obvious signs of bacterial contamination or of degradation. Table III shows the 14 types of medicaments contaminated. In 11 cases at least one of the contaminating organisms was a similar type to at least one of the strains of *Ps aeruginosa* isolated from the pharmacy environment.

TABLE III—Medicaments contaminated with *Ps aeruginosa* and possible environmental origin of strains

Pharmacy	Preparation	No of samples contaminated/ total no of samples	Environmental site
Barts	1% hydrocortisone in calamine cream	2/6	Basin, tap
	Calamine lotion without phenol	1/1	Basin, tap
	Steroid cream (half strength)	1/6	Tap, nailbrush
	Calamine cream BPC	9/9	Proprietary product
	0.5% hydrocortisone in aqueous cream base	3/3	Puddle of water
A	Oily cream BPC	1/1	Not found (NT) mop, rubber taps, sink, draining boards, jug
	Cetomacrogol cream A BPC	1/1 (NT)	Mop, rubber taps, sink, draining boards, jug
B	Aqueous chlorhexidine	1/1	Sink, surround, drain
	Oily cream BPC	6/6	Tank water supply, label damper
C	Chlorxylenol disinfectant	7/7	Tank water supply
	Pine disinfectant	7/8	Sink
D	Hand-cream	5/12	Sink, label damper
	Zinc oxide and ether soluble tar paste cream	1/1	Proprietary product
	Silicone cream	1/1	

NT = Non-typable.

Discussion

Ps aeruginosa is a hardy organism that may often be isolated from moist places in hospital and from the environment of the hospital patient. Its presence, however, cannot be condoned in medicaments made for use on patients' skin or for swallowing, even if the preparations are not intended to be sterile. Our results suggest that in the hospitals in which we worked too many preparations were leaving the pharmacy containing pseudomonads, and we know that in at least one hospital the rate was increased by contamination of preparations with pseudomonads during use in the wards.

Although the evidence was not conclusive, we felt that pseudomonads in medicaments had most often probably come from the environment of the pharmacy where the medicament was made. With one exception, all our pharmacies were partially housed in basements. Their state of repair was not uniformly good and the lighting was often poor. Cracked sinks and wooden draining boards were not easily cleaned. Partially blocked open drains, permanently wet floors, and cleaning mops and brushes left standing overnight in water all contributed to providing *Ps aeruginosa* with a chance to grow. In the absence of these unsatisfactory features the organism might still be isolated from sink units or from such items as the rubber tubing on taps or bottle washers. At one stage when we believed we had eliminated *Ps aeruginosa* from the pharmacy in this hospital we found it in the pharmacy's distilled water supply.

Elimination of pseudomonads from a pharmacy is not an easy task, but a large reduction in their numbers may be obtained fairly cheaply if simple rules of hygiene are followed, cleaning material is properly used, and staff are available for cleaning. Undoubtedly, some of the problems we met were due to staff shortage. Some preparations seem to be more at risk from contamination than others, and it would seem sensible to restrict their making to areas over which environmental control is possible.

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Is the x ray treatment of arthroses of the spine, particularly the cervical spine, reputable?

I assume that the term arthrosis is used to indicate purely degenerative change in the cervical spine as opposed to an inflammatory arthritis. There is no evidence that radiotherapy has any beneficial effect on cervical, thoracic, or lumbar arthrosis. Radiotherapy is still occasionally used in long-standing cases of ankylosing spondylitis when pain in a peripheral joint or spinal segment fails to respond to phenylbutazone or indomethacin. It must always be remembered that irradiation of the spine in young patients carries a definite risk of inducing leukaemia.¹

¹ Court Brown, W M, and Doll, R, *British Medical Journal*, 1965, 2, 1327.

Is it better to immunise all girls against rubella, irrespective of their medical history, unless there are good medical reasons for withholding it or the parents refuse to give permission?

I agree. The clinical diagnosis of rubella is not sufficiently reliable and it is a wise and safe precaution to immunise all girls around puberty before they become pregnant. In this way the congenital rubella syndrome will be prevented.