0022-5347/99/1621-0018/0
THE JOURNAL OF UROLOGY
Vol. 162, 18–22, July 1999
Printed in U.S.A.


# PETROLEUM JELLY IS AN IDEAL CONTACT MEDIUM FOR PAIN REDUCTION AND SUCCESSFUL TREATMENT WITH EXTRACORPOREAL SHOCK WAVE LITHOTRIPSY

ARMIN J. BECKER, CHRISTIAN G. STIEF, MICHAEL C. TRUSS, MATTHIAS OELKE, STEFAN MACHTENS AND UDO JONAS

*From the Department of Urology, Medizinische Hochschule Hannover, Hannover, Germany*

ABSTRACT

Purpose: Various minimally invasive approaches to reduce pain during extracorporeal shock wave lithotripsy (ESWL*) have been described. We compared petroleum jelly (Vaseline†) and ultrasound gel in vitro as a contact medium based on the stone fragmentation rate. The analgesic effect of cutaneous petroleum jelly was tested against eutectic mixture of local anesthesia. We also evaluated the outcome of ESWL in a large group of patients treated with petroleum jelly.

Materials and Methods: In vitro 3 artificial stones were completely fragmented with a MFL 5000* lithotriptor using petroleum jelly or ultrasound gel as a contact medium. A total of 110 patients (group 1) received petroleum jelly before treatment with the same lithotriptor. After retrospective analysis of group 1 we matched 32 patients (group 2) receiving cutaneous eutectic mixture of local anesthesia. Because of the favorable results with petroleum jelly, we used it in another 148 patients, for a total of 258 patients (group V). Treatment dependent pain was scored using a questionnaire as 1—no, 2—minor, 3—tolerable and 4—intolerable. ESWL without additional analgesics had a pain score of 1 to 3.

Results: In vitro petroleum jelly had a superior fragmentation rate compared to ultrasound gel. Our long-term experience with the lithotriptor indicated that only 30% of patients required no additional analgesics with cutaneous ultrasound gel. In contrast, no additional analgesics were needed in only 38% of group 2 compared to 81.8% of group V. The stone fragmentation rate did not differ statistically between groups.

Conclusions: Cutaneous petroleum jelly offers a noninvasive, highly effective, inexpensive treatment modality with no side effects and significant reduction in pain. This ointment is our contact medium of choice.

KEY WORDS: lithotripsy, pain, petrolatum, lidocaine, prilocaine

Since its introduction in 1980 extracorporeal shock wave lithotripsy (ESWL) has revolutionized urolithiasis.[1] This technique, combined with auxiliary endoscopic procedures, has replaced open stone surgery almost completely.[2,3] Furthermore, it is a highly efficacious treatment modality with low morbidity.[4] Due to increasing experience with this therapy and technical improvement in lithotriptors the stone fragmentation-to-trauma ratio has improved continuously.

Although regional or general anesthesia was commonly used for treatment with first generation lithotriptors,[1] it is not required with third generation machines in most cases. Specific data about the need for analgesics differ in the literature, especially for the lithotriptor used in our study, and vary depending on stone location from 30% (proximal ureter) to 78% (distal ureter) to 72% (mid/distal ureter).[5,6] According to our retrospective experience with this lithotriptor in 400 unselected treatments per year for more than 7 years, about 70% of patients required intravenous analgesics (for example 7.5 to 15 mg. per single dose piritramide). Opiate associated side effects (nausea, hypotension) were observed in 20% of patients. In 5% of these cases termination of the procedure was necessary.

Since 1986 several studies have investigated the effect of different local anesthetic substances on therapy dependent pain with varying results.[7–14] Cavitation phenomena have been discussed as the possible source of cutaneous pain during ESWL and the application of viscous ointment alone seems to reduce this pain.[5] We initially tested in vitro petroleum jelly against routinely used ultrasound gel as a contact medium. Because of the positive stone fragmentation results, a pilot study was performed comparing 110 patients treated with cutaneous petroleum jelly (group 1) to 32 treated with eutectic mixture of local anesthesia (EMLA‡) (group 2). After an unexpected analgesic effect with petroleum jelly (87%) compared to EMLA (38%) and ultrasound gel (30%) was revealed, another 148 patients were prospectively treated with petroleum jelly in an effort to decrease treatment related discomfort without limiting stone fragmentation. We report the results of our study.

## MATERIALS AND METHODS

Petroleum jelly is a physiologically well tolerated and inexpensive basic substance in numerous cutaneously applied drugs.[15] One gm. EMLA cream, an oil and water emulsion, contains 25 mg. lidocaine and 25 mg. prilocaine, and is used as superficial anesthesia for cutaneous surgical procedures. The ultrasound gel we used contains 835.2 gm. distilled water, 3.5 gm.carbopol-940, 150 gm. propylene glycol and 11.3 gm./1,000 gm. 10% sodium hydroxide saline solution.

Standardized in vitro experiments with 3, 1 cm. artificial stones were performed to evaluate the quality of contact with petroleum jelly compared to ultrasound gel. The stones were fragmented with 18, 22 and 25 kV., and the number of shock

Accepted for publication February 19, 1999.
* Dornier Medical Systems, Inc., Marietta, Georgia.
† Beiersdorf A. G., Hamburg, Germany.
‡ Astra USA, Inc., Westborough, Massachusetts.

waves needed for complete stone fragmentation was recorded (fig. 1). A thin but complete layer of the coupling agent was applied to the polyvinyl chloride membrane of the shock wave generator, and then the container filled with water from the lithotriptor tube and the stone net was fixed against the machine. The artificial stones were soaked before use for 20 minutes in the lithotriptor tube water. The end point of the fragmentation procedure was when the net containing the stones was empty.

A total of 290 patients treated with urolithiasis of the upper urinary tract were included in the in vivo study. Children younger than 15 years and patients requiring anesthesia due to auxiliary treatments were excluded from study. The procedure was performed without premedication. After our initial experience with petroleum jelly (110 patients, group 1) we recruited 32 additional patients to evaluate the analgesic potential of EMLA (group 2). Patient characteristics did not differ statistically in regard to age, sex, stone location and treatment parameters between these groups (table 1). Mean patient age was 50.9 ± 14.3 years in group 1 and 54.4 ± 14.5 in group 2 ($p > 0.7$). Both groups comprised 69% and 31% women After the pilot study another 148 consecutive patients were treated with petroleum jelly. Finally, all 258 patients treated with petroleum jelly (group V) were evaluated regarding age, sex, stone location, stone size, number and energy of shock waves, stone fragmentation rate and intensity of pain. Patients were informed about possible side effects of treatment and especially about the development of pain. During the entire procedure visual and vocal contact with the patient was maintained so that questions were immediately clarified. Furthermore, patients were asked about the experience and scored the intensity of pain as 1—no, 2—minor, 3—tolerable and 4—intolerable.

In group V an approximately 1 mm. thick layer of ointment was applied to the skin area immediately before ESWL. Treatment began with an energy level of 14 kV. and successively increased to a maximum of 26. In cases of intolerable pain the procedure was interrupted, 7.5 to 15 mg. single dose intravenous piritramide was given and after a 10-minute break treatment was continued. Regional or general anesthesia was given in cases of insufficient response to intravenous analgesics. In group 2 the pretreatment procedure was more time-consuming. From 45 to 90 minutes before ESWL 20 gm. EMLA were applied to the skin area depending on radiological findings. For better absorption the approximately 20 × 10 cm. skin surface was covered with synthetic foil. After 45 to 90 minutes the foil was removed and ultrasound gel was applied as a contact medium. Treatment was performed under the same conditions as in group V. Student's t test was used for statistical analysis with $p < 0.05$ considered significant. Results were calculated as mean plus or minus standard deviation.

## RESULTS

Stone fragmentation rate in vitro was superior with petroleum jelly at 18, 22 and 25 kV. (fig. 1). Average stone size was 11.0 ± 5.7 × 11.5 ± 7.0 mm. in group 1 and 9.1 ± 4.1 × 11.4 ± 6.3 mm. in group 2 ($p > 0.08$). Average number of applied shock waves was 2,918 ± 432 in group 1 and 2,881 ± 433 in group 2 ($p > 0.6$). Mean shock wave energy was calculated as 20.7 ± 2.5 kV. for group 1 and 21.7 ± 2.3 kV. for group 2 ($p > 0.05$). There were 70% kidney and 30% ureteral stones (table 1). The stone fragmentation rate, determined by comparing pretreatment and posttreatment radiological results was 94 and 92% for groups 1 and 2, respectively. There were no serious side effects in either group.

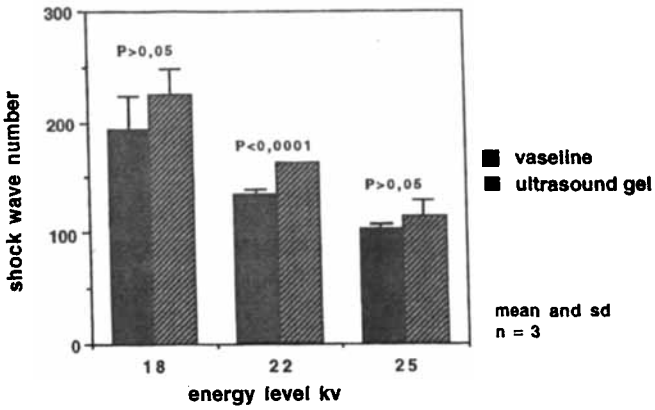


FIG. 1. In vitro stone fragmentation rate of artificial stones using petroleum jelly or ultrasound gel as contact medium, and mean plus standard deviation (*sd*) number of shock waves.

In 96 group 1 patients (87%) the entire procedure was performed with no, minor or tolerable pain after the application of petroleum jelly (pain score 2.2 ± 1.1). In 14 group 1 patients (13%) therapy was interrupted because of intolerable pain and continued after intravenous piritramide. The analgesic effect of EMLA was sufficient for treatment in 12 group 2 patients (38%, pain score 3.4 ± 0.6). In 20 group 2 patients (62%) therapy was interrupted because of intolerable pain. After the application of petroleum jelly the procedure was resumed with no, minor or tolerable pain in 18 of these patients (90%), and additional intravenous analgesic was necessary in 2. Regional or general anesthesia was not necessary in either group. The difference in pain score between groups 1 and 2 was statistically significant ($p < 0.0001$).

Group V was retrospectively subdivided to identify possible predisposing factors for the perception of pain into group Va—211 patients who were able to tolerate ESWL after application of petroleum jelly only and group Vb—47 who required additional analgesia or anesthesia. Group Va tolerated ESWL with no, minor or tolerable pain (score 1.9 ± 0.8), whereas treatment in group Vb was interrupted immediately because of intolerable pain (score 4.0 ± 0.0) and an intravenous analgesic was given. In 5 group Vb patients regional or general anesthesia was necessary (fig. 2).

Mean patient age was 52.2 ± 14.5 years in group Va and these patients were significantly older than group Vb patients (47.3 ± 12.2, $p < 0.03$). The distribution of sex was also significantly different between these groups ($p < 0.0001$). Group V comprised 65.5% men and 34.5% women. However, group Va comprised 70.1% men and 29.9% women compared to 44.7 and 55.3%, respectively, for group Vb. Average stone size did not differ significantly between groups Va and Vb, and was 11.7 ± 7.1 × 9.3 ± 5.9 mm. for group V. Mean number of applied shock waves varied between 3,142.4 ± 466 in group Va and 2,900 ± 997 in group Vb, which was statistically significant ($p < 0.01$). Mean shock wave energy was significantly higher in group Va (21.2 ± 2.3 kV.) than in group Vb (20.1 ± 2.7 kV., $p < 0.05$). The difference in stone location is shown in table 1. The correlation between stone location, and the development and intensity of pain is demonstrated in table

TABLE 1. *Stone location in groups 1, 2, Va and Vb*

| | No. Group 1 | No. Group 2 | No. Group Va | No. Group Vb |
|---|---|---|---|---|
| Men/women | 76/34 | 22/10 | 148/63 | 21/26 |
| Renal pelvis | 50 | 15 | 90 | 14 |
| Upper calix | 2 | 0 | 11 | 1 |
| Mid calix | 3 | 1 | 8 | 1 |
| Lower calix | 23 | 6 | 41 | 12 |
| Proximal ureter | 6 | 2 | 22 | 7 |
| Mid ureter | 12 | 3 | 19 | 2 |
| Distal ureter | 14 | 5 | 20 | 10 |
| Total No. kidney/ureteral stones | 78/32 | 22/10 | 150/61 | 28/19 |

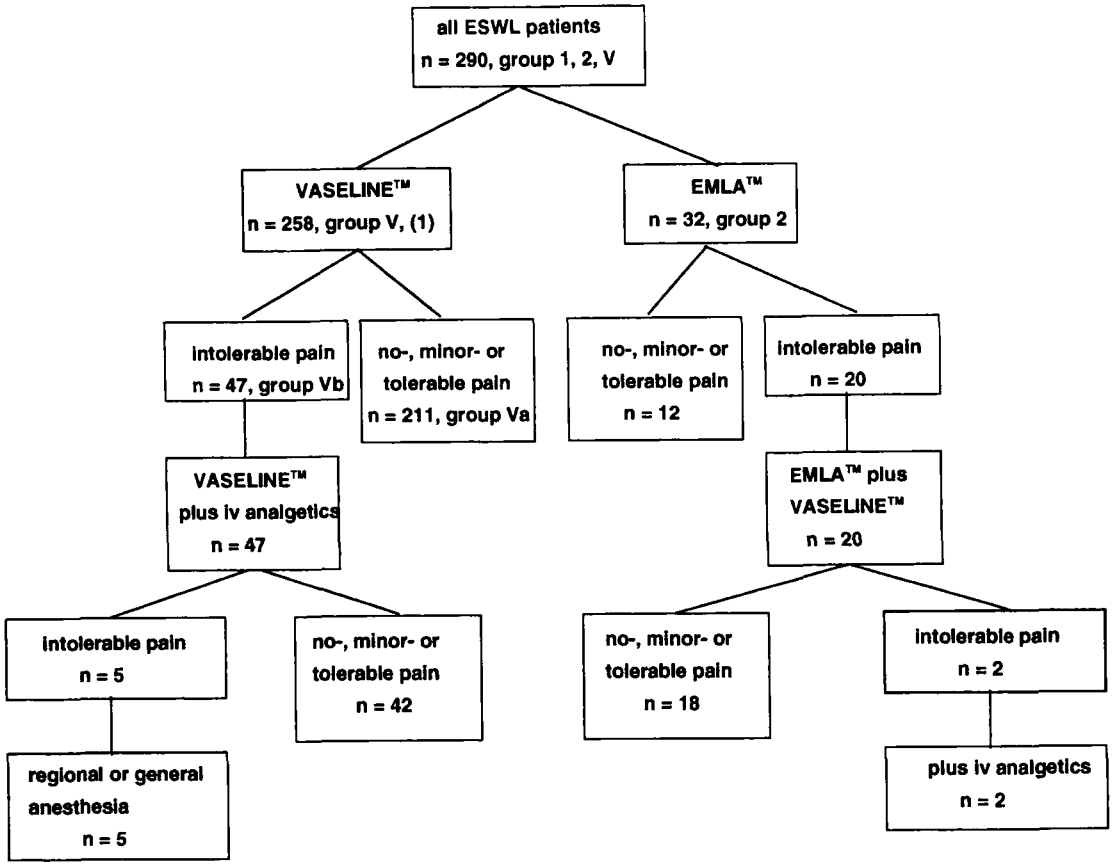


FIG. 2. Patient population relative to different coupling agents and therapeutic approach. *iv*, intravenous

2. Intolerable pain occurred mainly during treatment of distal ureteral stones (33.3%). The stone fragmentation rate did not differ statistically between groups Va (94.3%) and Vb (91.5%). There were no serious side effects in group V.

## DISCUSSION

With correct indication and handling ESWL is a safe and efficacious treatment modality[16–18] but related pain is of major importance to patients. Comparability of pain development during ESWL is limited due to major differences in technical procedures (different lithotriptor generations) and pain management (premedication and different forms of anesthesia). In our experience 70% of patients treated with ultrasound gel only required additional analgesics or anesthesia. Our results differ substantially from those of Heidenreich et al who described the need for intravenous analgesics in only 36% of patients using the same type of lithotriptor.[5] However, they also demonstrated a sufficient analgesic effect of cutaneous petroleum jelly in 93% of patients, and suggested a possible effect of viscous petroleum jelly on cavitation as the underlying source of pain reduction. Therefore, reduced stress on cutaneous nociceptors might be responsible for the decrease in pain phenomenon.

TABLE 2. *Intolerable pain relative to stone location in group V*

| | No. Location | % Intolerable Pain |
|---|---|---|
| Renal pelvis | 104 | 13.5 |
| Upper calix | 12 | 8.3 |
| Mid calix | 9 | 11.1 |
| Lower calix | 53 | 22.6 |
| Proximal ureter | 29 | 24.1 |
| Mid ureter | 21 | 9.5 |
| Distal ureter | 30 | 33.3 |

Further studies report different results with cutaneous EMLA for pain reduction during ESWL.[8,9,14,19–23] Barcena et al used a second generation lithotriptor and demonstrated an analgesic effect of EMLA, eliminating the need for intravenous fentanyl in 9 of 20 ESWL procedures.[21] Similar results were noted by de Lichtenberg et al comparing the analgesic effect of EMLA with subcutaneous infiltration of lidocaine in patients who received intravenous morphine as premedication.[9] Bierkens et al reduced fentanyl from 53% in a placebo to 30% in an EMLA group, which was not statistically significant.[19] Monk et al noted a significant decrease in cutaneous pain with EMLA cream.[20] Complete failure of EMLA to act analgesically was described by Ganapathy et al using a third generation lithotriptor in 83 patients who received intravenous alfentanil as premedication.[22] In addition to the indication for EMLA use during ESWL this substance has proved to be an effective topical anesthesia for venipuncture, harvesting of split thickness skin grafts, laser therapy of male genital warts and lumbar puncture.[24]

Because of the high absorption rate from EMLA, which is cutaneously applied 45 to 90 minutes before treatment, ultrasound gel must be used as a contact medium. The absorption rate of viscous petroleum jelly is minimal, and so it can be used as a contact medium only. Trials with artificial stones demonstrated a higher stone fragmentation rate with petroleum jelly compared to ultrasound gel. The thickness of petroleum jelly seems important since a 2 to 4 mm. layer resulted in reduced artificial stone fragmentation.[25]

Characteristics of groups 1 and 2 differed only in the number of patients, as recruitment of group 2 was terminated for ethical reasons due to significantly more intense pain. These

findings are supported by Ganapathy et al who failed to demonstrate a positive analgesic effect of EMLA in 83 patients using the same lithotriptor as in our study.[22] No supportive analgesic application was necessary in 87% of group 1 in contrast to only 38% of group 2 in our pilot study. This difference could also be documented in mean pain score, which was 2.2 ± 1.1 for group 1 versus 3.4 ± 0.9 for group 2 ($p < 0.0001$). Of 20 patients who had insufficient analgesia with EMLA 18 were able to complete ESWL after petroleum jelly application and only 2 required additional intravenous analgesics. These results for EMLA using ultrasound gel as a coupling agent may not explain why supplemental analgesia (out of study about 70%) is necessary more often for patients at our ESWL center than for those in the study by Heidenreich et al.[5] However, they confirm petroleum jelly as a topical analgesic for ESWL.

A second evaluation was performed to confirm the results of our pilot study in 148 patients who were prospectively treated under the same conditions. Finally, the 258 patients receiving petroleum jelly were retrospectively evaluated. In regard to predisposing criteria for pain development only, stone size and fragmentation rates were not statistically significant. Younger individuals were more sensitive to pain than older patients ($p < 0.03$). Group Vb comprised 55.3% and group Va comprised only 29.9% women ($p < 0.0001$). Similar results were reported by Monk et al who reduced pain with EMLA only in men.[20] A possible explanation might be a sex dependent difference in resorption of cutaneously applied substances. Differences between the sexes in skin blood flow and hormonal levels, which may influence cutaneous penetration of topically administered drugs, are well known.[26] Other theories for gender related differences in pain relief include variations in skin thickness or subcutaneous fat content.[27] Also, the location of stones was related to the assessment of pain. ESWL of lower caliceal (22.6%) and distal ureteral (33.3%) stones was associated with the most intense pain (table 2). An almost identical correlation between stone location and development of pain was also described by Heidenreich et al.[5] Their hypothesis was that petroleum jelly is able to block pain deriving from the skin surface but not from the visceral or periosteal tissues. Treatment related pain was not influenced by the number and energy of shock waves. Both parameters in our study were lower for group Vb than group Va. The pain score was 1.9 ± 0.8 for group Va versus 4 ± 0 for group Vb ($p < 0.0001$). The difference in pain score between groups 1 (2.2 ± 1.1) and V (2.3 ± 1.1), both treated with petroleum jelly, reflects the fact that only 81.8% of group V versus 87% of group 1 had no, minor or tolerable pain during the procedure. Although Heidenreich et al reported a mean pain score of 2.5 ± 1.05 their 7% rate of discontinued ESWL treatment was lower than our rate of 18.2%. Interpretation of these results remains controversial.

As petroleum jelly represents a noninvasive, inexpensive and well tolerated contact medium,[15] potential loss of efficacy with respect to stone fragmentation in favor of a significant pain reliever would argue against regular use for ESWL. However, no reduction in the stone fragmentation rate was observed during the in vitro or in vivo trials. In vivo results are supported by Heidenreich et al who reported a stone fragmentation rate of up to 96.5% with 1 mm. petroleum jelly applied to the skin.[5] This experience was also confirmed by our results (94.3%).

There is no clear evidence of the analgesic effect of petroleum jelly used as a coupling agent for ESWL but our data show that petroleum jelly reduces pain during ESWL. Combined with the improved in vitro stone fragmentation rate, this finding could indicate a better coupling quality of petroleum jelly compared to ultrasound gel. According to this hypothesis, the sound reflection on the skin area could be diminished, leading to better transformation of the energy applied to the stone, and reduced stress on cutaneous nociceptors might be responsible for the decrease in pain. To our knowledge there is no study on the effect of petroleum jelly on the smooth polyvinyl chloride membrane of the shock wave generator. Petroleum jelly might dissolve substances which are responsible for the softness of the membrane. Our experience with petroleum jelly as a coupling agent reveals a hardening of the membrane, and so it has to be changed twice as often as usual. We chose this strategy because of the advantage in reducing pain, analgesics and time. This problem should be avoided with a silicone membrane.

## CONCLUSIONS

Although the precise mechanism of pain reduction using petroleum jelly for ESWL is not completely understood, we recommend its routine use. Furthermore, petroleum jelly offers a noninvasive, inexpensive and well tolerated alternative to intravenous analgesics and anesthesia. For young women with a distal ureteral stone additional intravenous analgesics during ESWL seem justified. Further basic and clinical studies are needed to corroborate our results, and possibly motivate lithotriptor companies to change the polyvinyl chloride to a silicone membrane.

## REFERENCES


1. Chaussy, C., Schmiedt, E., Jocham, D., Brendel, W., Forssmann, B. and Walther, V.: First clinical experience with extracorporeally induced destruction of kidney stones by shock waves. J. Urol., **127:** 417, 1982.
2. Chaussy, C.: ESWL: past, present and future. J. Endourol., **2:** 97, 1988.
3. Eisenberger, F., Miller, K. and Rassweiler, J.: Extracorporeal Shock Wave Lithotripsy (ESWL). Stone Therapy in Urology. New York: Georg Thieme Verlag, pp. 29–82, 1991.
4. Jocham, D., Liedl, B., Lunz, CH., Schuster, C. and Chaussy, C.: Langzeiterfahrungen nach ESWL von Harnsteinpatienten. Urol. A, **28:** 134, 1989.
5. Heidenreich, A., Bonfig, R., Wilbert, D. M. and Engelmann, U. E.: Schmerzfreie ESWL durch kutane Applikation von Vaseline. Urol. A, **34:** 343, 1995.
6. Yip, S. K., Lee, F. C., Tam, P. C. and Leung, S. Y.: Outpatient treatment of middle and lower ureteric stones: extracorporeal shock wave lithotripsy versus ureteroscopic laser lithotripsy. Ann. Acad. Med. (Singapore), **27:** 515, 1998.
7. Aeikens, B., Fritz, K. W. and Hoehne, E.: Initial experience with local anaesthesia in extracorporeal shock wave lithotripsy. Urol. Int., **41:** 246, 1986.
8. Bierkens, A. F., Maes, R. M., Erdös, A., Hendrikx, J. M. and Debruyne, F. M. J.: Anaesthetic effect of eutectic mixture of local anaesthesia (EMLA) during extracorporal shock wave lithotripsy (ESWL). Eur. Urol., suppl., **18:** 366, 1990.
9. de Lichtenberg, M. H., Miskowlak, J., Mogensen, P. and Andersen, J. T.: Local anaesthesia for extracorporeal shock wave lithotripsy: a study comparing eutectic mixture of local anaesthetics cream and lidocaine infiltration. J. Urol., **147:** 96, 1992.
10. Loening, S., Kramolowsky, E. V. and Willoughby, G.: Use of local anaesthesia for extracorporeal shock wave lithotripsy. J. Urol., **137:** 626, 1987.
11. London, R. A., Kudlak, T. and Riehle, R. A.: Immersion anaesthesia for extracorporeal shock wave lithotripsy. Urology, **28:** 86, 1986.
12. Pettersson, B., Tiselius, H.-G., Andersson, A. and Eriksson, I.: Evaluation of extracorporeal shock wave lithotripsy without anaesthesia using a Dornier HM3 lithotripter without technical modifications. J. Urol., **142:** 1189, 1989.
13. Tiselius, H. G.: Anaesthesia-free in situ extracorporeal shock wave lithotripsy of ureteral stones. J. Urol., **146:** 8, 1991.
14. Tiselius, H.-G.: Cutaneous anaesthesia with lidocaine-prilocaine cream: a useful adjunct during shock wave lithotripsy with analgetic sedation. J. Urol., **149:** 8, 1983.
15. Sucker, H.: Vaselinen, Gebrauchseigenshaften und Guetebeurteilung. Pharm. Unserer Zeit. **2:** 87, 1973.

16. Schultz-Lampel, D., Lampel, A., Lazica, M. and Thuroff, J. W.: Extracorporeal shockwave lithotripsy in childhood. Urol. A, **36:** 200, 1997.
17. Sauter, G., Kullak-Ublick, G. A., Schumacher, R., Janssen, J., Greiner, L., Brand, B., Stange, E. F., Wengler, K., Lochs, H., Freytag, A., Wissing, A., Holl, J., Sackmann, M. and Paumgartner, G.: Safety and efficacy of repeated shockwave lithotripsy of gallstones with and without adjuvant bile acid therapy. Gastroenterology, **112:** 1603, 1997.
18. Kostakopoulos, A., Stavropoulos, N. I., Louras, G., Deliveliotis, C. and Dimopoulos, C.: Experience in 3,500 patients with urinary stones treated with the Dornier HM-4 bath-free lithotriptor. Int. Urol. Nephrol., **29:** 147, 1997.
19. Bierkens, A. F., Maes, R. M., Hendrikx, A. J. M., Erdos, A. F., de Vries, J. D. M. and Debruyne, F. M. J.: The use of local anesthesia in second generation extracorporeal shock wave lithotripsy: eutectic mixture of local anesthetics. J. Urol., **146:** 287, 1991.
20. Monk, T. G., Ding, Y., White, P. F., Albala, D. M. and Clayman, R. V.: Effect of topical eutectic mixture of local anesthetics on pain response and analgesic requirement during lithotripsy procedures. Anesth. Analg., **79:** 506, 1994.
21. Barcena, M., Rodriguez, J., Gude, F., Vidal, M. I. and Fernandez, S.: EMLA cream for renal extracorporeal shock wave lithotripsy in ambulatory patients. Eur. J. Anaesth., **13:** 373, 1996.
22. Ganapathy, S., Razvi, H., Moote, C., Parkin, J., Yee, I., Gverzdys, S., Dain, S. and Denstedt, J. D.: Eutectic mixture of local anaesthetics is not effective for extracorporeal shock wave lithotripsy. Canad. J. Anaesth., **43:** 1030, 1996.
23. Keller, R. J. and Elliott, C.: Eutectic mixture of local anesthetic cream-topical anesthesia for extracorporeal shock wave lithotripsy. Clin. Forum Nurse Anesthetists, **5:** 136, 1994.
24. Raveh, T., Weinberg, A., Sibirsky, O., Caspi, R., Alfie, M., Moor, E. V., Stein, Y., Wexler, M. R., Lipton, H. A. and Neuman, A.: Efficacy of the topical anesthetic cream, EMLA, in alleviating both needle insertion and injection pain. Ann. Plast. Surg., **35:** 576, 1995.
25. Heidenreich, A., Bonfig, R., Wilbert D. M. and Engelmann, U. E.: Schmerzfreie ESWL durch kutane Applikation von Vaseline. In: Jahrbuch der Urologie. Edited by U. Jonas. Munster, Germany: Regensburg & Biermann, pp. 207–211, 1995.
26. Coffman, J. D.: Cutaneous changes in peripheral vascular disease. In: Dermatology in General Medicine, 4th ed. Edited by T. B. Fitzpatrick. New York: McGraw-Hill, pp. 2077–2102, 1993.
27. Freinkel, R. K.: Cutaneous manifestations of endocrine disease. In: Dermatology in General Medicine, 4th ed. Edited by T. B. Fitzpatrick. New York: McGraw-Hill, pp. 2113–2131, 1993.