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A Comparison of Microbial Contamination in Commercial Intravenous Fluids Packaged in Glass and Flexible Plastic Containers

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A COMPARISON OF MICROBIAL CONTAMINATION IN COMMERCIAL INTRAVENOUS FLUIDS PACKAGED IN GLASS AND FLEXIBLE PLASTIC CONTAINERS

by

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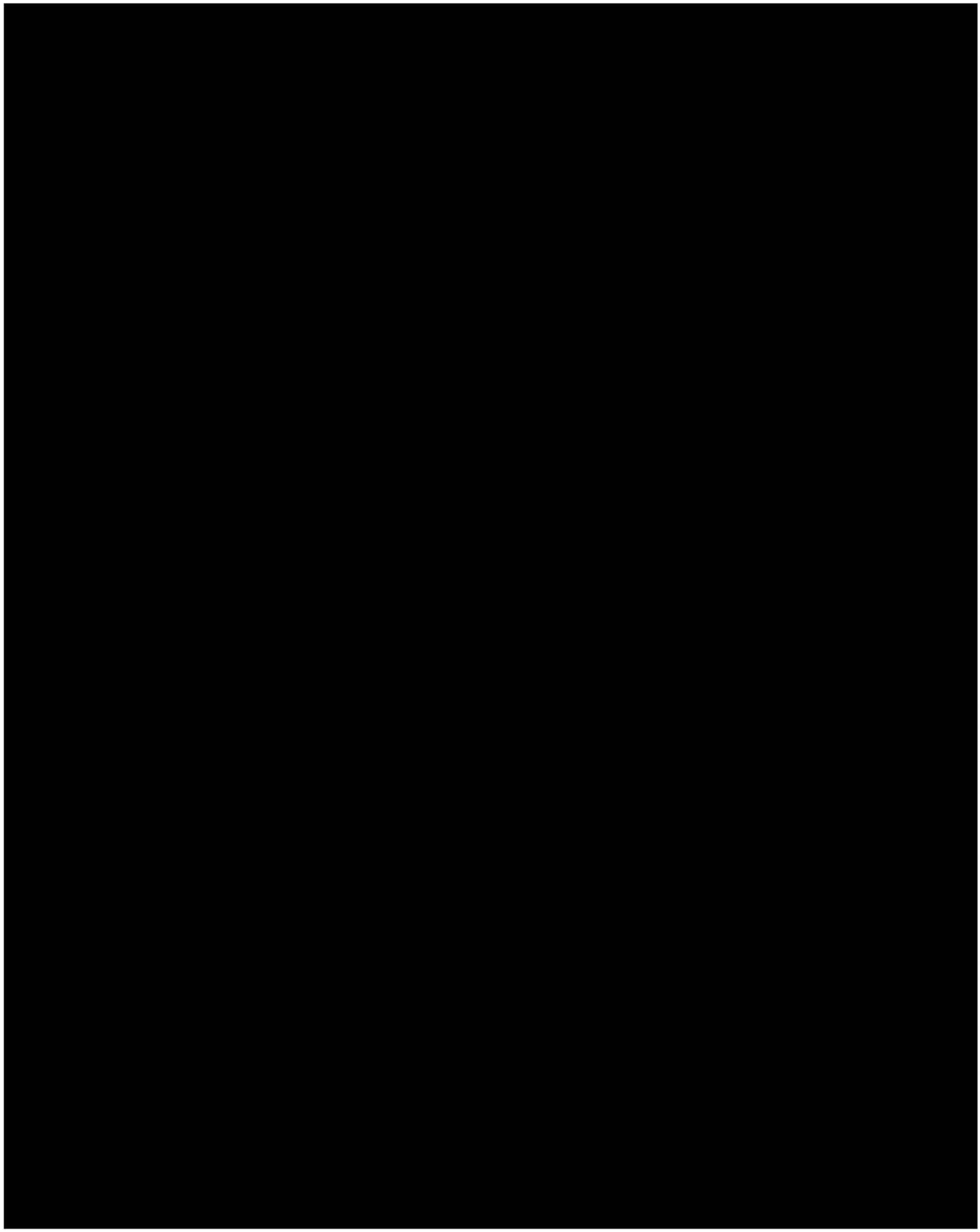
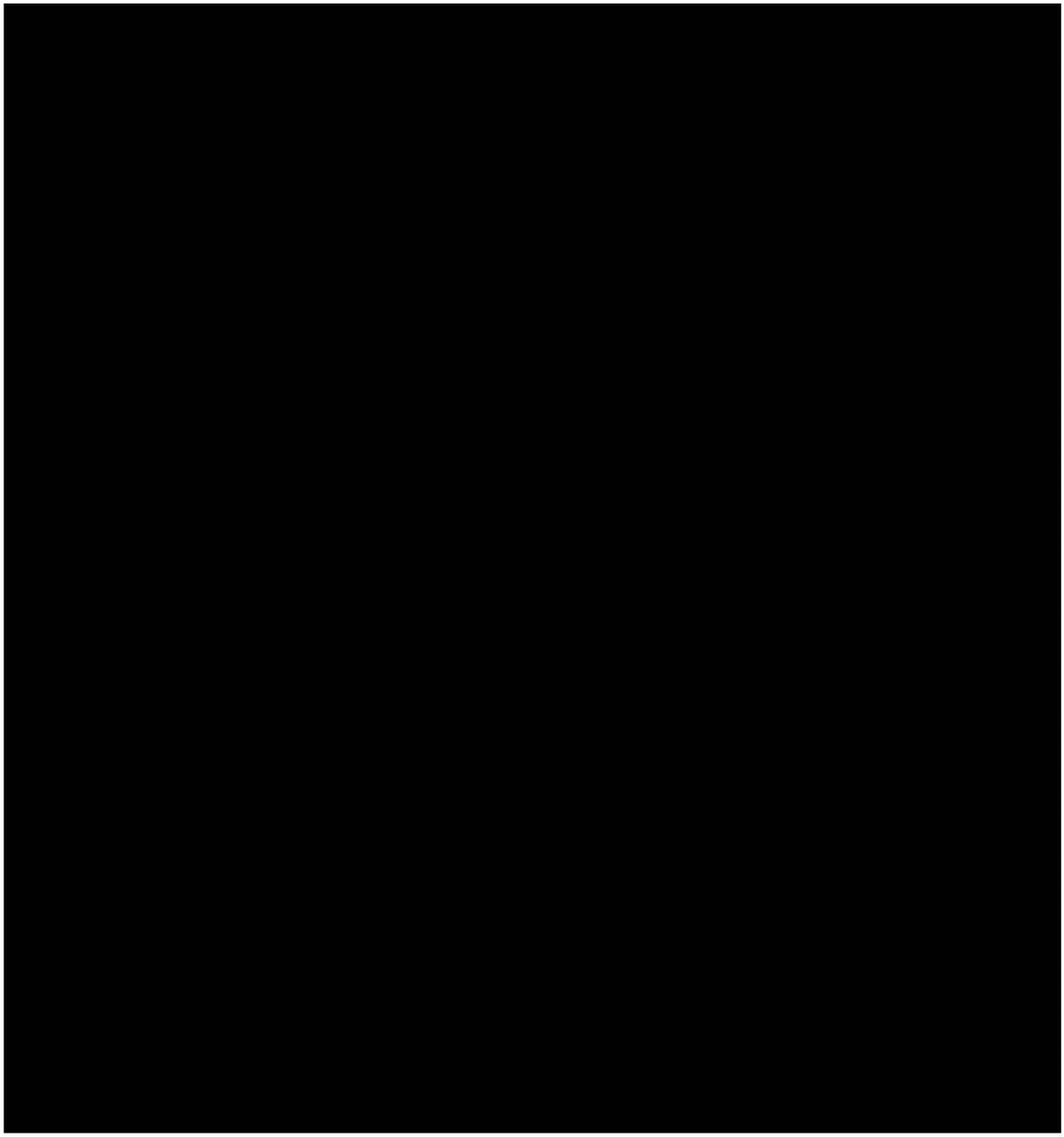
CURRICULUM VITAE





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INTRODUCTION

O'Shaughnessy[1] first suggested the treatment of patients with intravenous fluids in the early 1800's. Subsequently, Dr. s Latta[2] and Weatherill[3] and others treated patients by administering solutions of selected salts intravenously. Until the 1920's, hospitals depended exclusively upon solutions prepared in their own laboratories. Techniques allowing large volume commercial production were not developed until the late 1920's and in 1929 Dr. Don Baxter (Don Baxter, Inc.) began providing commercial intravenous fluids in the Los Angeles, California, area and nationwide in late 1931.[4]

A greater awareness is now recognized for the complexities of intravenous fluid production, not just from the standpoint of sterility but for pyrogenicity, formulation and administration. Basically, the formulae and methods of administration today are little different from the earlier hospital produced fluids.

The delivery system of the intravenous fluid has traditionally been the rigid glass bottle with some device to allow air venting. The venting allows equalization of air pressure by permitting ambient air to enter the bottle. This has been accomplished in one of two ways. First, a ball-check valve (many early systems used a "butter-fly" device) that permitted the ambient air to enter the bottle and pass through the fluid. Usually the devices provided some type of gross filtration of the air, but by no means was sterilization achieved. Second, a vent tube running the length of the bottle and directing ambient air

into the bottle over the surface of the fluid. It should be noted that in each case the non-sterile ambient air comes into intimate contact with the intravenous fluid. The delivery system as a unit represents an open pathway into the patients' veins and the non-sterile ambient air is a potential vehicle for introducing organisms into this pathway.

There was no alternative available if the physician wanted to administer intravenous fluids to his patient. Any system used relied upon non-sterile ambient air in order to function; however a new intravenous fluid administration system is now available in the United States. Travenol Laboratories has now marketed intravenous fluids in a flexible plastic bag (Viaflex^{R}) that does not rely on entry of ambient air to function. The plastic bag simply collapses to allow the fluid tovacate the container.

The official literature disseminated by Travenol Laboratories refers to the Viaflex^{R} system as "an innovation in parenteral packaging." Advantages sited for this system are: reduced weight, reduced bulk, freedom from breakage as a result of careless handling or exposure to freezing. However, a patient would benefit only indirectly from these advantages. A more important consideration for the patient is safety. Does this "innovation in parenteral packaging" subject the patient to less risk of septicemia resulting from a contaminated intravenous fluid administration system?

Microbial contamination of an intravenous fluid may occur in many ways, but among these, three are foremost.

1. During manufacture of the fluid and components
2. In preparation of the delivery system prior to administration
3. During actual administration of the fluid to the patient

By utilizing recognized good manufacturing practices plus adequate controls, the manufacturer is able to virtually eliminate the first source of contamination. During the course of this study, background data was collected to verify this observation.

Contamination occurring during assembly of the system and that encountered during actual administration becomes more difficult to eliminate. The propensity for contamination during assembly of the system is determined by the design of the system and the technique utilized by the individual preparing the system. A poorly engineered delivery system or one with serious design deficiencies would require meticulous technique from the individual. Such a system would be constantly challenged and subject the patient to an undue risk. Contamination arising during the administration of the fluids would be determined by the basic design of the system and its dependence on environmental factors.

The intent of this study was to methodically explore microbial contamination of a traditional glass bottle system and the newer flexible plastic bag system simultaneously. Utilizing nurses in a patient care area and pharmacists in a central additive service configuration each system was subjected to conditions approximating actual situations. The frequency of microbial growth in either system was used to serve as a comparison between the two systems.

REVIEW OF THE LITERATURE

For many years authors have been expressing fears of airborne microbial contamination. Wells and Wells[5] accurately stated the problem although, in a somewhat flowery manner; "In the dissemination of plant life, the atmosphere is nature's prime sower of the seed and thus vitally affects all living things." The suggestion that common air supplies be rendered free of microbial contamination, while impractical on the scale outlined by Wells and Wells[6], is precisely what is being attempted today on a limited basis in laminar air flow hoods and in clean rooms. Elaborate filtration devices are not the only means of achieving an atmosphere with fewer bacteria. By the use of sterile dust-free surgical gowns, Duguid and Wallace[7] showed that one source of bacterial contamination, i.e. dust-borne bacteria, could be drastically reduced. The study conducted by Cole and Bernard[8] indicated that careful housekeeping techniques could be expected to reduce the contamination level. Other workers have found that very basic matters such as the number of personnel in a given area and the extent of physical activity also played key roles in the levels of air-borne microbial contamination encountered.[9] Ford, Petersen, and Mitchell[10] came to the same conclusions and suggested the control of traffic in the operating rooms to reduce the level of air-borne microbial contamination.

The role of technique and the person preparing the intravenous fluids for administration in contributing to microbial contamination of the intravenous

fluids was shown by the work of Love.[11] This study indicated that improper assembly of the intravenous fluid administration system was an important factor in the rate of microbial contamination resulting.

In examining a series of actual in use intravenous fluids, Deeb and Natsios[12] attempted to provide a value for the frequency of microbial contamination. Their study showed that the patient receiving intravenous fluids must be considered a being at risk. Herman[13] endeavored to provide the practicing pharmacist with an appreciation of the role he may play in contributing to microbial contamination by pointing out that healthy hospital workers may carry recognized pathogens. This point was corroborated by the work of Williams[14] showing that transient carriage of Staphylococcus aureus by healthy individuals could be harmful to patients.

The prominent epidemic of septicemias arising from the use of contaminated intravenous fluids, first documented by Duma, Warner and Dalton[15] is an example of contamination occurring at the point of manufacture. The extent and possible underlying source of the contamination was subsequently noted by the Center for Disease Control.[16] Reports are still appearing in the literature documenting specific cases[17] and various methodologies employed in other outbreaks studied.[18]

The report of Rupp and Forni[19] documents a previously unrecognized means of contamination of an intravenous fluid, that of actual entry of an insect into the container via the vent tube. The potential of this means of contamination was suggested in an editorial from England[20] pointing out that these insects may be carriers of pathogenic microorganisms. This break in the integrity of the system was directly related to the basic design of the administration container.

Henry and Harrison[21] warned of the potential for contamination resulting from the improper use of volume control sets in administering intravenous fluids; a warning also voiced by Duma, Warner, and Dalton.[15]

The literature abounds with articles describing septicemias resulting from in-dwelling intravenous catheters.[22-33] Other reports appear in which intravenous fluid therapy is indicted as the most frequent source of infection[34] or evidence strongly suggests the fluid as the source of contamination.[35]

The gentle flow of air into the vacating fluid container does not alone represent the means of introducing the microbial contaminants into the fluid. Michaels and Ruebner[36] detected bacterial growth in intravenous fluids during administration and concluded the contamination occurred "either while the bottles were being changed or by contaminated air sucked into one of the bottles through the air-replacement tube." It was subsequently shown experimentally by Perceval[37] that the inrush of ambient air upon opening the fluid bottle with a partial vacuum could be the vehicle for introducing organisms into the intravenous fluid. Concurrent environmental air sampling was used by Perceval to serve as a comparison of the risk factor. Perceval found that the degree of environmental contamination did affect the rate of fluid contamination. O'Hare, Shapiro and Creeden[38] concluded that air microbial contamination has to reach a certain level to become clinically significant, although that level was not defined.

In the study conducted by Arnold and Hepler,[39] the contamination rate of fluids opened in various areas of their hospital ranged from zero to nearly 10%. The overall contamination rate was approximately 5% and in their opinion raised serious questions regarding the safety of intravenous fluids being opened in a

contaminated environment. A subsequent study by Hansen[40] at the same institution concluded that an open or air-dependent system was more likely to become contaminated through the entry of non-sterile air when the partial vacuum was released. Hansen further suggests these air-dependent systems be opened only in a laminar air flow hood to minimize the contamination potential.

Clearly, the literature shows that a great many people have been concerned for a number of years with the potential for infections in the hospital environment. This concern has included the administration of intravenous fluids and any source that may be contributary, i.e. manufacture, assembly of the unit and administration.

DESCRIPTION OF THE STUDY

The study in question was designed to examine a new intravenous fluid delivery system from the standpoint of microbial contamination. To serve as the base-line, a traditional delivery system was subjected to identical procedures concurrently with the new system.

The major differences between the two systems being studied was the fluid container. The traditional container consisted of the glass bottle with a vent tube running the length of the bottle. The new system was a flexible plastic bag that did not require the entry of ambient air for evacuation.

In recognition of the alternatives that exist with regard to intravenous fluid preparation, both nurses and pharmacists were utilized in the study. Obviously, vastly different conditions existed in the areas used by the study personnel for actual preparation of the fluids. The pharmacists used a certified laminar air flow hood and the recognized procedures of the Medical College of Virginia Hospital Pharmacy of a lint-free gown, surgical mask and cap. The procedure also included a scrub using a sterile 3% hexachlorophene sponge and cleansing of the hood and all materials placed inside the hood with a solution of 70% isopropyl alcohol. The nurses prepared their fluids in a medication room, unaltered from the normal setting with regard to traffic, housekeeping, ventilation, and distractions.

The particular nurses were carefully chosen to find ones having had no prior experience with the new system and no prior instruction in the recommended procedures. Likewise the pharmacists had no instructions in handling the new system but they were somewhat familiar with the flexible plastic bag.

Each nurse and pharmacist then proceeded to prepare one liter of an intravenous fluid containing one additive and attached an administration set and a final filter distal to the administration set. At the nursing unit (the same medication room) the nurses then attached a needle and proceeded to run the intravenous fluid into a sterile evacuated collection bottle. (Figure 1)

When the fluids had almost emptied, they were clamped with the device provided by the manufacturer and allowed to stand at room temperature for approximately 24 hours undisturbed.

The fluids were next collected by study personnel and delivered to the laboratory for sampling. After collecting the necessary samples, the materials were delivered to the laboratory for incubation and speciation.

To provide a positive concurrent control on both sampling technique and microbiology detection methods, small quantities of Escherichia coli (ATCC 11229) were added to one bottle and one bag of fluids of each one-day run. The addition of the microorganism was performed by the nurse or pharmacist preparing the fluids and the unit contaminated was unknown to both the persons performing the sampling and those in the microbiology laboratory.

Specifically the study was to proceed in the following fashion:

Phase One: collection of laboratory background data of individual components, by the study personnel.

Phase Two: preparation of the intravenous fluid systems by nurses on a patient care unit.

Phase Three: preparation of the intravenous fluid systems in a laminar air flow hood by pharmacists, using the prevailing standards of the department.

MATERIALS AND METHODS

MATERIALS

The intravenous fluids and administration sets utilized were manufactured by Baxter-Travenol Laboratories, Inc. (Morton Grove, Ill. 60053). The intravenous fluid selected was 5% Dextrose in Lactated Ringer's packaged in one liter quantities in the traditional glass bottle (catalog number 2A2074) and the Viaflex^{R} flexible plastic bag (catalog number 2B2074). The administration set was the Plexitron^{R} R-42 set (catalog number 2C0005). The additive selected to be included in each unit was 0.9% Sodium Chloride without a preservative, packaged in 30 ml single dose vials, manufactured by Baxter-Travenol Laboratories, Inc. (catalog number 2D4543). All supplies were purchased on the open market through normal distribution channels.

Millipore Corporation (Bedford, Mass.) manufactured the Swinnex-25^{R} 0.45μ in-line final filter (catalog number SXHA0250S) used throughout the study. Empty Vacuum Plasma collection bottles were used to collect the filtered intravenous fluids and were manufactured by Baxter-Travenol Laboratories, Inc. (catalog number 2A8504).

METHODS

All bacteriological manipulations were performed in a laminar air flow hood (Abbott Clean Air Center, Bench Model BK No. 1024) by the same two individuals, a physician and a pharmacist. The laminar air flow hood itself was certified during the course of the study (November 3, 1971, and June 29, 1972) by Contamination Control Labs (located in Livonia, Michigan). Prior to use the laminar air flow hood was prepared by allowing to run for at least one hour and swabbing the inside surfaces (top, sides and work area) with 70% isopropyl alcohol. Before beginning any sampling procedures, blood agar settling plates were placed on either side of the work area and fastened to the sides (approximately 8-12 inches from the outside edge) at a 45° angle to interdict the flow of filtered air. The settling plates were left in place until the sampling procedures had been completed; the last activity to be removal of the blood agar settling plates, secure the top in place, and deliver the exposed plates to the bacteriology laboratories for incubation and identification. Incubation was for seven days at 37°C, being checked daily for growth.

Phase One: Background Data Collection

Background data was collected to prove the sterility of all individual components and to provide a check on the technique of those performing the sampling. In this phase of the study, fifty (50) one liter glass bottles of 5% Dextrose in Lactated Ringer's, fifty (50) one liter flexible plastic bags of 5% Dextrose in Lactated Ringer's, forty (40) intravenous infusion sets, and fifty-four (54) final in-line filters were sampled. Actual sampling was performed in the following

manner for the glass bottles. First, the metal ring and metal disc were removed outside of the laminar air flow hood. Next the surface of the latex covering was dried with sterile gauze and the surface then flamed. The intravenous fluid bottle was then placed in the laminar air flow hood in a horizontal configuration with the vent tube in the lower position. The vacuum was next released by inserting a sterilized air filter through the hole provided for the infusion set. (The sterilized air filter was prepared by removing the plunger of a five cc syringe and placing a plug of cotton in the barrel and attaching a one and one-half inch twenty guage needle; the entire unit was wrapped and sterilized.) Ten ml of the intravenous fluid was removed with a syringe through the vent tube of the bottle. The opening of a bottle containing eighty ml of fluid thioglycollate media was next flamed and the ten ml of intravenous fluid then aseptically added. The opening of the bottle was again flamed and the top replaced. The contents of the bottle were then incubated at 37°C for seven days and any resulting growth speciated.

The flexible plastic bags were next sampled using a similar procedure with a few exceptions. After removing the intravenous fluid in the plastic bag from the outer plastic wrap, an Oschner clamp was used to support the medication port and the latex surface flamed. Since no procedures were required to equalize pressure as seen with the traditional glass bottle, the 10 ml sample of the fluid was next withdrawn. Addition of the sample to the bottle containing fluid thioglycollate media was performed in an identical manner to that described for the glass bottle.

In order to subject the intravenous infusion sets to the same sterility and procedural checks performed on other components of the study, fluid thioglycollate

media was flushed through each set. A rubber-stoppered container of fluid thioglycollate media was flamed, swabbed with a sterile alcohol swab, and 20 ml of media withdrawn by a needle and syringe in the laminar air flow hood. After passing the media through the length of the intravenous infusion set, it was collected in a sterile screwcapped test tube. The opening of the screw-capped test tube was flamed before and after addition of the media.

The final-in-line filters were removed from the manufacturers package and a sterile intravenous infusion set and 20 guage 1 1/2" needle attached. The complete unit, filter, needle and set, was then allowed to stand for 24 hours in the same medication room to be used by the nurses in the study in their assembly of bottles and bags of fluids. At the end of this incubation period, the filter, needle, and infusion set units were transported to the hospital pharmacy for sampling. The unit was dis-assembled in the laminar air flow hood and the filter case opened, the filter membrane and gasket removed using flamed forceps and placed top down on a blood agar plate for one to two hours. In the microbiology laboratory, the filter membrane and gasket were removed and placed in a test tube containing fluid thioglycollate media. Both media were then incubated as other media used in the study and any resulting growth noted.

Phase Two: Preparation by Nurses on a Patient Care Unit

Fifty-five (55) glass bottles and fifty-five (55) flexible plastic bags were sampled in addition to the control solutions by registered nurses accustomed to handling intravenous fluids. In this phase of the study, all supplies required by the nurses to prepare the intravenous fluids were delivered to the unit and

the nurses left alone to prepare them without intimate supervision. While the study personnel were available (by either paging or telephone) for any problems that may be encountered, they were not physically on the unit during the manipulations. The nurses were allowed to read any literature that accompanied the fluid but no additional instructions were forthcoming. The intravenous fluids were to be prepared as for any patient except (1) the additive to be used was 0.9% Sodium Chloride (2) a final in-line filter was to be used (3) instead of inserting the needle into the patient's vein, the fluid was allowed to run into the empty vacuum bottles supplied.

The additives were prepared in the following manner. The nurse, using a 20 ml syringe, withdrew 20 ml of the 0.9% Sodium Chloride without a preservative from the 30 ml single dose vial. Ten ml of the additive was injected into the intravenous fluid container and the remaining 10 ml in the syringe left for the study personnel. The following day when the completed fluids were retrieved, the 10 ml of additive in the syringe was transported to the pharmacy with all other supplies, and in a laminar air flow hood injected into a bottle containing 80 ml of fluid thioglycollate media and incubated at 37°C for seven days. This procedure provided a method of checking each additive for sterility and therefore, subjected the system to another check of its integrity.

After the nurse completed the assembly of the system, she regulated the flow rate to allow one liter to be emptied in approximately two hours. Before the entire liter was emptied, the nurse was requested to stop the flow leaving 50-100 ml of fluid remaining in the container. The entire unit was then allowed to stand until the following day (18-24 hours) undisturbed, on the nursing unit.

Next, the study personnel picked up all of the units and transported them intact to the hospital pharmacy for sampling. In transportation the units were carried along the same pathway a patient would follow if movement were required.

In the laminar air flow hood the samples were collected as follows. The first 10 ml of the remaining intravenous fluid to pass through the needle still attached to the final filter and set was collected in a bottle containing 80 ml of fluid thioglycollate media. The top of the screw-capped bottle was flamed before and after the sample was added. The remainder of the intravenous fluid was allowed to run through the intact set and filter, the last 5 to 10 ml being collected in an empty sterile screw-capped test tube. The test tube top was flamed before and after addition of the sample. Next the final in-line filter was removed from the set-up. The unit was disassembled and using flamed forceps, the gasket and the filter membrane aseptically removed in the laminar air flow hood to a blood agar plate; top side of each facing the media surface.

The 10 ml sample of the additive in the syringe was added to the media in a manner previously described.

The samples were then transported to the microbiology laboratory and the same technician performed the following actions. The two bottles containing the fluid thioglycollate media (the first 10 ml of fluid drawn from the set-up after overnight on the ward and the 10 ml additive control) were placed in the incubator at $37^{o}C$. From the test tube containing the last fluid to pass through the set and filter, a 0.5 ml sample was removed and streaked on a blood agar plate. Next another 0.5 ml sample was removed and streaked on an EMB plate (eosin methylene blue). Finally, 1 ml was removed to a sterile petri dish and a pour plate prepared

using Soybean Casein Digest Agar. All three of these samples were also incubated at 37°C.

The blood agar plates containing the gasket and filter membrane were opened and each removed to a separate test tube containing fluid thioglycollate media. The three samples were likewise incubated at 37°C. Each day the incubating samples were checked and any resulting growth speciated. Incubation and daily checking of the samples continued for seven days.

Phase Three: Preparation of the Intravenous Fluids in a Laminar Air Flow Hood by Pharmacists

In this phase of the study, a pharmacist accustomed to handling intravenous fluids prepared the set-up as would be expected in a central additive service. The pharmacists prepared a total of fifty-five (55) glass bottles and fifty-four (54) flexible plastic bags containing the intravenous fluids. The same supplies were provided to the pharmacist as noted in phase two. Each pharmacist followed the usual pharmacy procedure for preparing intravenous fluids which included a hand scrub using a sterile 3% hexachlorophene scrub sponge (catalog number 3000, Pharmaseal Laboratories), and wearing a lint-free cap and gown, and a surgical mask. The fluids were prepared in a similar manner to phase two, with regard to the additive utilized. The 10 ml remaining in the syringe again served as the control for the additive. The pharmacist also inserted the fluid administration set and attached the final in-line filter. Since the fluids prepared in the glass bottle had an open vent tube, some means of plugging the vent tube for transit had to be devised. A sterile plastic device was aseptically inserted into the vent tube by the pharmacist to fulfill this purpose. The assembled unit

was transported to the nursing station by pharmacy personnel and left for her to "administer". The nurse then attached the appropriate needle, where indicated withdrew the sterile vent tube plug device, and ran the fluids into the empty collection bottle provided. Regulation of the flow rate, retrieval by study personnel, sampling procedures and microbiology methods were identical to phase two. The same room and conditions were also used for the nurses' portion of the experiment.

In both phase two and phase three, the nurse or pharmacist selected one bottle and one plastic bag and deliberately contaminated that unit with a solution containing Escherichia coli. The identity of the contaminated unit was unknown to the personnel performing the sampling and microbiological techniques.

RESULTS

Phase One: Background Data (Table 1)

The fifty (50) one liter plastic bags of 5% Dextrose in Lactated Ringer's did not exhibit any evidence of contamination by the study methodology employed. However, a like number of one liter glass bottles of the same fluid resulted in one bottle yielding a positive culture for a Penicillium species. This represents a rate of contamination of 2%. No positive cultures resulted from forty (40) intravenous infusion sets sampled. The fifty-four (54) final in-line filters sampled produced two positive cultures for a rate of 3.7%. The organisms isolated from the filters were a Staphylococcus epidermidis and a Flavobacterium species.

Blood agar settling plates placed in the laminar air flow hood during all of these sampling procedures yielded a Bacillus species, a Staphylococcus epidermidis, a Mycelium sterilia, a Penicillium species and an Aspergillus species.

Phase Two: Preparation By Nurses on a Patient Care Unit (Tables 2 & 3)

Three general duty registered nurses prepared a total of fifty-five (55) liters of intravenous fluids in the glass bottle and fifty-five (55) liters in the plastic bag. Of the fifty-five (55) glass bottles, four bottles were positive; a rate of 7.1%. The organisms isolated were a Bacillus species, a Streptococcus species and a Staphylococcus epidermidis. The same number of fluids in the plastic bag

produced six positive cultures or a rate of 10.9%. Here the organisms were a Bacillus species, a Micrococcus species, and a Staphylococcus epidermidis. Settling plates of blood agar in the laminar air flow hood concurrent with the sampling procedures revealed a Staphylococcus epidermidis, a Bacillus species, and a Micrococcus species. Blood agar settling plates placed in the same room during nurse preparation yielded an Aspergillus species, a Staphylococcus aureus, a Staphylococcus epidermidis, a Micrococcus species, a Streptococcus species, and a Bacillus species. With the fluids in glass bottles, one nurse (C) accounted for all four of the contaminated fluids detected. However, when utilizing the fluids in plastic bags, this same nurse had no fluids contaminated although the other two nurses (A and B) each contributed three contaminated fluids to the total of six detected.

Phase Three: Pharmacist Preparation in a Laminar Air Flow Hood (Tables 4 & 5)

The two pharmacists prepared fifty-five (55) liters of fluids in glass bottles and fifty-four (54) liters in plastic bags. Three glass bottles were found positive for a contamination rate of 5.4%. The organisms isolated were a Staphylococcus epidermidis, a Micrococcus species, and a Bacillus species. The fifty-four (54) liters in the plastic bag produced three positive cultures; a contamination rate of 5.5%. With the plastic bags the organisms were an Escherichia coli, a Bacillus species and a Staphylococcus aureus.

The blood agar settling plates from the laminar air flow hood during sampling yielded a Bacillus species, a Micrococcus species, and a Staphylococcus epidermidis. Pharmacist B contributed two contaminated fluids to pharmacist A's

one contaminated fluid for both the glass bottle and plastic bag series but in each instance, B prepared a greater number of fluids than did A.

Subsequent discussions with the pharmacist involved revealed that the plastic bag that became contaminated with the Escherichia coli was prepared immediately after purposely contaminating a glass bottle with the control organism, an Escherichia coli. The microbiology laboratory subjected both cultures to further testing and found each to give the same fermentation patterns with those sugar reactions known to be variable in the genus Escherichia; presumptive evidence that the organism emanated from same source as the control organism.

STATISTICAL ANALYSIS

The results of the study were subjected to statistical analysis by Fishers' Exact Test and the Chi Square Test.

The data indicate the contamination rate for nurse preparation of the plastic bags was significantly greater than the background when examined at the 5% level. (Table 6).

When small sample sizes are utilized, such as this study, rates of less than 50% occurrence will tend to be underestimated more often than overestimated. The example stated by Schor[41] provides a graphic demonstration of this tendency. Assuming a prevalence rate of 5% for an occurrence, and using very small sample sizes of five, 774 samples out of every 1000 will yield a 0% prevalence rate (an underestimate) and only 226 out of 1000 on the average will yield rates over 5% (an overestimate). Therefore, a larger sample size would be required to overcome this tendency.

DISCUSSION

As stated by Dudrick[42] "The intravenous route is generally recognized as the most definite and practical means of systemic administration of medication and rapid or massive infusion of electrolytes and fluids." This statement accurately justifies the need for a means of administering intravenous fluids in a practical and efficient manner. However, the patient should be afforded the benefits of this valuable therapeutic tool without being subjected to any unnecessary risk.

While the incident reported by Rupp and Forni[19] is probably an isolated occurrence, the undesirable nature of an air-dependent administration system cannot be denied. By utilizing a non-air dependent system, e.g. Viaflex^{R}, the potential indicated by Perceval,[37] Arnold and Hepler,[39] and Hansen[40] could be eliminated, although the clinical significance of the open airway has not been demonstrated. More concern must be shown for the mode of administering intravenous fluids, but at the same time, any new approach must undergo careful scrutiny.

In conducting a study of this nature, selection of the personnel is a vital factor. The operation of a centralized additive service, the configuration selected for the pharmacists participation in this study, requires that the personnel be familiar with the rudiments of aseptic technique and possess the ability to

perform these tasks without contaminating the system being utilized. It would be anticipated that personnel in this area would be somewhat familiar with the tasks to be performed, although likely of different degrees of proficiency. Therefore, the pharmacists selected for the study were experienced in an additive operation, exhibited a high level of proficiency and an above average awareness for contamination potential. In regard to the selection of nursing personnel for the study, it was felt that to utilize only those nurses thoroughly schooled and familiar with the new system would be somewhat unrealistic. The integrity of the delivery system must be examined in the light of the inevitable staff turnover of of nursing and the necessary time lag in training new personnel. To include only nurses proficient and experienced in a new delivery system would tend to produce spurious results and imply a lower contamination rate than would be encountered in the normal nurse population. In choosing nurses unfamiliar with the non-air dependent delivery system, the system was essentially being challenged to determine its limitations in the face of improper technique. However, to more fully answer this question of improper technique would require training of these same nurses, allowing them to become proficient and then repeating this phase of the study.

The pharmacists did perform one task that is not considered to be routine in many centralized additive programs. Each intravenous fluid prepared by the pharmacists had the administration set attached in the laminar air flow hood, along with the final in-line filter. As a result, when the units arrived at the nursing station the nurse had only to attach the needle to the filter and insert into the vacuum container.

In viewing the data one must appreciate the conditions that are identical and those dissimilar. The nurse assembly of the unit, including needle attachment to pharmacy prepared fluids, was affected in an area normally utilized for this purpose. The medication room had its normal traffic, no attempt being made to alter the environment. On the other hand, pharmacist assembly used an area free from excessive traffic, in a room with the air grossly filtered and the actual preparation in a laminar air flow hood. One condition standard to fluids prepared in both areas was the ward environment in which the fluids were run and allowed to incubate overnight. Here again, no attempt was made to alter the conditions from those normally encountered.

The value of positive concurrent controls cannot be underestimated. It would be most difficult to assess the findings of a study of microbial contamination in the absence of data to define the sensitivity of the procedures. Obviously, one must be able to retrieve organisms added as controls with a degree of reliability and sensitivity that produces a valid finding. For this purpose one unit of each system was innoculated with a known concentration of Escherichia coli for each series run. Although the microorganisms were added on a blind basis, the contaminated unit being known only to the nurse or pharmacist preparing the fluid, the control solution was identified in each instance.

The concentration of the control solution of Escherichia coli ranged from 113 Colony Forming Units per 10 ml to 230 Colony Forming Units per 10 ml with an average concentration of 171 Colony Forming units per 10 ml. No attempt was made to quantitate the Escherichia coli recovered from the control solutions.

Based on the concentrations of the control solutions added to the one liter containers, the lower limits of detection would appear to be less than one colony forming unit per milliliter. However, the ideal detection capability should be one colony forming unit in the entire container, since a solution with one microorganism is contaminated.

Chance observation revealed that microorganisms from the control fluids were not found in the filtrate, i.e. the fluid collected after passing through the final filter, except in one incident when the filter membrane was found to be ruptured when opened. This finding would appear to agree with others[43] indicating that the final filter effectively removes most bacteria from the fluid being administered.

When one begins to examine the microorganisms encountered in any work of this nature, the immediate tendency of the neophyte is to classify the organisms by pathogenicity, i.e. pathogenic or non-pathogenic. In reality, however, the potential for pathogenicity must include the organisms that constitute the body flora and may subsequently cause an opportunistic infection.[44] Dalton and Allison[45] showed that Staphylococcus epidermidis, usually considered non-pathogenic, was the causative agent in a significant percentage of bacteremias in their hospital. Although usually considered to be contaminants, the presence of microorganisms such as Staphylococcus epidermidis must be viewed with concern since bacterial endocarditis resulting from this agent cannot be considered a rarity.[45] Some workers have suggested that these facultatively pathogenic organisms may be an intermediate group between the really non-pathogenic strains and documented pathogenic strains of staphylococci.[46] In any event the presence

of microorganisms in intravenous fluids must be considered potentially harmful regardless of the origin of contamination.

The microorganisms encountered in this study appeared to be from touch contamination. The significance of air-borne contamination was not shown. Those microorganisms found in the collection of background data could easily be attributed to technique, but never-the-less, at a level acceptable to the study personnel and permitting advancement to the subsequent phases.

It is interesting to note that nearly one-fourth of the glass bottles prepared by one nurse were contaminated, the other two nurses having no bottles contaminated (Table 2). However, this same nurse, when utilizing the plastic bag had none contaminated while the other two nurses had approximately one-sixth of each of theirs contaminated (Table 3). The explanation for this finding was not apparent.

When the pharmacists prepared the fluids in a laminar air flow hood, the findings were the same for both glass bottles and plastic bags, no difference in either the rate of contamination or the individual preparing the fluid (Tables 4 & 5). The occurrence of the one plastic bag with Escherichia coli contamination was the cause of considerable concern. While it appeared the Escherichia coli was the same strain as used for control purposes, this contamination in the hands of a most capable pharmacist shows that the laminar air flow hood alone does not assure sterility of admixtures. Meticulous care must be exercised by the personnel at all times even in the laminar air flow hood. The standard procedures employed by the pharmacists in this study, i.e. a disposable lint-free gown with elasticized wrist bands, a surgical mask and cap and the scrub procedure

with sterile 3% hexachlorophene should be considered the minimum acceptable standard. Cleansing of all products placed in the hood with 70% isopropyl alcohol reduces particulate matter and keeps the microbial contamination to a minimum, both of vital concern to the practicing pharmacist.

The blood agar settling plates placed in the laminar air flow hood during each sampling procedure further indicates that the environment inside the hood is far from sterile (Tables 1-5). During the sampling procedures, study personnel wore surgical masks and sterile gloves while working in the laminar air flow hood and did not work between the filter and the blood agar settling plates.

The individual preparing admixtures must not undertake this task with a cavalier attitude on the false assumption the laminar air flow hood will cover up his shortcomings.

CONCLUSIONS & RECOMMENDATIONS

The following points can be concluded from this study:

1. Using personnel with no training in the proper use of the flexible plastic bag, no significant difference in the contamination rate could be seen when compared to the traditional glass bottle.
2. A non-air-dependent intravenous fluid administration system should prove safer for the patient in that non-sterile ambient air does not enter the container and come into intimate contact with the fluid.
3. Based on the organisms detected, the data show that touch contamination is the major source of contamination in the intravenous fluid delivery systems tested.
4. A central intravenous fluid additive service can be expected to reduce the level of contamination encountered in the fluids if the proper technique is employed.
5. A laminar air flow hood alone is not sufficient to insure sterile intravenous fluids. Hospital pharmacists should utilize the laminar air flow hood coupled with a greater awareness of the technique required to provide a sterile product.
6. The laminar air flow hood does have limitations and should not be challenged by the operator, his lack of proper attire, and improper technique.
7. Airborne contamination was not shown to be a major factor in overall contamination of intravenous fluids.

The intravenous fluid delivery system should be designed to require a minimum of manipulations to administer to the patient since touch contamination appears to play a major role in contamination.

The introduction of the non-air-dependent intravenous fluid delivery system is the first step in closing the entire intravenous administration system to entry of microorganisms. The airborne contamination, although of undocumented clinical significance, has been eliminated by the flexible plastic bag. The next area that should be attacked by first the pharmacist and then industry is the problem of touch contamination. The individual pharmacist in the hospital may take action by attaching the administration set in the environment of the laminar air flow hood, thereby, preventing exposure of the system to an uncontrolled situation. Next industry may take the initiative by providing an intravenous fluid administration system of proven sterility by manufacture of the container and administration set as an integral unit, eliminating manipulations at the patient bedside, the medication room, or even the laminar air flow hood. Admittedly, this approach would be less flexible from the standpoint of multiple administration sets, than is now seen, but the decision must be made. Is contamination of intravenous fluids the price to pay for the flexibility of numerous different administration sets?

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TABLE I

Number of Positive Cultures and Microorganisms Isolated
from Individual Components - Background Data

Component Cultured	Number of Components	Number of Positive Cultures	Species of Organism Isolated
Fluid in Flexible Plastic Bags	50	0	None Isolated
Fluid in Glass Bottles	50	1 (2%)	Penicillium species
Infusion Sets	40	0	None Isolated
Final In-line Filters	54	2 (3.7%)	Staphylococcus epidermidis Flavobacterium species
Blood Agar Settling Plates in Laminar Air Flow Hood	16	4 (25%)	Bacillus species, Penicillium species, Aspergillus species, Mycelium sterilia, Staphylococcus epidermidis

TABLE 2

Number of Positive Cultures and Microorganisms Isolated
from Units Assembled by Nurses
on a Patient Care Unit - Glass Bottles

Nurse	Number of Units Prepared	Number of Positive Cultures	Species of Organism Isolated
A	19	0	None Isolated
B	18	0	None Isolated
C	18	4 (22%)	Staphylococcus epidermidis, Bacillus species Streptococcus species
Controls	9	9 (100%)	Escherichia coli
Total Less Controls	55	4 (7.1%)	Staphylococcus epidermidis, Bacillus species, Streptococcus species
Blood Agar Settling Plates in Laminar Air Flow Hood	18	3 (16.7%)	Staphylococcus epidermidis, Micrococcus species, Bacillus species

TABLE 3

Number of Positive Cultures and Microorganisms Isolated
from Units Assembled by Nurses
on a Patient Care Unit - Plastic Bags

Nurse	Number of Units Prepared	Number of Positive Cultures	Species of Organism Isolated
A	19	3 (15.8%)	Bacillus species, Staphylococcus epidermidis, Micrococcus species
B	18	3 (16.7%)	Bacillus species, Micrococcus species
C	18	0	None Isolated
Controls	9	9 (100%)	Escherichia coli
Total Less Controls	55	6 (10.9%)	Bacillus species, Staphylococcus epidermidis, Micrococcus species
Blood Agar Settling Plates in Laminar Air Flow Hood	18	3 (16.7%)	Staphylococcus epidermidis, Bacillus species, Micrococcus species

TABLE 4

Number of Positive Cultures and Microorganisms Isolated from Units Assembled by Pharmacists in a Laminar Air Flow Hood - Glass Bottles

Pharmacist	Number of Units Prepared	Number of Positive Cultures	Species of Organism Isolated
AT	23	1 (4.3%)	Staphylococcus epidermidis,
BW	32	2 (6.2%)	Micrococcus species, Bacillus species
Controls	10	10 (100%)	Escherichia coli
Total Less Controls	55	3 (5.4%)	Staphylococcus epidermidis, Micrococcus species, Bacillus species
Blood Agar Settling Plates in Laminar Air Flow Hood	20	3 (15%)	Staphylococcus epidermidis, Bacillus species, Micrococcus species

TABLE 5

Number of Positive Cultures and Microorganisms Isolated from Units Assembled by Pharmacists in a Laminar Air Flow Hood - Plastic Bags

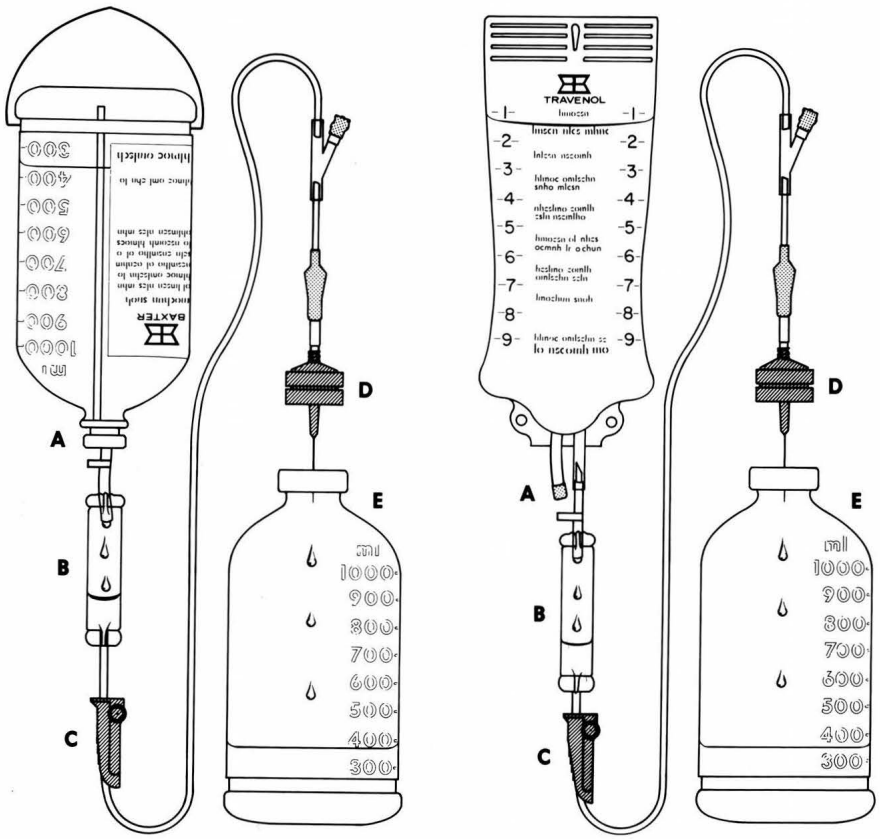
Pharmacist	Number of Units Prepared	Number of Positive Cultures	Species of Organism Isolated
A	24	1 (4.2%)	Escherichia coli
B	30	2 (6.7%)	Staphylococcus aureus, Bacillus species
Controls	10	10 (100%)	Escherichia coli
Total Less Controls	54	3 (5.5%)	Escherichia coli, Bacillus species, Staphylococcus aureus
Blood Agar Settling Plates in Laminar Air Flow Hood	20	3 (15%)	Staphylococcus epidermidis, Bacillus species, Micrococcus species

TABLE 6

Statistical Analysis
Confidence Limit at 95% Interval (P=O.O5)

	Background	Pharmacists	Nurses
Plastic Bags	0.08	0.02-0.17	0.06-0.27
Glass Bottles	0.01-0.13	0.01-0.17	0.025-0.19

FIGURE 1



Configuration of Complete Units as Tested

A. Site for insertion of administration set

B. Drip chamber of administration set

C. Roller clamp supplied by manufacturer

D. Final in-line filter

E. Vacuum collection bottle