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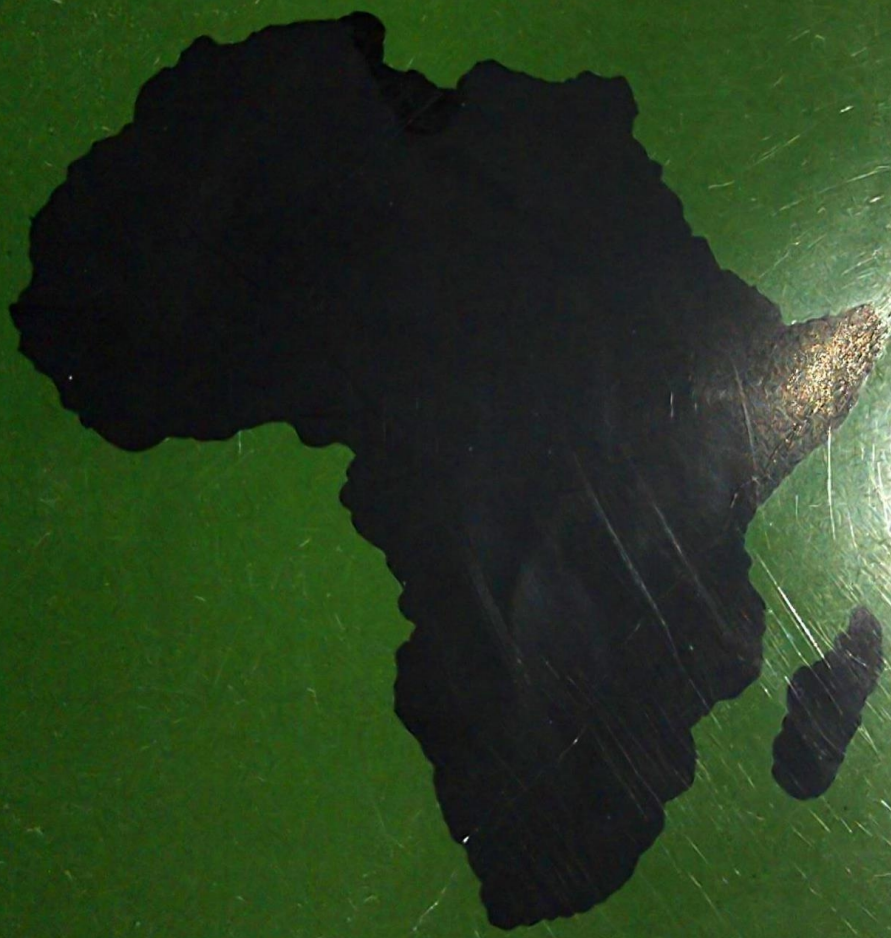

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# The influence of cuprophan and polysulfone membranes on dialyzer reusability and intradialytic complications

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**Summary**
The influence of cuprophan and polysulfone membranes on dialyzer reuse and intradialytic complications was examined in patients receiving chronic haemodialysis.Mean uses were 2.7±1.3 S.D. and 2.2±1.0 S.D. for cuprophan and polysulfone respectively ($P < 0.001$). 20.8% and 35..5% of cuprophan and polysulfone dialyzers respectively did not survive first use ($X^2 = 17.4$, $P < 0.001$), being unsuitable for further use. The most common number of uses obtainable was 3 for each type. 2.6% of cuprophan but none of the polysulfone dialyzers were usable over 5 times. Hypotension occurred in 12% and 29% of dialyses with cuprophan and polysulfone dialyzers ($P < 0.001$), and the difference persisted, but the frequency in each membrane group decreased, with reuse ($P < 0.001$). First use reactions occurred in 9.5% and 3.9% of dialyses with cuprophan and polysulfone respectively ($P < 0.001$), and the difference was not affected by reuse ($P > 0.1$), but the frequency decreased in each group ($P < 0.001$). Clotting of the dialyzer occurred in 2.2% and 1.9% of cases respectively ($P > 0.5$), diminished with reuse of cuprophan ($P < 0.001$), but not with polysulfone ($P > 0.5$). Cuprophan membrane was more reuseable and was associated with fewer episodes of hypotension, while polysulfone was associated with fewer episodes of first use reactions.Rational choice of membranes can be made during haemodialysis.

**Keywords:** *haemodialysis, membranes, reuse, biocompatibility.*

**Résumé**
L'influence du cuprophan et des membranes polysulfones sur re-usage du dialyseur et les complications intradialytiques a ete examinee chez des patients recevant une haemodialyse chronique les moryennes d'usage itaient de 2.7±1.3 S.D. et 2.2±0 S.D. pour le cuprophan et les dialy sour polysulfones respectivement ɳ'ont par survein le premier usage (X2=17.4, $P < 0.001$), etant insupportable pour usage futur.. Le plus grand numbre commun des usages obtenables itait trois pour chaue type. L'hypotension est apparue dans 12% et 29% des dialyses an cuprophan et dialyseurs poly sulfones ($P < 0.001$), et la difference a persiste, mais la frequence dans groupe. decroissait, avec re-usage ($P > 0.1$) rairs la frequence decroissant dans chaque groupe ($P < 0.001$). La coagulation du dialyseur a enlieu dans 2.2% et 1.9% des cas respectivement ($P > 0.5$), dim mait avec re-usage an cuprophan ($P < 0.001$), mais pas avec le polysulfone ($P > 0.5$). La membrane cuprophan etait plus reutilisable et etait associee aux episodes de fievre d'hypotension, alors que le polysulfone etait associe ounx episodes de fievre des reaction au premier usage un cloix rational de membranes pent fait an courant des hemodialyses.

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## Introduction

The functional essential component of the haemodialysis system is the dialyzer whose configuration is hollow fibre or parallel plate nowadays. Of these, the hollow fibre is the more efficient and more widely used, in Nigeria, and worldwide [1]. The dialyzer membrane is the critical component of the system, and can be assessed according to performance, biocompatibility and cost. Biocompatibility is the sum of the interactions between blood and materials used in dialysis, most notably the dialyzer membrane [2]. In Nigeria, the currently available dialyzers have membranes made of cuprophan (cuprammonium cellulose) or polysulfone. Cuprophan, the classic cellulose membrane is derived from cotton, a naturally occurring substance, while polysulfone is a synthetic membrane. Differing membrane, characteristics may cause substantial differences in the reusability of dialyzers [3] and complications associated with dialysis [4]; synsthetic membranes are thought to be more biocompatible than cellulose membranes such as cuprophan [4,5]. We examined the influence of dialyzer membrane type on these parameters of haemodialysis in our practice. The findings may be useful in the rational use of membranes in haemodialysis, a procedure which has recently come into rather wide use in Nigeria [6].

## Patients and methods

The study period covered nine years during which 989 patients with chronic renal failure received 2581 sessions of haemodialysis. Patients who were hepatitis and human immunodeficiency virus positive were excluded. Hepatitis positive patients were dialysed under a different arrangement which did not permit reuse.

Haemodialysis was carried out using single delivery automatic proportioning machines with acetate as base. Duration was normally for 3 hours at initiation and maintained at 4 hours thereafter. Dialysate flow rate was 500mL/min, maintenance blood flow rate 200mL/min and ultrafiltration was by automatic volumetric control as indicated. Hollow fibre dialyzers were used, and membrane was either cuprophan or polysulfone used as available and without selection bias. Cuprophan dialyzers had membrane surface areas 0.8m² to 1.3m², in vitro urea clearances 160 to 177mL/min and in vitro ultrafiltration co-efficient 4-6mL/mm.Hg/Hour. Polysulfone dialyzers had membrane surface areas 1.0 to 1.3m², in vitro urea clearances 170-180mL/min and ultrafiltration co-efficient 4-5.5mL/mm.Hg/Hour. Mode of sterilization was by ethylene oxide for all. Inradialytic monitoring was carried out automatically by the machine and by an attendant as appropriate. Hypotension was defined as a fall in blood pressure greater than systolic or diastolic of 25/10mm.Hg and was usually accompanied by feelings of unwell, dizziness, light headedness, nausea and muscle cramps [5]. First use reactions were characterized by itching, rhinor-

rhoea, urticaria, abdominal cramps, vomiting, chest pain back pain and dyspnoea [5].

Eligible patients entered a reuse programme in which the dialyzers and blood lines were processed before the first use and thereafter after each use in readiness for the next dialysis. Details of the reuse procedure have been previously described [6] and essentially consisted of flushing and storage in formalin. The reusability of a dialyzer was based on a volumetric test, whereby a dialyzer could be reused only if the blood compartment volume remained above 75% of the initial value [7].

*Statistics:* Comparison of means was by the z-test, and comparison of proportions was by chi-square test. Trend in proportions was examined by the Mantel-Haensczel test. Significance was at $p < 0.05$.

## Results

The number of dialyses by membrane type and the reusability of the dialyzers is shown in table 1. 2168 dialyses were obtained from 803 cuprophan dialyzers giving a mean use of 2.7±1.3 S.D, while 413 dailyses were obtained from 186

**Table 1**: Dialyzers by membrane type and their reusability

| No of Uses | Cuprophan | Polysulfone |
|---|---|---|
| 1 | 167 | 66 |
| 2 | 153 | 31 |
| 3 | 332 | 72 |
| 4 | 83 | 16 |
| 5 | 47 | 1 |
| 6 | 17 | 0 |
| 7 | 2 | 0 |
| 8 | 2 | 0 |
| Total | 803 | 186 |

*Values are n*

polysulfone dialyzers with a mean of 2.2±1.0 S.D. uses. The difference between the means was significant ($P < 0.001$). 332 (41%) and 72 (39%) of cuprophan and polysulfone dialyzers respectively, could be used 3 times and 21(2.6%) of the cuprophan dialyzers but none of the polysulfone dialyzers, could be used over 5 times. There was a disproportionately higher proportion of polysulfone dialyzers that were found to be unsuitable for further use after the first dialysis. (35.5%) vs. 20.8%, $X^2 = 17.8$, $P < 0.001$).

The relationship between the membrane type and the major complications encountered during haemodialysis is summarized in table 2. Data was unobtainable for the 4 dialyzers that were used up to 7 times, and these accounted for 30 of the 2168 sessions (1.4%). Hypotension occurred in 12% and 29% of dialyses employing cuprophan and polysulfone membranes, respectively ($X^2 = 83.7$, $P < 0.001$), and the difference was not affected by reuse ($X^2 = 2.43$, $P > 0.5$). However, in each membrane group, the frequency of occurrence of hypotension decreased significantly with reuse as shown by the Mantel-Haensczel test for trend ($X^2 = 370.9$, $P < 001$ for cuprophan, and $X^2 = 124.0,0$, $P < 0.001$ for polysulfone).

**Table 2:** Complications of haemodialysis in relation to membrane type and number of uses of dialyzer

| Complications | Uses of dialyzer 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|
| Hypotension | | | | | | |
| cuprophan | 112 (167) | 76 (306) | 50 (996) | 11 (332) | 2 (235) | 2 (102) |
| Polysulfone | 49 (66) | 41 (62) | 24 (216) | 6 (64) | 0 (5) | 0 (0) |
| First use reaction | | | | | | |
| cuprophan | 51 | 45 | 83 | 15 | 7 | 2 |
| Polysulfone | 7 | 4 | 4 | 1 | 0 | 0 |
| Clotting | | | | | | |
| cuprohan | 19 | 15 | 14 | 0 | 0 | 0 |
| Polysulfone | 1 | 4 | 2 | 1 | 0 | 0 |

*Values are n*
*Numbers in brackets are total number of dialyses*

First use reactions occurred in 203 of the 2138 dialyses with cuprophan (9.5%), and in 16 of the 413 (3.9%) with polysulfone membrane, the difference being statistically significant ($X^2 = 13.4$, $P < 0.001$). Because of the small numbers in the polysulfone group for the third to sixth uses, they were pooled for analysis. The difference in the occurrence of reactions was not affected by reuse ($X^2 = 3.63$, 2 df, $P > 0.1$), but the frequency decreased with reuse with cuprophan ($X^2 = 92.9$, $P < 0.001$) and with polysulfone ($X^2 = 11$, $P < 0.001$) membranes.

Clotting of the dialyzer occurred during 48 (2.2%) and 8 (1.9%) dialyses with cuprophan and polysulfone membranes, respectively, the difference being insignificant ($X^2 = 0.114$, $P > 0.5$). However, the frequency of occurrence showed a decreasing trend with reuse with cuprophan membranes ($X^2 = 61.8$, $P > 0.001$), but not with polysulfone membranes ($X^2 = 0.9$, $P > 0.5$).

## Discussion

It has been possible to examine the relative performances of cuprophan and polysulfone membranes used in a somewhat random manner, albeit, fortuitously and retrospectively, even though there had been no deliberate randomization from the outset. In similar manner, there was no reason to suppose that the patients were significantly different and the large numbers ensured some even distribution.

Of the membranes commonly in use today, cellulose membranes are the oldest. Derivatives of substituted cellulose in which hydroxyl group has been replaced, and later the synthetic membranes followed. Synthetic membranes other than polysulfone include polyacrylonitrile, polymethylmethacrylate and polycarbonate. The development of synthetic membranes made modifications to membrane thickness and pore size easier providing greater flexibility in dialysis. This has been utilized to the utmost in high flux dialyzers which give very high clearances and permit shorter dialysis lengths. In certain situations cost considerations may influence the choice of membrane [8], but this was not the case in our study, as the costs of the 2 types of dialyzers were similar in Nigeria.

Dialyzer reuse is crucial to our dialysis programme, and has been shown to be viable [6, 9] and cost effective in Nigeria [6] and elsewhere [10]. Although about 40% of either dialyzer type could be used 3 times, the findings from this study suggest the superior reusability of cuprophan mem-

branes, and barring other considerations, should be prescribed where cost considerations are paramount. A study which compared cuprophan and polyacrylonitrile, another synthetic membrane, reached a similar conclusion, although it applied only to small surface area dialyzers [3] such as those used in our study. In that study, larger dialyzers of surface area 1.8m² lost volume with formalin and were less reusable. A more recent study [11] involving high efficiency cuprophan and polysulfone dialyzers showed significant falls in urea and creatinine clearances with polysulfone, but not with cuprophan, and showed a rise in beta-2-microglobulin clearance with polysulfone but not with cuprohan dialyzers. The clearance of beta-2-microglobulin is a measure of middle molecules clearance and is associated with reduced morbidity on dialysis [12].

Another important consideration in membrance assessment is its biocompatibility. A membrane is more biocompatible if its use is accompanied by fewer or less severe complications. Hypotension is a common complication of haemodialysis, and is often due to excessive ultrafiltration, variablities in sodium levels in the dialysate and the use of acetate as base [5]. Cellulose membranes may stimulate interleukins and cause hypotension [13] while polysulfone membranes may be associated with excessive ultrafiltration because of the usually high ultrafiltration co-efficients. In this study however, ultrafiltration co-efficients were not high and ultrafiltration was achieved by automatic volumetric control, yet the polysulfone dialyzers were associated with a greater frequency of hypotension. The reason for the increased frequency of hypotension with polysulfone is not quite clear, but a previous study had failed to demonstrate a difference in intradialytic well being between cuprophan and polysulfone hollow fibre dialyzer [14]. The frequency of hypotension in that study was actually higher with polysulfone dialyzers, but the difference was not statistically significant. The decreasing occurrence with reuse observed in our study would suggest the roles of factors such as increased washout of offending agents and possibly, albumin coating of membranes, factors involved in biocompatibility. This view is not consistent across studies, as shown by a study of cuprophan dialyzers during reuse [15]. In that study [15] there were no differences in biocompatibility, intradialytic symptoms and signs including hypotension, when using single use and multiple use dialyzers.

First use reactions are so named because they most commonly occur during the first use of a dialyzer [16] and diminish as the dialyzer is reused. They consist of a collection of symptoms and signs which characteristically occur during the first 30 minutes of dialysis, and are considered to result from reactions of the blood with residual ethylene oxide used for sterilization of the dialyzer, and also from interactions with the dialyzer membrane [2]. In our study, they occurred more often with cuprophan membranes, suggesting a role of the membrane.They diminished with reuse, in agreement with some other studies [17,18), but not with others [15]. Cuprophan membranes have for long been considered to be less biocompatible [4,5] than synthetic membranes, they activate complement via the alternative pathway [19], and are associated with increased frequency of first use reactions. Reuse of dialyzers leads to the deposition of a thin layer of albumin on the membranes which prevents direct blood and membrane interactions and results in reduced frequency of reactions. This protection may be lost if bleach is used in the reprocessing as it removes the albumin from the membrane. In addition, reprocessing results in a gradual washout of residual ethylene oxide. Clotting of the dialyzer is more often related to inadequate heparinization, but can follow activation of complement and the clotting mechanism [2]. In this study clotting ocurred with about equal frequency in cuprophan and polysulfone dialyzers, but reuse had a favourable effect on only cuprophan dialyzers. The reason is not obvious, and the small numbers may make conclusions difficult.

The summary of our findings suggest that although 40% of both dialyzer types could be used 3 times, cuprophan dialyzers, are more reusable and are associated with fewer hypotensive episodes, while polysulfone dialyzers are associated with fewer first use reactions. Polysulfone dialyzers may therefore be more suitable for use in hypertensive patients. The influence of the use of bicarbonate as base during dialysis on membrane characteristics and the influence of the membrane type on long term dialysis have not been evaluated in this study. Bicarbonate dialysis is associated with fewer episodes of hypotension overall, [5]. It has been difficult to sustain dialysis for any length of time except in a few cases, due to the relatively high cost of dialysis [9]. In the absence of any organised health care subsidy programme, the cost of treatment is borne by the patients, and cost considerations become pre-eminent. Long term evaluation would permit the estimation of survival which is perhaps a better and encompassing index of biocompatibility. For the moment at least, short term evaluation is the only reality, and our findings must be interpreted in this context.

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