In a small praxis/ambulance study we evaluated data of 200 women with chronic recurrent cervical infections and with a cervix dysplasia (CIN 1, CIN 2) who got after the primary therapy a treatment with vitamin D vaginal suppositories (12500 IU, 3 nights a week, for 6 weeks). We found that—when compared with the lactobacillus vaginal suppositories—the high dose vitamin D vaginal treatment might be more effective. Vitamin D showed very good anti-inflammatory effects. In the survey after six weeks therapy, 79% of the women had “less vaginal problems,” “less discharge,” and “less problems with the sexual intercourse.” Objectively, after six weeks therapy, only 7% of the patients still had bacterial and/or fungal vaginal infections that required a treatment. We found that vitamin D is reabsorbed by the vaginal mucosa, but the reabsorption may be individually very different. In the CIN 1 group we found six weeks after treatment good antidysplastic effects, in the CIN 2 group we often found no or only temporary antidysplastic effects. So this vaginal vitamin D treatment method might be an option for the therapy and prevention of chronic cervical infections and maybe of a cervic dysplasia CIN 1 (good anti-inflammatory effects, antidysplastic effects). This small study is not representative. We need much bigger studies with much more dates and with a longer follow up. Caution: At the moment, we do not know if the vaginal vitamin D treatment with 12500 IE is possible in pregnancy. We have no experience. Therefore we recommend an effective contraception during the application.

**Introduction**

In the last almost 20 y in our praxis/ambulance we treated some thousands of patients suffering from vaginal and cervical infections, many of them with a dysplasia of the cervix uteri. Some hundreds of them were so called “problem patients”: they had persisting chronic vaginal and cervical infections, some of them four times a year—despite an adequate therapy (primary therapy with antibiotics/antimycotics according to the antibiogram and secondary vaginal lactobacillus treatment).

For this study, we evaluated data of 200 “problem patients” with chronic recurrent cervical infections:

- 100 of them with chronic bacterial and/or fungal infections had no dysplasia.
- 100 of them with chronic bacterial and/or fungal infections had dysplasia. 50 with a CIN 1 and 50 with a CIN 2. Of the 50 CIN 1 patients 86% and of the 50 CIN 2 patients 92% had high risk of HPV.

**Bacterial infections**

Of the 200 patients, 51 had an infection with *G. vaginalis*, *E. coli* and/or coccus (*Streptococcus, Staphylococcus*), 44 patients mainly with coccus (*Streptococcus, Staphylococcus*), 16 patients mainly with *G. vaginalis*. 45 patients had a *C. trachomatis* infection, partially combined with bacterial mixed and/or fungal infection. Five patients had an infection with *T. vaginalis*, all plus coccus and/or *C. trachomatis*. (Fig. 1).

**Fungal infections**

Of the 200 patients 39 patients had a fungal infection (above all with *C. albicans*), partially combined with a mixed bacterial infection. (Fig. 1).

**Viral infections**

Of the 50 CIN 1 patients 43 and of the 50 CIN 2 patients 46 had high risk of HPV (mostly type 16 and 18).
Results

Vaginal vitamin D Reabsorption

The standard values for 25-hydroxy vitamin D in the serum: <30 ng / ml insufficient, 30–50 ng / ml sufficient, 50–70 ng / ml satisfying, > 70 ng / ml good.\(^1\)

In our small praxis/ambulance study before the vaginal vitamin D treatment, 100 of the 200 patients (50%) had insufficient 25-hydroxy vitamin D serum values (< 30 ng/ml).

- Only 10 (5%) had good 25-hydroxy vitamin D serum values (> 70 ng / ml)
- 20 (10%) had satisfying 25-hydroxy vitamin D serum values (50–70 ng/ml)
- 70 (35%) had sufficient 25-hydroxy vitamin D serum values (30–50 ng/ml)
- and 100 (50%) had insufficient 25-hydroxy vitamin D serum values (< 30 ng/ml).

We could observe that most of our elder patients with estrogen deficiency colpitis had an extreme vitamin D deficiency. Obviously, in menopause with the increasing age, the vitamin D serum values are continuously decreasing. We suppose that this might be caused by the metabolic, endocrin and intestinal deficits increasing with the age—also, the decreasing outdoor activities might contribute to this.\(^1\)

We were astonished that some of our patients had insufficient 25-hydroxy vitamin D serum values (< 30 ng/ml) although they just had been in summer holidays and had got more than enough sun. Therefore, we come to the conclusion that the vitamin D food supply might be much more important than reported for many decades.

We could find that obviously vitamin D is reabsorbed by the vaginal mucosa. We found that the reabsorption was individually very different. But after treatment, 58 of these 100 patients (58%) had vitamin D serum values (> 30 ng/ml).

Cervicitis without dysplasia group

Most of the patients subjectively and objectively had a benefit of the therapy. In the survey after six weeks therapy, 79 of 100 women subjectively declared to have “less vaginal problems,” “less discharge,” and “less problems with the sexual intercourse.” This we also could find objectively: After six weeks therapy only 7% of the patients still had bacterial and/or fungal vaginal infections that required a treatment.

Cervicitis and CIN 1 group

Immediately after six weeks of treatment only 10% still had a bacterial and/or fungal cervicitis. Of the 50 patients immediately after six weeks of treatment, 24 patients were free of dysplastic cells (PAP III, PAP II or PAP I). Twenty-six patients still had a CIN 1. Of the 50 patients, 21 still had a high risk of HPV. Before the treatment, 43 had a high risk of HPV.

Cervicitis and CIN 1 group: Follow-up two years after

Unfortunately, not all of the patients are still in our praxis/ambulance. At the moment we also do not have the time and the manpower to make a perfect follow up evaluation. But of the 50 patients in the “Cervicitis and CIN 1” group, we now can present the data of 20 patients among them:

- Of these 20 patients in the Cervicitis and CIN 1 group, two years after the therapy 15 patients had a better PAP (PAP I, II, II W, III)
- Of these 20 patients in the Cervicitis and CIN 1 group, three patients had a CIN 1 again, one patient had a CIN 2–3, one patient a CIN 3. These three patients needed and got a conization and a curettage (15%). All three patients had a therapy resistant HPV high risk infection and chronic therapy resistant bacterial cervicitis (chlamydia trachomatis, coccus).
So of these 20 patients, in three cases (=15%) the vaginal vitamin D treatment was ineffective: Neither a cervicitis nor a higher grade dysplasia and operation could be prevented.

Cervicitis and CIN 2 group

Immediately after six weeks of treatment of the 50 patients in the Cervicitis and CIN 2 group, eight patients (16%) still had a bacterial and/or fungal cervicitis that required a treatment. Of the 50 patients in the Cervicitis and CIN 2 group, nine patients were free of dysplastic cells (PAP 2 or PAP 1). Seven of these nine patients were free of high risk HPV. Of the 50 patients in the Cervicitis and CIN 2 group, 22 patients still had dysplastic cells, but with a better trend (CIN 1). Five of these 22 patients had no more high risk HPV infection. Of the 50 patients in the Cervicitis and CIN 2 group, 19 patients immediately after the six weeks of treatment still had an unchanged CIN 2. All still had a high risk HPV infection. Of the 50 patients in the Cervicitis and CIN 2 group, 38 patients still had a high risk HPV infection (before the therapy of the 50 patients, 46 patients had a high risk HPV infection).

Cervicitis and CIN 2 group: Follow-up two years after

Unfortunately, not all of the patients are still in our praxis/ambulance. At the moment we also do not have the time and the manpower to make a perfect follow up evaluation. But of the 50 patients in the Cervicitis and CIN 2 group we now can present the data of 18 patients among them. Of these 18 patients in the “Cervicitis and CIN 1” group two years after the therapy, in ten cases so far a conization and abrasio could be prevented. Two years after the therapy these ten patients have a better PAP (three patients have a PAP II, one patient has a PAP II W, six patients have a CIN 1). The other eight patients needed and got a conization and a curettage. So we found that in CIN 2 this method obviously had no or only short time antidysplastic effects.

Discussion

Vitamin D and chronic infections

The vaginal vitamin D treatment method (e.g., with OVID®) showed very good anti-inflammatory effects. In the survey after six weeks therapy, 79% of the women had “less vaginal problems,” “less discharge,” and “less problems with the sexual intercourse.” Objectively, after six weeks therapy, only 7% of the patients still had bacterial and/or fungal vaginal infections that required a treatment.

So we found that when compared with the lactobacillus vaginal suppositories (e.g., with Vagiflor® etc.), the vaginal vitamin D treatment method (e.g., with OVID®) might be more effective. The OVID® vaginal vitamin D treatment seems to have good anti-inflammatory effects, and in case of a CIN 1, also antidysplastic effects.

Vitamin D: Hormonal effects

We know that Vitamin D is not only a vitamin but also a hormone. And it has important metabolic, endocrinological, immunological, and anticancer effects. It is regulating the growth of the endocrine cells and protecting them from malignant growth. If there is a predisposition, a chronic vitamin D deficiency can promote the growth of hormone-dependent tumors. New studies show that vitamin D might be an important cancer prevention and therapy factor. With a sufficient vitamin D supply (daily at least 1,000 IU) the colon cancer risk can be reduced to 50%. It even can be reduced to one-third by a daily vitamin D supply with 2000 IU.7-9 If there is a cancer predisposition, a chronic vitamin D deficiency can promote the formation and the growth of malignant tumors. Vitamin D deficiency can raise the risk of breast, ovarian, and prostate cancer.

Vitamin D deficiency and cancer

New studies show a correlation between vitamin D deficiency and lung, bladder, esophagean, gastric, rectal, larynx, and pancreas cancer.11-13 In vitro studies with prostate cell cultures showed that vitamin D could stop their growth. We do not know yet if there is also a correlation between a vitamin D deficiency and a cervix dysplasia and a higher cervix carcinoma risk. But we found in our small praxis/ambulance study that before the vaginal vitamin D treatment 100 of the 200 patients (=50%) had insufficient 25-hydroxy vitamin D serum values (< 30 ng/ml).

Vitamin D against HPV

In the Cervicitis and CIN 1 group, the vaginal vitamin D treatment method (e.g., with OVID®) seemed to have also some antiviral effects. In the Cervicitis and CIN 2 group we did not find this effect. At the moment we also do not know if the vaginal vitamin D treatment method (e.g., with OVID®) has any long time effect on high risk HPV infections. We do not believe that the vaginal vitamin D treatment method (e.g., with OVID®) could be an alternative to the HPV vaccination.

Vitamin D against cervix dysplasia

In the CIN 1 group we found six weeks after treatment good antidysplastic effects. In the CIN 2 group we often found no or only temporary antidysplastic effects. So this vaginal vitamin D treatment method might be an option for the therapy and prevention of chronic cervical infections and maybe of a cervix dysplasia CIN 1 (good anti-inflammatory effects, antidysplastic effects).

Unfortunately the vitamin D treatment method (e.g., with OVID®) was not as effective in the treatment of a CIN 2 as we had hoped starting the study. Regarding also the follow up, we unfortunately found either no or only few and/or short time anti-dysplastic effects.

Conclusion

Immediately after six weeks treatment, most of the 200 patients—subjectively and objectively—had a benefit. So this
vaginal vitamin D treatment method (e.g., with OVID®) might be an option for the treatment (and maybe also for the prevention) of lighter vaginal infections (colpitis and cervicitis) and maybe also of a CIN I.

Contraindication pregnancy
So far we do not know if the vaginal vitamin D treatment method with 12500 IE (e.g., with OVID®) can be problematic in pregnancy. In 2011, just when we were about to publish the method first time international in Arch Gyn Obs, one of our patients with chronic vaginal infections got pregnant during the vaginal vitamin D treatment. Unfortunately she had an early abortion (in the fifth/sixth week of pregnancy). We got some problems and very short time decided to withdraw the publication. We do not think that our vaginal vitamin D treatment method with 12500 IE (e.g., with OVID®) was the reason for this unfortunate course. Meanwhile there appeared some new publications (Holis et al., 2012, 2013) on the importance of vitamin D for the pregnancy and for the development of the embryo and fetus. But so far we are forced to make the following warning:

**WARNING**

So far, we do not know if the high dose vitamin D treatment with 12500 IE is possible in pregnancy. We have no experience. Therefore we recommend an effective contraception during the application.

This small praxis study is not representative. We need much bigger studies with much more dates and with a follow up.

### Materials and Methods

**Primary treatment**
We treated the bacterial and fungal infections according to the antibiogram. In case of infections with *G. vaginalis, C. trachomatis, Ureaplasma, Mycoplasma*, and *Trichomonas vaginalis*, the partner(s) was/were treated simultaneously. Infections with *C. trachomatis, Mycoplasma*, and *Ureaplasma* were treated with tetracyclines. Fungal infections were treated with combined antymycotic prescriptions (vaginal suppositories and cream for the vulva and the intimate area), including the partner(s) treatment.

**Secondary treatment**
After this primary treatment, all patients got a secondary treatment with high dose vitamin D.

- The first years we started with a treatment with vaginal tampons with 5000 IU vitamin D and olive oil (vitamin D on the long side of the tampon, every night, for six weeks).
- Since 2008 we treated with OVID® (=standardized 2 g vaginal suppositories containing 12500 IU vitamin D, neutral oil and adeps solidus), three nights a week, also for six weeks.

**Prescription**
Vitamin D vaginal ovules (for compounding pharmacies), e.g. OVID®, Klösterle Apotheke München, e.g., Rondell Apotheke München: 12500 IE Vit D (e.g., Vigantol®), neutral oil, adeps solidus q.s. XII/XXIV ovules, ad 2 g.

**Why Vitamin D?**
Meanwhile, a lot of studies prove not only the central function of vitamin D for the calcium and bone metabolismin but also its excellent anti-inflammatory immunomodulating and antioxidative effects. Vitamin D is more than only a vitamin. Simultaneously in Central Europe there seems to be an endemic vitamin D deficiency. Vitamin D is not only produced in the dermis and epidermis (induced by UV B) but also orally ingested. Today we know that the oral ingestion seems to be much more important than it was supposed for many decades. The endemic vitamin D deficiency seems to have three main causes obviously increasing with the age: Sunlight exposure deficits, vitamin D food supply deficits, and intestinal resorption deficits (e.g., by dysbiosis, metabolic dysbalance, leaky gut syndrome, etc.). Vitamin D has important metabolic, endocrinological, immunological, and anticancer effects. It is regulating the growth of the endocrine cells and protecting them from malignant growth. If there is a predisposition, a chronic vitamin D deficiency can promote the growth of hormone-dependent tumors. Vitamin D also can prevent chronic degenerative and cardiovascular diseases, from multiple sclerosis, rheumatoid arthritis, diabetes mellitus, Crohn’s disease, hepatitis C etc. New studies show that vitamin D might be an important cancer prevention and therapy factor. With a sufficient vitamin D supply (daily at least 1000 IU), the colon cancer risk can be reduced to 50%. It even can be reduced to one-third by a daily vitamin D supply with 2000 IU. If there is a cancer predisposition, a chronic vitamin D deficiency can promote the formation and the growth of malignant tumors. Vitamin D deficiency can raise the risk of breast, ovarian, and prostate cancer. New studies show a correlation between vitamin D deficiency and lung, bladder, esophagean, gastric, rectal, larynx, and pancreas cancer. In vitro studies with prostate cell cultures showed that vitamin D could stop their growth. After the vitamin D supply, the prostate cancer cells stopped their uncontrolled growth. The same reaction could be observed with colon and breast cancer cells. Mice getting injections with colon cancer cells showed a much slower tumor growth after vitamin D supplementation. Some gynecological publications are showing good vitamin D effects. Therefore, we had some reasons to do this small study.

**Disclosure of Potential Conflicts of Interest**
No potential conflicts of interest were disclosed.
References
1. Holick MF. Vitamin D deficiency. N Engl J Med 2007; 357:266-81; PMID:17634462; http://dx.doi.org/10.1056/NEJMra070553
2. Autier P, Gandini S. Vitamin D supplementation and total mortality: a meta-analysis of randomized controlled trials. Arch Intern Med 2007; 167:1736-7; PMID:17846391; http://dx.doi.org/10.1001/archinte.167.16.1730
3. Bayer W, Schmidt K. Besteht in Mitteleuropa ein endemischer Vitamin D Mangel? Erfahrungsheilkunde 2004; 53:609-13; http://dx.doi.org/10.1055/s-2004-834412
4. Lappe JM, Travers-Gustafson D, Davies KM, Recker RR, Heaney RP. Vitamin D and calcium supplementation reduces cancer risk: results of a randomized trial. Am J Clin Nutr 2007; 85:1586-91; PMID:17556697
5. Schulte-Uebbing C, Schlett S. Vitamin D bei PAP III D und Zervizitis. Dtsch Z Onkol 2010; 42:118-22; http://dx.doi.org/10.1055/s-0030-1257719
6. Schulte-Uebbing C, Schlett S. Kolpitis und Co. Vaginale Vitamin-D Applikation hilft. Gynäkologie und Geburtshilfe 2010.
7. Garland CF, Comstock GW, Garland FC, Helsing KJ, Shaw EK, Gorham ED. Serum 25-hydroxyvitamin D and colon cancer: eight-year prospective study. Lancet 1989; 2:1176-8; PMID:2572900; http://dx.doi.org/10.1016/S0140-6736(89)91789-3
8. Jenah M, Bueno de Mesquita H B, Ferrari P, et al. Association between prediagnostic circulating vitamin D concentration and risk of colorectal cancer in European populations: a nested case control study. BMJ 2010; 340:c5508.
9. Jenah M, et al. High vitamin D levels, lower colon cancer risk? EPIC Norfolk Publications 2010.
10. Garland CF, Gorham ED, Mohr SB, Grant WB, Giovannucci EL, Lipkin M, Newmark H, Holick MF, Garland FC. Vitamin D and prevention of breast cancer: pooled analysis. J Steroid Biochem Mol Biol 2007; 103:708-11; PMID:17368188; http://dx.doi.org/10.1016/j.jsbmb.2006.12.007
11. Grant WB. Relation between prediagnostic serum 25-hydroxyvitamin D level and incidence of breast, colorectal, and other cancers. J Photochem Photobiol B 2010; 101:130-6; PMID:20570169; http://dx.doi.org/10.1016/j.jphotobiol.2010.04.008
12. Ingraham BA, Bragdon B, Nohe A. Molecular basis of the potential of vitamin D to prevent cancer. Curr Med Res Opin 2008; 24:139-49; PMID:18034918
13. Pilz S, Tomatschitz A, Obermayer-Pietsch B, Dobnig H, Pieber TR. Epidemiology of vitamin D insufficiency and cancer mortality. Anticancer Res 2009; 29:3699-704; PMID:19667167
14. Wang TT, Dabbas B, Laperriere D, Bitton AJ, Soualhine H, Tavares-Mendoza LE, Dionne S, Servant MJ, Bitton A, Seidman EG, et al. Direct and indirect induction by 1,25-dihydroxyvitamin D3 of the NOD2/CARD15-defensin beta2 innate immune pathway defective in Crohn disease. J Biol Chem 2010; 285:2227-31; PMID:19948723; http://dx.doi.org/10.1074/jbc.C109.071225
15. Levin J. Vit D suppl. Improve SVR in chron. Hep. C 2010; www.natap.org
16. Pilz S, Tomatschitz A, Grammer TB, März W. Vitamin D Supplementation. Zukünftige Standardtherapie in der Gynäkologie? Gynäkologie und Geburtshilfe 2010; 6:28-30
17. Bonkhoﬀ H, Fiserer T, Hunsicker I, Remberger K. Progesterone receptor expression in human prostate cancer: correlation with tumor progression. Prostate 2001; 48:289-91; PMID:11536308; http://dx.doi.org/10.1002/pros.1108
18. Schulte-Uebbing C. 7-keto-DHEA - ein kurzer Überblick. CO MED 2010; 8:1-4.
19. Schulte-Uebbing C. Ursachen von Endometriose: Schlussfolgerungen aus Praxiserfahrung und Nachuntersuchung. ZKM 2010; 1-1.5
20. Schulte-Uebbing C, Dibbelt L, Kuss E. Steroids as Inhibitors of Human Placental Glutathione-S-Transferase by Steroids. Placenta-Kongreß, Aachen 1986.
21. Schulte-Uebbing C, Dibbelt L, Kuss E. Human Placental Glutathione-S-Transferase: Interactions with Steroids. Biol Chem Hoppe Seyler 1988; 369:23-8; http://dx.doi.org/10.1515/bchm3.1988.369.1.25