the "winter vomiting disease" or epidemic gastroenteritis which seem to be due to virus infections and yet no agents have so far been cultivated from such cases; so we need more studies by virologists to find new methods for cultivating these. Finally, a group of compounds which was originally presented to virologists as a tool for studying the nucleic acid of the virus has just been shown to have a chemotherapeutic effect on herpetic infections of the eye of man. Perhaps specific virus chemotherapy is not so far off after all (Kaufman, 1962).


### Summary

A combination of improved laboratory methods and clinical observation is rapidly advancing our understanding of virus infections of man. Some recent examples are given. Certain acute infections with a prominent rash and affecting children have been shown to be due to enteroviruses. Chicken-pox and herpes zoster are due to infections with the same virus. Herpes simplex virus may cause a whitlow. The Eaton agent is now known to be a mycoplasma (pleuropneumonia-like organism), and the pneumonia it produces can be effectively treated with demethylchlortetracycline. The common-cold syndrome can be produced by a variety of viruses, including parainfluenza viruses, respiratory syncytial viruses, and rhinoviruses.


### Addendum

The REOviruses, once called E.C.H.O. 10 virus, are biologically quite distinct from the enteroviruses, but, like them, may be found in the throat and faeces. Lerner *et al.* (1962) have reported on patients infected with REOvirus type 2 and five of these had an itchy maculopapular rash, while one had a vesicular rash. Perhaps this is yet another virus which can cause a rash disease.

Large numbers of rhinoviruses have now been isolated in various laboratories from cases of the common-cold syndrome (Johnson *et al.*, 1962; Ketler *et al.*, 1962; Mogabgab, 1962; Reilly *et al.*, 1962). The position is confused, as names such as "coryza virus" and "entero-like virus" have been used, and all the strains have not yet been compared with each other, but there are probably scores of serotypes. Virus isolations from more severe types of acute respiratory illness have been reported, but it was not proved that the virus isolated caused the disease.

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# EFFICIENCY OF ANTISEPTICS WHEN ACTING ON DRIED ORGANISMS


BY

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Antiseptics are frequently employed to deal with organisms that are dry and adherent to textiles or impervious surfaces made of metal, glass, plastics, or paint. Unfortunately, the choice of an antiseptic for such purposes is rendered difficult because, other than the Rideal-Walker or Chick Martin coefficients, the only available information in regard to their efficiency is the highest dilution that will kill certain species of organisms suspended in broth, saline, or water within a specified time, which is seldom less than 10 minutes. Such information is virtually useless, because the antiseptic must generally be able to kill the organisms in a very much shorter time if it is to be of any practical value, and the organisms will not only be dry but will probably be embedded in films which, almost certainly containing protein, may delay its action considerably.

We have therefore tested a number of antiseptics by a method first suggested by our colleague Dr. W. D. Foster which is much more economical of time, glassware, and effort than the use of threads (Koch, 1881),

garnets (Krönig and Paul, 1897), coverslips (Jensen and Jensen, 1933), glass slides (Johns, 1947), glass cylinders Mallmann and Haynes, 1945), or metal surfaces (Neave and Hoy, 1947 ; Stedman, Kravitz, and Bell, 1954).

The new method makes use of the outer surface of the flat base of tubes in which tablets are marketed. An overnight culture of the organism under test is spread evenly over the surface, allowed to dry in the air, and is then immersed in the antiseptic for a specified time ; the antiseptic is removed by holding the tube in a rapid stream of tap-water, surviving organisms being detected by apposing the film to the surface of a suitable solid culture medium.

No attempt was made to obtain extreme accuracy by using replicates in any series of tests. And, except for the fact that well-grown overnight cultures were invariably employed, so that heavy confluent growth was obtained from control films not treated with antiseptic, the number of organisms submitted to the action of the antiseptics was not standardized. It should, however, be mentioned that many of the more important estimations were repeated three or even four times with extremely little variation in the results obtained.

## Methods

*Strains Employed.*—These comprised: *Staphylococcus aureus,* phage type 80 ; *Streptococcus pyogenes,* N.C.T.C. 8198 ; *Str. faecalis,* N.C.T.C. 775; *Str. viridans,* N.C.T.C. 3165 ; *Escherichia coli,* N.C.T.C. 9703 ; *Pseudomonas pyocyanea,* N.C.T.C. 8060 ; *Klebsiella pneumoniae,* N.C.T.C. 7761 ; *Proteus vulgaris,* N.C.T.C. 8751 ; *Corynebacterium diphtheriae,* N.C.T.C. 3989 ; and a strain of *Bacillus subtilis* isolated some time ago in this hospital. In addition to these strains, 14 strains of *Ps. pyocyanea* were also employed—seven from infections in this hospital and seven from other hospitals, two of which (522, 523) were known to be relatively resistant to chloroxylenol. A further six strains of *Staph. aureus* with different phage patterns were derived from cases in this hospital.

Cultures in plain broth were generally used, but for *Str. pyogenes, Str. viridans, Str. faecalis, and C. diphtheriae* it contained 5% horse serum. *Myco. phlei* was grown on agar, the growth scraped off and ground in a mortar to break up clumps, and suspended in broth before use. When the spores of *B. subtilis* were required the culture was heated for 30 minutes at 60° C. and films were examined to confirm the presence of spores.

All the cultures were incubated at 37° C. for 16 hours and shaken with an eccentric bung-shaker before use.

*Media.*—The broth employed consisted of 1% Evans peptone, 1% Lemco beef extract, and 0.5% NaCl in distilled water adjusted to *p*H 7.4–7.6. Nutrient agar plates were employed for the explant media used for most organisms, but 5% horse blood agar was used for the streptococci and Hoyle's tellurite medium for *C. diphtheriae.*

*Preparation of Films.*—The tubes employed were 10 cm. long with an external diameter of 2.5 cm. and were sterilized by dry heat while covered with aluminium foil. They were stood bottom up in a rack, and, employing a sterile pasteur pipette, 0.25 ml. of the culture was placed on the base of each tube, care being taken to prevent, so far as was possible, its reaching the slight concavity in the centre which was present on all the tubes. As much excess fluid as possible was removed by a filiform pipette and the films were allowed to dry for three hours in a quiet part of the laboratory.

*Preparation of Antiseptic Solutions.*—Concentrated solutions of each antiseptic were suitably diluted in distilled water immediately before each series of tests.

*Exposure to Antiseptic Solution.*—The base of each tube was held in a shallow layer of the antiseptic in a Petri dish or beaker for the time required, when excess antiseptic was shaken off and the lower end of the tube held for 25 seconds in a sterile 1-litre beaker through which tap-water was flowing at the rate of 3 litres per minute. As much water as possible was removed by shaking, the bottom of the tube apposed to the surface of a culture plate, and after slight rotation removed. After incubation for 48 hours the number of colonies was counted. Very little trouble was encountered by reason of contaminants, and even if they appeared their colonies were easily detected.

In general, films were exposed to the antiseptic for 0.5, 2.5, 5, 10, and 15 minutes, but for some it was necessary to employ 20, 30, and 60 minutes as well. Spore suspensions were tested at intervals up to 24 hours. The shortest period of exposure to the antiseptic which resulted in no growth of the organism under test was taken as the end-point.

*Controls.*—In any series of tests, one film was immersed in distilled water for five minutes and treated in the same way as those subjected to the action of the antiseptic. A second film was similarly immersed in distilled water, but for the longest period of immersion to which any of the films were kept in the antiseptic, and it was then treated in the same way.

## Results

In Table I are given the times of immersion required to obtain no growth of the organisms after treatment with a number of antiseptics, all of which were employed in dilutions or concentrations recommended by the manufacturers or which have become established by custom. It will be noted that most of them acted so rapidly that there was no growth following immersion for only 0.5, 2.5, or, exceptionally, 5 minutes.

There seems no doubt that the organisms were killed and that such factors as detachment of the films from the glass or carry-over of antiseptic to the explant medium played no part. There was, for example, good growth from control tubes treated in distilled water instead of the antiseptic, or from films containing *B. subtilis* spores which had been immersed for as long as 24 hours in all the antiseptics except sodium hypochlorite and formaldehyde, which are known to kill spores.

Nor is it at all probable that the absence of growth was due to inhibition caused by traces of antiseptic reaching the explant medium. The fact that *B. subtilis* spores germinated renders this improbable, but many other experiments were also carried out in which organisms such as *Staph. aureus* which are not killed unless immersed for 2.5 to 5 minutes in an antiseptic were shown to be capable of full growth after immersion for shorter periods than this and then washed in the usual way. Other experiments also showed that longer periods and more violent methods of washing, such as holding the tubes under a running tap, did not alter the results. Lastly, *Staph. aureus, Ps. pyocyanea, Pr. vulgaris,* and *C. diphtheriae* heavily seeded on culture plates grew readily following application of

tubes with dried films of broth after immersion in all the antiseptics employed and then washed in the usual way.

It was largely because of this that at no stage in the process was any attempt made to employ compounds neutralizing the antiseptics. Additional reasons for this were that, so far as we are aware, there are no recognized neutralizing agents for some of the antiseptics tested and none of them have ever been suspected of acting as bacteriostatic rather than bactericidal agents in the concentrations we employed. It should also be added that antiseptics for which neutralizers are essential, such as salts of mercury and quaternary ammonium compounds, were not tested.

If, therefore, it can be assumed that when no growth occurred on the explant medium the organisms had been killed by the antiseptic, the mixture of cresols constituting lysol, the coal-tar phenolic distillate "sudol," and the solution of sodium hypochlorite "Milton" were all powerful enough to kill dried non-sporing pathogens in films of protein as a result of contact for only 0.5, 2.5, or, exceptionally, 5 minutes when used in dilutions of 1/100 or less. Since none of these antiseptics are employed in higher dilutions than this, no attempt was made to ascertain how much they could be diluted before ceasing to act.

These results had been anticipated, but not the apparently equal efficiency of ethyl alcohol and the chloroxylenol "dettol." The former, even when used in the optimum concentration, 70%, is not generally considered to be a sufficiently powerful antiseptic for most purposes, largely as a result of the work of Bigger, Blacklock, and Parish (1940) and others (M.R.C., 1945). But the results given in this paper show that when the organisms are more accessible than they are likely to be in a syringe or needle the efficiency of ethyl alcohol, even in "abnormal" concentrations such as 50% and 90%, is equal to that of other antiseptics.

Dettol, originally introduced because of its high bactericidal action on *Str. pyogenes*, was shown by Lowbury (1951) to have little action on *Ps. pyocyanea*, and Colebrook (1941) found that it was unable to kill staphylococci on human skin. But according to our results the efficiency of this antiseptic would appear to be fully equal to that of those referred to above. Largely because this antiseptic, being comparatively non-toxic, has much to recommend it, 14 more strains

TABLE II.—*Time in Minutes Required to Obtain No Growth of Staph. aureus and Ps. pyocyanea Following Immersion in Three Antiseptics*

| Organism | Chloroxylenol (Dettol 1/100) | Chlorhexidine "Hibitane" 0·5% | Chlorhexidine "Hibitane" 0·02% | Cresol (Lysol 1/100) |
|---|---|---|---|---|
| *Staph. aureus:* | | | | |
| 80/81 | 2·5 | 30 | 30 | 2·5 |
| 29/52/80+ | 2·5 | 20 | 60 | 2·5 |
| 71 | 2·5 | 20 | 60 | 5·0 |
| 75/77/42D | 2·5 | 20 | 60 | 2·5 |
| 42E/83A | 2·5 | 30 | 60 | 2·5 |
| 83A | 2·5 | 20 | 15 | 2·5 |
| *Ps. pyocyanea:* | | | | |
| S.T.H. 7 | 0·5 | 2·5 | 15 | 0·5 |
| „ 8 | 2·5 | 2·5 | 10 | 0·5 |
| „ 9 | 0·5 | 0·5 | 2·5 | 0·5 |
| „ 10 | 0·5 | 2·5 | 2·5 | 0·5 |
| „ 13 | 2·5 | 2·5 | >15 | 0·5 |
| „ 17 | 2·5 | 0·5 | 10 | 0·5 |
| „ 21 | 0·5 | 2·5 | 5 | 0·5 |
| 509 | 0·5 | 0·5 | 10 | 0·5 |
| 519 | 0·5 | 0·5 | 5 | 0·5 |
| 522 | 0·5 | 0·5 | 10 | 0·5 |
| 523 | 0·5 | 2·5 | 10 | 2·5 |
| 542 | 2·5 | 2·5 | 10 | 0·5 |
| 544 | 0·5 | 0·5 | 5 | 0·5 |
| 549 | 0·5 | 0·5 | 5 | 0·5 |

Depending on the antiseptic under test, the films were immersed for 0·5, 2·5, 5, 10, 15, 20, 30, and 60 minutes.

TABLE I.—*Time in Minutes Taken by Antiseptics to Kill 11 Species of Organisms in Dried Films*

| Antiseptic | Organism: *Staph. aureus* | *Str. pyogenes* | *Str. viridans* | *Str. faecalis* | *E. coli* | *K. pneumoniae* | *Pr. vulgaris* | *Ps. pyocyanea* | *C. diphtheriae* | *Myco. phlei* | *B. subtilis* spores |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Cresol: | | | | | | | | | | | |
| Lysol 1/20 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | >15 |
| „ 1/100 | 2·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | | | >1,440 |
| Phenolic distillate: | | | | | | | | | | | |
| Sudol 1/80 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | >15 |
| „ 1/100 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | | | >1,440 |
| Chloroxylenol: | | | | | | | | | | | |
| Dettol 1/40 | 2·5 | 0·5 | 0·5 | 2·5 | 2·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | >15 |
| „ 1/100 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | | | >1,440 |
| Instrument dettol 1/80 | 2·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | 5 | 0·5 | >1,440 |
| Sodium hypochlorite: | | | | | | | | | | | |
| Milton 1/80 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | 30 |
| „ 1/100 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | 30 |
| Ethyl alcohol: | | | | | | | | | | | |
| 90% | 2·5 | 5 | 0·5 | 0·5 | 0·5 | 2·5 | 0·5 | 0·5 | 2·5 | 0·5 | >15 |
| 70% | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | >1,440 |
| 50% | 2·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | >15 |
| Chlorhexidine: | | | | | | | | | | | |
| Hibitane 0·02% | >15 | 5 | 5 | 5 | 0·5 | 10 | 5 | 10 | 0·5 | 2·5 | >15 |
| „ 0·5% | >15 | 2·5 | 0·5 | 10 | 0·5 | 0·5 | 0·5 | 2·5 | 0·5 | 0·5 | >1,440 |
| 0·5% in 70% alcohol | 2·5 | 0·5 | 0·5 | 2·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | >15 |
| 70% alcohol control | 0·5 | 0·5 | 0·5 | 2·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | >15 |
| Phenol: | | | | | | | | | | | |
| 5% | 5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | >1,440 |
| 1% | 10 | 5 | 2·5 | >15 | 10 | 5 | 0·5 | 2·5 | 0·5 | 10 | >15 |
| 0·5% | >15 | >15 | >15 | >15 | >15 | >15 | >15 | >15 | 5 | >15 | >15 |
| Formaldehyde: | | | | | | | | | | | |
| 40% | 2·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | 0·5 | 30 |
| 4% | 15 | 2·5 | 0·5 | 10 | 2·5 | 5 | 2·5 | 2·5 | | | >15 |
| 2% | >15 | 10 | 0·5 | 2·5 | 2·5 | 5 | 5 | 2·5 | | | >15 |
| 1% | 30 | 30 | 10 | 120 | 2·5 | 10 | 15 | 10 | 10 | 10 | 240 |
| Liquor formaldehydi chirugicalis | >20 | 15 | 5 | >20 | 2·5 | 2·5 | 2·5 | 2·5 | 5 | 10 | 240 |

The figures refer to the number of minutes required to obtain no growth of the organism after immersion for 0·5, 2·5, 5, 10, 15 and 20 minutes. Spore suspensions were immersed for periods up to 24 hours.

*of Ps. pyocyanea* and six of *Staph. aureus* were employed in similar tests. The results, given in Table II, show clearly that this antiseptic would appear to be quite as efficient as lysol. When the discrepancy between our findings and those of previous workers was brought to the attention of the manufacturers we were informed that an improved formulation was adopted in 1952.

### Chlorhexidine, Phenol, and Formaldehyde

In contrast to all the antiseptics referred to in the previous section, the behaviour of these three was very different because considerably longer periods of immersion were required to obtain no growth on the plates.

So much is this so that chlorhexidine ("hibitane") at the concentration of 0.02%, which is recommended by the manufacturers for general purposes, requires over 15 minutes to kill *Staph. aureus* and between 5 and 10 minutes for *K. pneumoniae* and *Ps. pyocyanea*. Even when the strength was increased to 0.5%, *Staph. aureus* was still alive after 15 minutes. Further tests carried out with six more strains of *Staph. aureus* and longer periods of exposure (see Table II) showed that even the 0.5% solution required between 15 and 20 minutes to sterilize four strains and between 20 and 30 minutes for the remaining two strains. At a concentration of 0.02% its action was even slower, between 30 and 60 minutes being generally required. On the other hand, this antiseptic acts more rapidly on *Ps. pyocyanea*, all 14 strains being killed in a minute or so in the 0.5% solution. Longer periods of 10, 15, or even more minutes were required in the 0.02% solution.

Chlorhexidine is also employed at a concentration of 0.05% in 70% alcohol for the rapid sterilization of instruments and, as will be seen in Table I, there is no doubt that the organisms are killed much more rapidly than in watery solution. But a control series, set up at the same time employing 70% alcohol only, gave equally good results, suggesting that it was the alcohol rather than the chlorhexidine that was the more active ingredient of the mixture.

Phenol also proved to be weaker than had been anticipated. Although a dilution of 1/20 kills organisms quickly, a less toxic solution such as 1/100 took between 5 and 10 minutes to kill *Staph. aureus* and *E. coli*, and *Str. faecalis* were still alive after 15 minutes. When the concentration was reduced to 1/200 it was even slower, so that surviving organisms were nearly always present after 15 minutes' immersion.

Formaldehyde in the form of a 40% solution of the gas usually known as formalin is undoubtedly a good antiseptic which possesses the great advantage of being able to kill spores. It retains this property even after dilution, but quite long periods of immersion are required to kill non-sporing organisms. So much is this so that 4% formaldehyde requires from 10 to 15 minutes to kill *Staph. aureus*. Even longer periods were required in the 1% solution, from 60 to 120 minutes being necessary for *Str. faecalis* and 20 to 30 minutes for *Staph. aureus* and *Str. pyogenes*.

Largely because neither phenol nor formaldehyde appeared to be very powerful, tests were also carried out with liquor formaldehydi chirugicalis, recently advocated as a useful general-purpose antiseptic (Williams, Blowers, Garrod, and Shooter, 1960) which, besides borax and fluorescein, contains 0.5% phenol and 1% formaldehyde. As will be seen from Table I, the mixture is in fact slightly more powerful than either alone. Nevertheless, it cannot be said that a solution which requires over 20 minutes to kill *Str. faecalis* and *Staph. aureus* is a particularly good antiseptic. Its one advantage would seem to be that it kills spores, but this requires immersion for between three and four hours.

## Discussion

Although antiseptics have been rightly condemned as sterilizing agents, they are employed a great deal in the hope of killing non-sporing pathogens on solid surfaces such as floors, walls, furniture, trolley tops, plastic mattress covers, and many pieces of surgical and anaesthetic apparatus. They are also used for the treatment of bedpans, urinals, baths, and bedding, and, perhaps with less justification, for gloved hands and instruments. If the antiseptic is to be of any value at all in most of these situations it must not only kill organisms that are dry and probably embedded in films of some kind but it must act rapidly before it is removed by evaporation, gravity, or washing. Speed of action is even more necessary if the antiseptic is suspected of having become contaminated, because they are often required for use again within a few minutes.

If the conditions in which the antiseptics are tested in the experiments reported in this paper can be assumed to represent those in which they must act when employed for such purposes, there is no doubt that some at least are sufficiently powerful. These include cresol lysol, the coal-tar phenolic distillate sudol, the chloroxylenol dettol, the sodium hypochlorite solution Milton, all employed in dilutions of 1/100 or thereabouts. Ethyl alcohol in cencentrations of from 50 to 90% would appear to be equally useful. It is not suggested that this list is in any way exhaustive. Other antiseptics of essentially the same composition, but which we have not tested, may well be equally valuable.

Three antiseptics are, however, much less suitable. The first is chlorhexidine, which even when used in the highest concentration suggested by the manufacturers takes the best part of half an hour to kill *Staph. aureus*. Phenol, too, in 1/100 dilution is slow and at 1/200 virtually useless. Lastly there is formaldehyde. Even when employed in the form of a 4% solution it is slower than most antiseptics, and when only 1% is present very long periods of immersion would be required to ensure complete sterilization. The mixture of formaldehyde and phenol called liquor formaldehydi chirugicalis gave a better performance, and will eventually kill spores. But except for this rather dubious quality it has little to recommend it.

## Summary

The ability of different antiseptics to kill several species of organisms embedded in dried films of broth on glass surfaces was estimated by a new technique. One-per-cent. solutions of cresol, a phenolic coal-tar distillate, chloroxylenol, sodium hypochlorite, and 70 to 90% ethyl alcohol killed all species tested in less than five minutes, whereas longer periods were required with 0.5% and 0.02% chlorhexidine, 0.5% and 1% phenol, 1 to 4% formaldehyde, and the mixture of 0.5% phenol and 1% formaldehyde constituting liquor formaldehydi chirugicalis.

Spores of *B. subtilis* were unaffected by all the antiseptics except sodium hypochlorite and formaldehyde.

Further tests with six more strains of *Staph. aureus* showed that chlorhexidine in 0.5% concentration might

take 20 to 30 minutes to kill all the organisms, whereas the same strains were killed in less than five minutes by 1% chloroxylenol and 1% lysol. Similar tests with 14 more strains of *Ps. pyocyanea* showed that 1% chloroxylenol and 0.5% chlorhexidine were as powerful as 1% lysol.

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# $^{131}$I-"HIPPURAN" RENOGRAPHY IN DETECTION OF UNILATERAL RENAL DISEASE IN PATIENTS WITH HYPERTENSION

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The recognition of unilateral renal disease in hypertension is often of therapeutic importance. In renal artery stenosis the results of surgical treatment are particularly favourable in comparison with those obtained in other forms of unilateral renal disease (Page *et al.*, 1959; Connor *et al.*, 1960; Brown *et al.*, 1960; Howard and Connor, 1962), and much attention is currently being focused on the diagnosis of this condition. Intravenous pyelography, an essential preliminary investigation, may show differences in renal size and in pyelographic density, suggesting the possibility of renal artery stenosis (Brown *et al.*, 1960). Tomography has proved of value in defining renal outlines and in assessing the thickness and symmetry of the renal cortex (Hodson, 1960). However, normal pyelograms have been reported in patients with renal artery stenosis (Squire and Schlegel, 1959; Block *et al.*, 1960; Whitley *et al.*, 1962) and additional simple methods of investigation are required to enable better selection of hypertensive patients for aortography and divided renal-function tests.

Isotope renography, which was introduced by Taplin *et al.* (1956), has been used for this purpose; the procedure involves the recording of the counting rate registered by detectors placed over the kidneys after an intravenous injection of a radioisotope-labelled compound showing rapid urinary excretion. The initial substance used, $^{131}$I-labelled "diodrast," is concentrated in the liver and has been superseded by other substances, the most satisfactory being $^{131}$I-labelled "hippuran," sodium salt of orthoiodohippuric acid (Nordyke *et al.*, 1960). Published reports on the detection of unilateral renal disease using radioactive diodrast or diatrizoate have been both favourable (Winter *et al.*, 1959; Serratto *et al.*, 1959; Denneberg and Hedenskog, 1959; Block *et al.*, 1960; Straffon and Garcia, 1960) and unfavourable (Poker *et al.*, 1960; Säterborg, 1960; Dollery, 1960; Moses *et al.*, 1961). In this paper we report the results of $^{131}$I-hippuran renography in 203 hypertensive patients and assess the value of the test when used in conjunction with the intravenous pyelogram to select individuals for aortography and divided renal-function tests.

## Methods

*Apparatus.*—The unit consists of two matched scintillation counters connected to ratemeters and recorders. The activated sodium iodide crystal of the scintillation counter is 1.7 cm. in diameter and 2.5 cm. deep: collimation is fairly wide, the aperture being 4 cm. in diameter at a distance of 3 cm. from the end of the crystal. The time-constant setting of the ratemeters is 5 seconds and the counting-rate range 100 counts per second. The chart speed of the recorders is quarter-inch per minute (half-inch per minute in our earlier tracings).

*Procedure.*—The patient is seated comfortably on a stool and leans forward with his elbows resting on a table; the scintillation counters are placed over the surface markings of the kidneys at right angles to the back. The dose of $^{131}$I-hippuran (obtained from the Radiochemical Centre, Amersham, Bucks) is given intravenously, and continuous records are made of the activity from each renal area for 15–20 minutes. Whenever possible the surface markings are taken from an intravenous pyelogram. Accuracy of location is further checked by varying the position of the counters during the test. Our average dose of $^{131}$I-hippuran is 8 $\mu$c. (0.07–7.5 mg.), and it varies according to the size and renal function of the patient; care is taken to avoid extravascular deposition of hippuran, which may give rise to "abnormal" tracings. The radiation dose received by the patient is low, being a small fraction of that received during intravenous pyelography, and the test can be repeated one hour after the original injection unless renal function is severely impaired. When abnormalities occurred in the renogram the test was repeated at least once; remarkably consistent results were obtained in individual patients, including those taken after intervals as long as six months.

*Interpretation of Renogram.*—The normal $^{131}$I-hippuran renogram shows three phases (Fig. 1) which are usually called "vascular" (A to B), "secretory" (B to C), and "excretory" (C to D). While these are influenced by the blood flow to the kidney and adjacent tissues, renal blood volume, renal excretory activity, the size of the renal pelvis, and the rate of urine flow from the kidney to the bladder, it is important to recognize that each segment of the curve is the resultant of at least three of these functions (Taplin *et al.*, 1956; Klapproth *et al.*, 1962). In normal subjects the curves obtained over the two kidneys are similar in amplitude and contour. In this study the renograms were assessed independently by at least two observers who made a visual comparison of the tracings and measured the maximum amplitude of each curve. The renograms were used to detect differences in function between the two kidneys, and disparity was considered to exist if there was a difference in contour of the two tracings or