High-Flux Hemodialysis without Hemoperfusion Is Effective in Acute Valproic Acid Overdose

Sandra L Kane, Marigel Constantiner, Alfred E Staubus, Curt D Meinecke, and John R Sedor

OBJECTIVE: To report a case of valproic acid overdose treated successfully with high-flux hemodialysis without the addition of charcoal hemoperfusion.

CASE SUMMARY: A 25-year-old white woman with a history of multiple suicide attempts and schizophrenia presented after ingesting an unknown amount of valproic acid. She became comatose and developed hypotension and lactic acidosis as valproic acid concentrations increased to >1200 µg/mL (therapeutic concentration 50–100). High-flux hemodialysis was performed for four hours; the calculated elimination rate constant (k_e) during the procedure was 0.2522 h⁻¹ with a half-life (t_{1/2}) of 2.74 hours compared with posthemodialysis k_e of 0.0296 h⁻¹ and t_{1/2} of 23.41 hours, suggesting that high-flux hemodialysis effectively eliminates valproic acid. The patient’s hemodynamic status and mental function improved in conjunction with the acute reduction in valproic acid concentrations. Her subsequent hospital course was complicated only by transient thrombocytopenia.

DISCUSSION: Most literature reports of valproic acid overdose have described the use of charcoal hemoperfusion alone or in combination with hemodialysis to accelerate valproic acid clearance at toxic concentrations. However, the pharmacokinetic properties of valproic acid indicate that hemodialysis alone would be effective therapy for an acute valproic acid overdose.

CONCLUSIONS: We suggest that toxic concentrations of valproic acid can be effectively reduced with high-flux hemodialysis without the addition of charcoal hemoperfusion and its attendant risks.

KEY WORDS: hemodialysis, valproic acid, overdose, thrombocytopenia.

Valproic acid is commonly used for focal and generalized seizures, bipolar disorders, and migraines. In the setting of accidental or intentional ingestion of valproic acid overdose, serious toxicities have been reported including leukopenia, thrombocytopenia, hemodynamic compromise, respiratory failure, cerebral edema, renal failure, hepatotoxicity, and coma. More than 8000 toxic exposures of valproic acid were reported to the American Association of Poison Control Centers in 1998.

The optimal treatment for life-threatening valproic acid intoxication has not been determined. Forced diuresis to accentuate valproic acid excretion is unlikely to be efficacious, since only 1% of the drug is excreted unchanged in the urine. Valproic acid usually has a rapid absorption; therefore, treatment with lavage and a single dose of activated charcoal is useful if the patient is treated prior to complete drug absorption. Repeated administration of activated charcoal does not enhance the rate of elimination of valproic acid at therapeutic concentrations; however, toxic concentrations have been reduced by bolus or continuous infusion of multiple-dose activated charcoal (MDAC). Charcoal hemoperfusion alone or in combination with hemodialysis is reported to be an effective treatment option for valproic acid intoxication.

The pharmacokinetic properties of valproic acid suggest that hemodialysis without charcoal hemoperfusion could be effective therapy for an acute valproic acid overdose. Valproic acid has a low molecular weight and a small volume of distribution. Additionally, treatment with hemodialysis alone avoids the risks associated with charcoal hemoperfusion. Serum valproic acid concentrations >150 µg/mL saturate protein binding sites and result in elevated unbound concentrations. Given these premises, we successfully treated a patient with valproic acid intoxication exclusively with high-flux hemodialysis.

CASE REPORT

A 25-year-old white woman presented to the emergency department at MetroHealth Medical Center, Cleveland, Ohio, via emergency medical services after reportedly ingesting an unspecified amount of valproic acid and doxepin, as well as consuming large...
quantities of alcohol. The patient’s past medical history included multiple suicide attempts, schizophrenia, alcohol dependence, and alcohol dependence–associated depression, for which she was being treated with valproic acid and fluoxetine.

The patient was unresponsive on arrival to the emergency department, although she reportedly was combative and argumentative at home. She developed shallow respirations and a diminished gag reflex, and subsequently was intubated for airway protection. Her BP was 160/90 mm Hg and her HR was 126 beats/min. After intubation, arterial blood gas analysis revealed pH 7.32, PaCO$_3$ 30.5 mm Hg, PaO$_2$ 151.2 mm Hg, and HCO$_3$ 15.4 mEq/L. Gastric contents were emptied via nasogastric tube after instillation of 500 mL of NaCl 0.9% and 50 g of charcoal. The lavage fluid was dark brown, with no sign of unabsorbed medications. Gastric lavage was continued until the fluid was clear. Complete blood count was significant for macrocytosis (mean corpuscular volume 100.9 µm$^3$). Routine laboratory test results showed a hematocrit of 45%, albumin of 3.8 g/dL, and electrolytes within normal limits. Electrocardiogram revealed sinus tachycardia without widening of the QRS complex. A toxicology screen demonstrated ethanol and valproic acid concentrations of 261 mg/dL and 948 µg/mL, respectively. Doxepin concentrations were not immediately available, but were later determined to be <10 ng/mL. The patient was transferred to an intensive care unit for further management of a probable valproic acid overdose.$^{17}$

In the intensive care unit, the patient remained obtunded. Her sodium concentration was elevated (152 mEq/L), with an anion gap of 21 mEq/L. The free water deficit was calculated to be 3 L, which was gradually corrected with D$_5$W over the next 48 hours. Serum osmolality was 334 mOsm/kg, and the calculated osmolar gap normalized to 50 mOsm/kg when corrected for the serum alcohol concentration. Liver function test results were normal (aspartate transaminase 31 IU/L, alanine transaminase 21 IU/L). Approximately two hours after admission, the patient developed serious metabolic acidosis while still intubated (pH 7.21, PaCO$_2$ 25.1 mm Hg, PaO$_2$ 152.4 mm Hg, HCO$_3$ 9.9 mEq/L), despite receiving two bolus doses of sodium bicarbonate 50 mEq. The metabolic acidosis subsequently worsened (pH 7.16, PaCO$_2$ 24.4 mm Hg, PaO$_2$ 112.0 mm Hg, HCO$_3$ 7.0 mEq/L on forced inspiratory oxygen at 30%), and a sodium bicarbonate infusion was initiated. Concurrent with the development of worsening acidosis, she became hypotensive (systolic BP 81 mm Hg). NaCl 0.9% volume resuscitation restored the blood pressure to normal, but the serum calculated anion gap decreased to 17 mEq/L, and serum lactate was 9.8 mEq/L. Given the clinical deterioration of the woman approximately 20 hours after her arrival, high-flux hemodialysis was initiated to accelerate valproic acid removal and treat metabolic acidosis.

A highly permeable polysulfone dialyzer membrane (F80, Fresenius, Ogden, UT) was used for dialysis. During a four-hour hemodialysis session, the blood flow rates ranged between 200 and 350 mL/min via femoral vein dialysis catheter, and dialysate flow rate was 800 mL/min. Valproic acid concentrations were drawn at 20 minutes, and one, two, three, and four hours after dialysis initiation from the arterial (A) and the venous (V) ports of the hemodialysis system and then randomly throughout her hospitalization. Serum valproic acid concentrations were measured using a standard assay (CEDIA Valproic Acid II Homoge-

Table 1 lists the valproic acid concentrations and the pharmacokinetic variables for four hours of high-flux hemodialysis. K$_p$ is the partition coefficient of the drug between red blood cells and the plasma, which is reported to be 0.28 ± 0.06 for valproic acid.

![Figure 1. Valproic acid concentrations during the patient’s hospitalization. The inset illustrates the effect of four-hour high-flux hemodialysis to the valproic acid concentrations.](image)

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Valproic Acid Serum Concentration (µg/mL)</th>
<th>Q$_b$ (mL/min)</th>
<th>E (mL/min)</th>
<th>Cl$_p$ (mL/min)</th>
<th>Cl$_b$ (mL/min)</th>
<th>dAe/dt (mg/h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.00</td>
<td>948</td>
<td>900</td>
<td>0.47</td>
<td>141</td>
<td>95.3</td>
<td>4283.4</td>
</tr>
<tr>
<td>10.33</td>
<td>1294</td>
<td>1000</td>
<td>0.40</td>
<td>140</td>
<td>94.6</td>
<td>3270.8</td>
</tr>
<tr>
<td>20.33</td>
<td>High-flux hemodialysis started</td>
<td>1200</td>
<td>0.33</td>
<td>126</td>
<td>69.9</td>
<td>1287.7</td>
</tr>
<tr>
<td>24.33</td>
<td>High-flux hemodialysis completed</td>
<td>1400</td>
<td>0.52</td>
<td>187</td>
<td>126.4</td>
<td>2252.6</td>
</tr>
</tbody>
</table>

Cl$_b$ = blood clearance; Cl$_p$ = plasma clearance; dAe/dt = rate of drug elimination by hemodialysis; E = extraction ratio; NA = not appropriate; Q$_b$ = blood flow rate.

*Elapsed time from arrival to the emergency department.
Valproic acid. These data were used to determine the whole blood to plasma ratio (Cv/Cp = 0.676) with the equation:

\[ C_b = (C_v - C_p)/C_v \]

Whole blood hemodialysis clearance was calculated using the equation \( CL = Q (\text{blood flow rate, mL/min}) \times E \). The rate of drug elimination was determined by \( dAe/dt = C_p (\text{arterial blood concentration, } \mu g/mL \times CL_p (\text{whole blood hemodialysis clearance, mL/min}) \). Since \( dAe/dt \) remains unchanged for blood and plasma, the clearance was \( CL_p = (C_v/C_p) \times CL \). The patient’s apparent plasma volume of distribution \( V_p^D \) at supratherapeutic concentrations was 0.3608 L/kg; values reported at therapeutic concentrations were 0.13–0.14 L/kg. \( V_p^D \) is necessary in order to quantitate the amount of drug effectively eliminated via hemodialysis compared with the patient’s normal elimination process (Table 2).

During the four-hour hemodialysis session, the extraction ratio ranged between 0.33 to 0.62, and calculated whole blood hemodialysis clearances ranged from 99 to 187 mL/min. Calculated plasma hemodialysis clearances ranged between 67 to 126 mL/min. The calculated first-order rate constant \( (k_{HD}) \), during hemodialysis was 0.2522 h\(^{-1} \), with a corresponding \( t_{1/2} \) of 2.74 hours. The posthemodialysis first-order rate constant, the \( k_p \), was 0.0296 h\(^{-1} \), with a corresponding \( t_{1/2} \) of 23.41 hours. During the course of hemodialysis, the patient’s clinical status improved as her valproic acid concentration decreased to 149 \( \mu g/mL \). She became alert and responsive with improvement in hemodynamics (systolic BP between 130 and 140 mm Hg, HR 110 beats/min). A small increase in valproic acid concentration occurred between hours 6 and 13 after hemodialysis was terminated, which was not associated with clinical deterioration. The patient was extubated without incident 20 hours after hemodialysis and was transferred to an inpatient psychiatry unit.

### Discussion

Most reports of the treatment of valproic acid overdose with extracorporeal techniques include hemoperfusion with or without hemodialysis. Drug characteristics that aid in determining effective removal with hemodialysis include water solubility, \( V_d \), molecular weight, and the extent of protein binding. Valproic acid is poorly water-soluble, suggesting that it would be poorly dialyzed from the blood into the dialysate. In contrast, other pharmacokinetic characteristics of the drug suggest it would be effectively removed from circulation by dialysis. These properties include a \( V_d \) for valproate (0.1–0.5 L/kg) and a low molecular weight. Furthermore, the protein binding of valproic acid suggests that an overdose can be effectively managed with high-flux hemodialysis.

Valproic acid is approximately 80–95% protein-bound at therapeutic concentrations. However, in healthy individuals, the protein binding decreases to 70% when drug concentrations are > 150 \( \mu g/mL \). At valproic acid concentrations of 300 \( \mu g/mL \), protein-bound drug diminishes to 35%.

The percentage of unbound drug that increases as valproic acid concentrations exceed therapeutic concentrations illustrates a saturable process.

Patients with end-stage renal disease (ESRD) receiving valproic acid have protein-binding properties similar to those of patients with overdose. Patients with ESRD have elevated unbound valproic acid concentrations due to displacement of protein binding by uremic by-products, and as a result of low serum albumin concentrations. Therapeutic valproic acid concentrations decrease approximately 20% during four hours of hemodialysis in patients with chronic renal failure.

The removal of valproic acid by hemodialysis in patients with ESRD supports the potential efficacy of hemodialysis in an acute overdose.

Hemoperfusion removes drugs that are highly protein bound and adsorbed by activated charcoal, hence, valproic acid should be effectively removed with this process. However, reports of hemoperfusion with valproic acid are equivocal. Van der Merwe et al.\(^{14} \) stated that hemoperfusion did not accelerate valproic acid extraction in a patient with a peak concentration of 1080 \( \mu g/mL \). In contrast, the use of hemoperfusion plus MDAC resulted in a three-hour \( t_{1/2} \) of valproic acid after an acute ingestion, with peak concentration of 1380 \( \mu g/mL \). This patient continued MDAC therapy alone, achieving a 4.8-hour \( t_{1/2} \). Hemoperfusion appeared to contribute to the clearance of MDAC.

### Table 2. Calculated Amount of Valproic Acid Eliminated, Plasma Clearance, and Half-Life of Drug for the Patient During and After High-Flux Hemodialysis

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Total</th>
<th>Hemodialysis</th>
<th>Patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amount eliminated (g)</td>
<td>11.95(^{b})</td>
<td>10.55(^{c})</td>
<td>1.40(^{d})</td>
</tr>
<tr>
<td>Plasma clearance (mL/min)</td>
<td>105.50(^{a})</td>
<td>93.17(^{f})</td>
<td>12.33(^{g})</td>
</tr>
<tr>
<td>Half-life (h)</td>
<td>2.74(^{h})</td>
<td>23.41(^{i})</td>
<td></td>
</tr>
</tbody>
</table>

\( \Delta A_{HD} = \text{amount eliminated by high-flux hemodialysis; } \Delta A_{patient} = \text{amount eliminated by the patient during hemodialysis; } \Delta A_{total} = \text{total amount eliminated during hemodialysis; } AUC_{t1-t2} = \text{AUC from time 1 to time 2; } CL_{HD} = \text{total body clearance during hemodialysis; } CL_{patient} = \text{normal clearance of patient at time of hemodialysis; } Cp = \text{plasma concentration at time 1; } Cp^{2} = \text{plasma concentration at time 2; } (dAe/dt)^{1} = \text{the rate of elimination by hemodialysis at time 1; } (dAe/dt)^{2} = \text{the rate of elimination by hemodialysis at time 2; } k_{HD} = \text{elimination rate constant during high-flux hemodialysis treatment obtained from calculated elimination rate-time data; } V_{p}^{D} = \text{volume of distribution during high-flux hemodialysis.} \)

\( ^{a} \text{Calculations available from corresponding author.} \)

\( ^{b} \text{Calculations available from corresponding author.} \)

\( ^{c} \text{Calculations available from corresponding author.} \)

\( ^{d} \text{Calculations available from corresponding author.} \)

\( ^{e} \text{Calculations available from corresponding author.} \)

\( ^{f} \text{Calculations available from corresponding author.} \)

\( ^{g} \text{Calculations available from corresponding author.} \)

\( ^{h} \text{Calculations available from corresponding author.} \)

\( ^{i} \text{Calculations available from corresponding author.} \)
Tank and Palmer used a combination of hemodialysis/hemoperfusion (HD/HP) to treat a valproic acid overdose in a patient whose peak plasma concentration was 1262 µg/mL. The calculated $k_d$ before the treatment was 0.053 h$^{-1}$, with a $t_{1/2}$ of 13 hours. During the procedure, the $k_d$ was 0.41 h$^{-1}$, with a $t_{1/2}$ of 1.7 hours. A definitive comparison between hemodialysis and hemoperfusion does not exist. We chose to proceed with high-flux hemodialysis alone, based on the favorable pharmacokinetic properties of valproic acid and the risks associated with hemoperfusion.

In our patient, the calculated $k_d$ during hemodialysis was 0.2522 h$^{-1}$, with a $t_{1/2}$ of 2.74 hours, results similar to those obtained with combination HD/HP. After completion of four hours treatment with high-flux hemodialysis, the valproic acid concentration reached a minimum of 297 µg/mL (arterial port that reflects the plasma concentration in the rest of the body). We were able to successfully increase the rate of elimination with four hours of high-flux hemodialysis. Unfortunately, we were unable to calculate a predialysis $k_d$ since insufficient valproic acid concentrations were available. The calculated $t_{1/2}$ after hemodialysis was 23.41 hours. Assuming that this is the patient’s normal rate of elimination for valproic acid, the approximate time to reach concentrations of <100 µg/mL would be 147.4 hours. We realize that the patient’s normal $k_d$ prior to hemodialysis may have been faster if the rate of elimination was proportional to the unbound plasma concentrations. After reviewing the case reports on the combination of HD/HP and comparing them with our results, the combination approach may be unnecessary. An additional reason to avoid hemoperfusion would be the added complications of thrombocytopenia, leukopenia, and hypocalcemia that can result from this technique.

A detailed case report supporting our findings was recently published. Johnson et al. treated a patient with an acute valproic acid overdose with high-flux hemodialysis alone. The 43-year-old woman had a $t_{1/2}$ of 7.2 hours prior to the initiation of hemodialysis. The valproic acid concentration was 940 µg/mL at commencement of six hours of hemodialysis. During hemodialysis, the $t_{1/2}$ was reduced to 2.4 hours and resulted in the removal of an estimated 15.5 g of valproic acid, similar to our four hours of hemodialysis.

Of interest, our patient’s valproate concentrations did rebound to 195 µg/mL 13 hours after hemodialysis. A rebound effect can be expected if the rate of drug removal from plasma during dialysis exceeded the rate of drug transfer from the peripheral to the central compartment. This rebound effect was also noted by Johnson et al. approximately five hours after hemodialysis, causing the extracorporeal therapy to be restarted. More information about this phenomenon would be valuable for determining optimal concentrations during treatment, establishing the duration of dialysis therapy and establishing monitoring guidelines. Our patient experienced an apparent 31% increase in the valproic acid concentration between six and 13 hours after dialysis, with no apparent clinical significance.

During the first 24 hours of hospitalization, our patient also developed hypernatremia. Valproic acid has been reported to cause syndrome of inappropriate antidiuretic hormone; hyponatremia is more commonly associated with valproic acid than hypernatremia. Although the lungs can be a significant source of free water loss, our patient was intubated, her respiratory rate was controlled, and she was oxygenated with appropriate tidal volumes using humidified air. The hypernatremia probably was due to excessive renal hypotonic fluid loss from an ethanol-induced osmotic diuresis. Consistent with this diagnosis, her urine was dilute (specific gravity <1.005, urine osmolality 435 mOsm/kg).

Lactic acidosis, which developed in our patient, has previously been reported with valproic acid and appears to result in part from circulatory compromise due to extracellular fluid volume depletion. The hypotension in our patient responded to infusion of NaCl 0.9%, but the patient described above required vasopressor support in addition to volume resuscitation. Lactic acidosis may also have contributed to the osmolar gap identified in our patient.

Transient thrombocytopenia can be viewed as a dose-related, adverse effect of valproic acid. Our patient also developed thrombocytopenia during her hospitalization. A minimum platelet count of 57,000 cells/mm$^3$ was documented approximately 150 hours after drug ingestion. Comparison of serum valproic acid concentrations and platelet counts indicated a tight correlation between recovery of thrombocytopenia and reduction in valproic acid concentrations (Figure 2). The patient’s platelet concentration began to recover six days after the drug was discontinued.

![Figure 2. Valproic acid concentrations and platelet counts from the time the patient was admitted. ⊕ = valproic acid concentrations after admission; □ = platelet count.](image-url)
The rebound thrombocytosis that followed has also been reported.1,2

Summary

In conclusion, the saturable protein binding of valproic acid at supratherapeutic concentrations allows this drug to be a good candidate for removal by hemodialysis after ingestion of an overdose. Rapid removal of valproic acid with extracorporeal systems can result in significant clinical improvement. Treatment with high-flux hemodialysis for valproic acid overdose appears to be as effective for drug elimination as the combination of hemodialysis and charcoal hemoperfusion. We suggest that toxic concentrations of valproic acid can be effectively treated with high-flux hemodialysis without the addition of charcoal hemoperfusion and its attendant risks for the patient.

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References


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Case Reports

EXTRACTO

OBJETIVO: Reportar un caso de sobredosis con ácido valproico tratado exitosamente con hemodiálisis de alto flujo sin tener que recurrir a hemoperfusión con carbón activado.

RESUMEN DEL CASO: Una mujer de 25 años con historial de esquizofrenia y múltiples intentos de suicidio se presentó a sala de emergencia después de ingerir una cantidad desconocida de ácido valproico. La paciente estaba comatosa; desarrolló hipotensión y acidosis láctica con concentraciones séricas mayores de 1200 µg/mL (concentración sérica terapéutica = 50–100 µg/mL). Se inició la hemodiálisis de alto flujo por cuatro horas, y k3 calculada durante el procedimiento fue 0.2522 h-1 y una vida media de 2.74 horas comparado con la k3 y la vida media después de la hemodiálisis de 0.0296 h-1 y 23.41 horas, respectivamente. Esto indica que la hemodiálisis de alto flujo elimina el ácido valproico de forma efectiva. El estado hemodinámico y función mental mejoró como también una aguda reducción de las concentraciones séricas de ácido valproico. El subsecuente curso de la hospitalización fue complicado debido a una trombocitopenia transitoria, y este efecto aparece reportado en la literatura en los pacientes con sobredosis de ácido valproico.

DISCUSIÓN: En muchos reportes de casos han usado la hemoperfusión de carbón activado sola o en combinación con hemodiálisis de alto flujo para acelerar la depuración de ácido valproico en concentraciones tóxicas. Sin embargo las propiedades farmacocinéticas del ácido valproico indican que la hemodiálisis de alto flujo sola podría ser una alternativa efectiva para el manejo de una sobredosis de ácido valproico. Se sugiere que las concentraciones tóxicas de ácido valproico pueden ser reducidas efectivamente con hemodiálisis de alto flujo sin recurrir a la hemoperfusión de carbón activado y sus conocidos riesgos.

Wilma M Guzmán

RÉSUMÉ

OBJECTIF: Décrire un cas de surdose d’acide valproïque traité avec succès à l’aide d’hémodialyse à haute performance, sans l’addition d’hémoperfusion sur charbon de bois activé.

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RÉSUMÉ DU CAS: Une femme de 25 ans s’est présentée à l’urgence après avoir ingéré une quantité indéterminée d’acide valproïque. La patiente avait des antécédents de schizophrénie, de dépendance à l’alcool, et de tentatives multiples de suicide. Elle devint comateuse et développa de l’hypotension et de l’acidose lactique alors que les concentrations d’acide valproïque atteignirent plus de 1200 µg/mL (concentrations thérapeutiques: 50 à 100 µg/mL). La patiente fut placée sous hémodialyse à haute performance pendant quatre heures; le k_during la procédure était de 0.2522 h$^{-1}$ avec une demi-vie de 2.74 heures, comparativement à la période post-hémodialyse où le k et la demi-vie étaient de 0.0296 h$^{-1}$ et 23.41 heures. Ces données suggèrent que l’hémodialyse à haute performance élimine efficacement l’acide valproïque. L’état hémodynamique et mental de la patiente se sont améliorés parallèlement à la chute des concentrations sanguines d’acide valproïque. Le reste de son séjour hospitalier ne fut compliqué que par de la thrombocytopenie transitoire, phénomène qui a déjà été rapporté lors de surdosage d’acide valproïque.

DISCUSSION: La plupart des cas décrits dans la littérature ont rapporté l’emploi d’hémoperfusion sur charbon de bois activé, seule ou en association avec l’hémodialyse, dans le but d’accélérer l’élimination de concentrations toxiques d’acide valproïque. Cependant, les paramètres pharmacocinétiques de l’acide valproïque calculés ici, indiquent que l’hémodialyse seule serait un traitement efficace pour un épisode de surdose aiguë à l’acide valproïque.

CONCLUSIONS: Notre expérience suggère que des concentrations toxiques d’acide valproïque peuvent être efficacement réduites à l’aide d’hémodialyse à haute performance, sans l’addition d’hémoperfusion sur charbon de bois activé, évitant ainsi les risques qui y sont associés.

Pierre Martineau

SPECIAL INVITATION

Christian Pharmacists Fellowship International invites you to a luncheon fellowship on November 7, 2000, in Los Angeles, California

While enjoying a delicious luncheon, leaders and researchers in the profession of pharmacy will be intrigued and delighted to hear the inspirational content of Dr. Fazale Rana’s latest research as he speaks on —

“New Discoveries from Genomics and Implications for the Origin of Life and Intelligent Design.”

Dr. Rana is a research biochemist, author, editor, lecturer, and Vice President for Apologetics at the nonprofit group “Reasons to Believe” in Pasadena, California. The luncheon will be held at —

Westin Century Plaza Hotel
Los Angeles, California
November 7, 2000
12–1:30 p.m.

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Reservations are required by October 20 (cancellations may be accepted by October 27).

This luncheon coincides with the ACCP Annual Meeting to accommodate clinical pharmacists interested in its content; however, the ACCP does not sponsor nor endorse this event, nor is there any connection with the ACCP.