FIG. 6—Effect of intravenous propranolol and atropine on beat-to-beat variation in healthy man aged 30 years (i) before drug administration, (ii) after 10 mg propranolol, (iii) after 1.8 mg atropine. Arrows mark points between which deep breaths were taken.

The dominance of vagal control over beat-to-beat variation (Levy and Zieske, 1969) is indicated by the raised heart rate of

the pharmacologically denervated heart (Turner, 1969) and of the transplanted heart, which is, of course, denervated (Griep et al., 1971). Moreover, sympathetic inhibition by the administration of propranolol to normal subjects has no effect on beat-to-beat variation (fig. 6). These observations lend further support to the theory that loss of vagal tone is responsible for the absence of beat-to-beat variation in diabetics with autonomic neuropathy.

Measurement of cardiac beat-to-beat variation provides objective evidence for the presence of autonomic neuropathy. The test is simple and reproducible and serial observations can easily be made. Certain clinical observations such as the persistent sinus tachycardia found in some patients may be accounted for by vagal denervation of the heart. Two patients (cases 1 and 3) each had two "unexplained" cardiac arrests, and one might speculate that these episodes were in some way the consequence of cardiac denervation.

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From PhisoHex to Hibiscrub

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Summary

In a field trial of three disinfectant-detergent preparations for the surgical scrub Hibiscrub (a 4% chlorhexidine detergent solution) maintained a significantly greater residual antibacterial action on the skin of the gloved hands of an operating team than was obtained with Disadine (povidone-iodine detergent preparation) ($P < 0.001$). In comparison with PhisoHex (3% hexachlorophane in detergent cream), the established surgical scrub of the operating team for many years, Hibiscrub

maintained marginally more significant residual disinfection ($P < 0.05$). Of the three preparations the members of the team found Hibiscrub to be more acceptable for use than either Disadine or PhisoHex.

Introduction

Since the first British report on PhisoHex (Smylie et al., 1959), 3% hexachlorophane detergent preparations have dominated the choice of safe and effective agents for the surgical scrub regimen. There is no doubt that both in this field (Lowbury et al., 1960, 1963) and in others, notably infant care (Plueckhahn and Banks, 1963; Baber et al., 1967), the disinfectant hexachlorophane has been shown to contribute significantly to the control of hospital cross-infection. As a narrow spectrum agent acting mainly against skin cocci the continuous use of this compound has been criticized (Forfar et al., 1968) because it gives a selective encouragement to Gram-negative infections. This, together with recent reports on the possibility of its toxic absorption

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(Curley *et al.*, 1971; Kimbrough, 1971), has emphasized the need for an efficient and acceptable alternative.

Such a preparation would require to be non-toxic, hypo-allergenic, cumulatively microbicidal, effectively detergent, non-irritant, and pleasant to handle—a tall order which over the past decade has disqualified numerous competitors in this field. The marketing of a new product Hibiscrub (a 4% chlorhexidine detergent preparation) by I.C.I., Ltd. laying claim to the above properties stimulated the professorial surgical unit in Aberdeen Royal Infirmary to carry out a field trial of Hibiscrub and one other currently popular product, the povidone-iodine detergent preparation Disadine, as possible alternatives to Phiso-hex.

Conduct of Field Trial

OPERATING TEAM

This was taken to mean surgeon, nurse, and assistants. As these roles were filled from a unit staffing pool the composition of the team could change between operations, but lists were generally completed by the same team. Phiso-hex has been used exclusively for many years by this unit.

METHOD OF ASSESSMENT

In this type of field trial elaborate methods of sampling are generally unsuccessful, either ruining collaboration by inducing impatience in clinical staff or because they are physically traumatic. Thus skin biopsy, self-adhesive tape stripping, and the cylinder-scrub technique (Selwyn and Ellis, 1972) were not considered. Price's (1938) technique and all its subsequent modifications is suitable only for laboratory experiments. The recently evolved glove fluid procedure (Peterson, 1972) which measures near total numbers of removable organisms from the gloved hand is cumbersome and has yet to be proved free from experimental error. For these reasons the original plate-streak technique used by this unit in their earlier work with Phiso-hex was retained. The finger and thumb pads of both hands of each member of the team were streaked in a regular pattern across agar plates incorporating disinfectant inhibitors (1% Tween 80, 0.5% lecithin, and 1% sodium thiosulphate) immediately gloves were removed after operation. Samples showing no growth were tested with sensitive cultures to assess carry-over of disinfectant. All plates were incubated aerobically for 24 hours at 37°C and stored on the bench for a further 48 hours before colony identification and counting. Records were kept of each operative procedure and the progress of all wounds was followed up to show any change in the incidence of postoperative sepsis.

The trial contained four consecutive periods of study. Period 1—Base-line measurement of the efficiency of the current hexachlorophane detergent (Phiso-hex) regimen (154 operations studied). Period 2—Change to chlorhexidine detergent (Hibiscrub) (228 operations studied). Period 3—Return to Phiso-hex

and re-establishment of baseline measurement (262 operations studied). Period 4—Change to povidone-iodine detergent (Disadine) (222 operations studied).

At the end of period 4 each member of the team completed a questionnaire which required an opinion on lathering power, after-use skin dryness, irritation, colour, scent, and, assuming all three agents to have equal microbicidal properties, their overall preference.

Results

BACTERIOLOGY

Plate-streak Sampling

The results of the trial are shown in the table. In each period all counts obtained from individual finger-streaks from both hands were totalled, combined, and averaged against the number of operations involved. This average mean postoperative colony count could then be used to show the state of the hands for each role in the operating team during each period of disinfection and as a comparison of one disinfection period with another. Because many operations were performed with one rather than two assistant surgeons this group has been treated as a single individual.

All cultures from individual members of the operating team yielding fewer than five colonies per operation were classed as negative, five and more as positive. A χ^2 analysis of negative versus positive counts was then applied to each individual team role. This showed that periods 1, 2, and 3 (Phiso-hex and Hibiscrub usage) for each role did not differ significantly ($P > 0.1$), that the two Phiso-hex treatment periods did not differ ($P > 0.1$), but that on combining these two baseline measurement periods for comparison with period 2 Hibiscrub appeared to be a better treatment than Phiso-hex though the difference was of borderline significance ($P 0.05$). The major difference was for period 4 which gave counts above 5 significantly more often ($P < 0.001$) than did the other periods.

It is apparent that average mean postoperative counts are proportional to the manual activity of the individual. The diagram illustrating this (fig. 1) also shows the dominant hand count for surgeon and nurse to be right and left respectively. The thumb and index finger pads were the most heavily contaminated in all three roles.

The comparative inefficiency of hexachlorophane incorporated in bar soap rather than in Phiso-hex has been well documented (Lowbury and Lilly, 1960), and it emerged again during this trial. The team was joined latterly by an operator preferring Deryl soap (hexachlorophane 2% incorporated in ordinary bar soap) to Phiso-hex. From 48 scrubs with Deryl he produced an average postoperative colony count of 100.5. This compared so unfavourably with his average count of 4 from the 24 scrubs contributed to period 2 (Hibiscrub) that he voluntarily followed the format of the remainder of the field trial. Subsequently 24

Cultural Result from Each Trial Period showing Average Mean Postoperative Colony Counts for Individual Team Roles and Negative versus Range of Positive Plate-streak Counts. All counts above 500 were given the value 500

Disinfection Period	Team Role	Average Mean Colony Count	Negative Cultures (< 5)	Positive Cultures (5 or > 5)	Range of Colony Counts from Positive Cultures			
					5-99	100-199	200-499	500 +
Phiso-hex I	S.	15	137	19	15	1	1	2
	N.	12	129	27	20	5	2	—
	A.	5	120	8	6	1	1	—
	S.	15	208	16	12	1	—	3
Hibiscrub	N.	10	196	28	21	2	1	4
	A.	4	179	4	2	1	—	1
	S.	20	217	23	12	6	—	5
	N.	10	244	32	28	1	—	3
Phiso-hex II	A.	4	216	15	15	—	—	—
	S.	82	113	115	82	10	9	14
	N.	43	139	89	67	13	4	5
	A.	14	121	56	51	5	—	—

S. = Surgeon. N. = Nurse. A. = Assistant.

FIG. 1—Total and right/left-hand colony counts from postoperative "streak plates." (To ease illustration of such a large amount of data, counts have been drawn to represent levels and not comparative areas, and should be read accordingly.)

FIG. 2—Average mean postoperative colony counts for different team roles after one-, two-, and three-hour operative procedures.

scrubs in period 4 (Disadine) by this operator yielded an average count of 129.7.

The pattern of residual disinfectant action during the wearing of rubber gloves was detected by separating operations into one-, two-, and three-hour procedures. A comparison of average mean postoperative colony counts for each role in the team at the end of each type of procedure is shown in fig. 2. At the end of one-hour procedures counts from period 4 of the trial (Disadine) were already three to four times higher for the surgeon and nurse compared with those obtained from the first three trial periods (Phisoex and Hibiscrub). This difference increases for the surgeon engaged in two-hour procedures, but not for nurses or assistants. By the end of three-hour procedures all members of the team using Disadine yielded counts ranging from four to nine times larger than those obtained with either Hibiscrub or Phisoex.

The low counts obtained during Hibiscrub usage were not significantly increased in relation to either length of operative procedure or team role. Counts obtained during Phisoex usage followed a similar order and pattern except for the surgeon who

appears to have increased his count according to length of operative procedure.

Staphylococcus epidermidis was the dominant growth. *Staph. pyogenes* was identified on three occasions, twice during period 1 and once during period 4. There were never more than two colonies in a mixed growth.

Follow-up of all patients showed no significant difference in the incidence of postoperative wound sepsis or of cross-infection. The systematic study of the incidence of post-operative wound infection has been continuous in this unit since 1964.

ACCEPTABILITY OF PRODUCT

This was assessed from the questionnaire answers given by the 23 members of the team. A clear preference for Hibiscrub emerged. Undesirable side effects occurred mostly with Disadine (18 subjects), then Phisoex (11), and Hibiscrub (4).

Discussion

In this field trial the professorial surgical unit in collaboration with the department of bacteriology of the University of Aberdeen provided material from 870 operative procedures to permit comparison of two previously unused disinfectant-detergent preparations with an already well-established surgical-scrub regimen. The direct contact method of sampling chosen to suit the exigencies of this type of field trial is free from many of the experimental errors which beset indirect sampling methods.

A gratuitous experimental control was provided by the operator who joined the team latterly using Deryl soap in preference to Phisoex. The resultant postoperative colony counts fall directly in line with the observations of Lowbury and Lilly (1960) which showed the size of the discrepancy in the antibacterial action of hexachlorophane in bar soap as opposed to Phisoex. We think this is confirmatory evidence that the plate-streak technique is an adequately sensitive indicator of disinfectant action in this type of field trial.

Prewash and initial postwash sampling, omitted from this trial, has already been accurately assessed for all three disinfectant principles (Lilly and Lowbury, 1971; Michaud, *et al.* 1972; Peterson, 1972; Lowbury and Lilly, 1973). The latter show a significantly greater mean immediate reduction of prewash bacterial counts after one application of Hibiscrub (86.7%) in comparison with either Disadine (68.0%) or the hexachlorophane detergent cream Disfex (61.34%). Their observations show that after six successive hand washes spread over two days there was little difference between the three preparations in the eventual reduction of skin flora, both Disadine and Disfex having virtually caught up with the Hibiscrub effect. Measurements, however, were made from the ungloved hand. Some indication of an entirely different cumulative result from gloved hands is given in Peterson's (1972) report on the glove-fluid procedure. In this study the immediate initial reductions of prewash counts for Phisoex in comparison with Betadine (povidone-iodine detergent) match those of Lowbury and Lilly. However, after rubber gloves had been worn for two hours Betadine-treated hands regularly yielded counts more than double the initial count while as expected a further 80% reduction of initial Phisoex counts took place. In the Aberdeen field trial, with Phisoex to establish a baseline against which the other two products were measured, it was seen that the average mean postoperative colony counts obtained during period 4 were significantly higher (about four times) than in any of the other three periods. This indicates failure of povidone-iodine detergent to maintain an adequate residual or cumulative disinfectant action on the working gloved hand. This is apparent during one- and two-hour procedures, is most

pronounced over three-hour procedures, and appears proportional to the degree of manual activity within the team.

There is no doubt that palmar sweat contains a variety of substances capable of inactivating iodine. Unless the Disadine scrub is followed by a continuous release of available iodine throughout the operative procedure, failure to deal with recolonizing skin bacteria may be expected. This hypothesis is the subject of further studies.

The dominance of right and left hand contamination of surgeon and scrub-nurse respectively remains an unexplained observation. It was not due to a majority of left-handed nurses. In an earlier study in this unit Davidson (1969) showed glove puncture to occur most commonly on the left hand of the surgeon and the right hand of the scrub-nurse. This was thought to be due to the different way in which they handled suture needles. In the current trial the glove puncture rate remained constant throughout.

Conclusion

It is felt that the bacteriological result of this field trial adds significantly to the information required in an approach to an ideal surgical scrub technique. It is clear that on gloved hands Disadine failed to achieve the residual or cumulative antibacterial action shown by both PhisoHex and Hibiscrub. Correlative interpretation of our own results with those of other workers suggest that of the small list of products available for the preparation of the hands of operating teams the new 4% chlorhexidine detergent performs as well if not better than

PhisoHex during even the longest operative procedure. It has, moreover, a broader antibacterial spectrum, and produces a greater initial reduction of the bacterial contamination of the skin of the hands. It was found to be more acceptable in use and cheaper than either Disadine or PhisoHex. These factors combined to convince the members of the trial team that Hibiscrub should now displace PhisoHex in their surgical scrub regimen.

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New Type of Allergic Asthma due to IgG "Reaginic" Antibody

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Summary

This study was undertaken to examine the possibility that IgE is not the only immunoglobulin responsible for immediate allergic reactions. A group of asthmatics were investigated in whom immediate allergic reactivity of the bronchi to common inhalant allergens had been confirmed by provocation tests. Their sera were fractionated and the reaginic activity of the immunoglobulin classes was studied by passive cutaneous anaphylaxis testing in monkeys. The results showed that the immediate allergic reactions were due to IgE antibodies in most patients, but there was a group with reactions due to short-term anaphylactic IgG antibodies. It was not possible to inhibit the IgG-mediated responses with disodium cromoglycate. As these two groups had clearly different serum IgE levels the estimation of IgE provided an important guide to the management of these patients.

Introduction

Though it is generally accepted that the antibodies responsible for immediate allergic reactions in man belong to one immunoglobulin class—IgE (Ishizaka and Ishizaka, 1967)—there is circumstantial evidence that other antibodies may be acting as reagents in some asthmatic patients.

It has been shown that circulating IgE levels may be normal in some allergic asthmatic subjects (Bennich and Johansson, 1971), and specific IgE antibodies have not been found in 25% of those who have a positive bronchial response to specific allergens (Aas and Johansson, 1971; Stenius *et al.*, 1971). Furthermore, though disodium cromoglycate (DSCG) is an effective inhibitor of IgE-mediated allergic reactions (Cox, 1971), in several clinical trials it has been shown that it is effective in treating only 70% of patients with allergic asthma (Munro-Ford, 1971; Silverman *et al.*, 1972). In addition disodium cromoglycate does not always suppress immediate allergic reactions elicited by bronchial provocation tests (Muittari, 1971).

Immediate allergic reactions in experimental animals are mediated by two types of antibody (Bloch and Ohman, 1971), one of these having the features of human IgE, the other being an IgG antibody. There is one report of "short-term anaphylactic IgG antibodies" occurring in man, and that was in a group of patients with food allergy (Parish, 1970).

The present study was undertaken to determine whether a group of asthmatic patients with immediate allergic bronchial

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