Dear Readers,

In the first months of 2019, many things have changed in the Dr. Bayer laboratory. There was a change in the medical management in January. In February, a new laboratory information system was installed, giving the findings layout a new design. And at the end of March, Labor Dr. Bayer also moved to the new location in the course of the relocation of SYNLAB MVZ Leinfelden-Echterdingen Ltd.

In this issue of Labor Bayer newsletter, I would like to introduce myself briefly. My name is Dr. Christoph Milczynski and in January 2019, I took over as medical director of the laboratory Dr. Bayer. I am a specialist in laboratory medicine and have many years of experience in the field of clinical chemistry, microbiology and endocrinology. The clinical experience in internal diseases I get during the work in hospital of Ludwigshafen Ltd. Further training in laboratory medicine I completed in the laboratories of Limbach Group. One of the most significant achievements in of this time was the development and establishment of the investigation procedure of the intestinal microbiome for this laboratory group.

The special field of complementary medicine also offers the possibility to deal mainly with topics of preventive medicine. There are also clinical pictures, their diagnostic and therapeutic Approaches are often still little established in classical medicine. For example, stool diagnostics or hormonal saliva diagnostics are Topics that will become more and more important.

In this issue

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We dedicate this issue to saliva analysis.

Saliva is a biological fluid that is used in medical diagnostics for more than 30 years for estimation of different markers. Saliva can be considered for the most part as a filtrate of the blood. There are electrolytes, hormones, antibodies and therapeutics in it. The secretion performance of the salivary glands under physiological conditions contains between 1000 and 1500 ml per day. The steroidal hormones that you can find in saliva are especially in their „free“, biologically active fractions. In this way the measured hormones represent the decisive part of hormones.

We hope you enjoy reading it.

With best regards

Dr. med. Christoph Milczynski
Saliva analysis as reliable and non-invasive endocrinological diagnostics

**Advantages of saliva analysis**

Although saliva is a physiological fluid and as already mentioned, many, especially low-molecular substances in it have not reached the right position in medical diagnostics yet. This can be achieved by its property of being relatively tough, foaming and sometimes difficult to collect as test material. Furthermore, the concentrations of biological active substances are significantly lower than in the blood. Through the technological progress in recent years it was able to establish methods with reliable measurements without costly extraction steps. One of the most widely used investigations is the measurement of cortisol in saliva. The measurements shown in figure 1 a gut correlation between serum and saliva. This is a good established application in the medical diagnostics.

Moreover, this type of investigation has more advantages than the determination in blood. The most important of them are:

- non-invasive and stress-free method of sampling and therefore especially recommended for children,
- samples can easily be taken several times a day, thus it is possible to calculate an average daily value or to determine a hormonal daily profile,
- Saliva can be collected by the patient on themselves,
- the saliva samples can be stored in appropriate containers and can be sent by post.

**The regulation of the circadian rhythm and its disruption by stress**

The secretion of steroid hormones like cortisol, testosterone or dehydroepiandrosterone (DHEA) is subject to a circadian rhythm. The highest quantities are used to be found in the wake-up phase and released in the early morning hours. The release of cortisol from the adrenal cortex is controlled by the Corticotropin Releasing Hormone (CRH) from the hypothalamus and through the adrenocorticotropic hormone (ACTH) from the anterior pituitary gland via a negative feedback mechanism. In this way the organism can respond to the mental and physical “physiological stress”. During the day the released rate of these hormones decreases and reaches its physiologically minimum around midnight (see Figure 2).

**Figure 1:** Correlation between the concentrations of free cortisol in plasma and the concentration of cortisol in saliva. Vining et al. Ann Clin Biochem 1983; 20: 329–35

**Figure 2:** Diurnal course of salivary cortisol levels (data in hours after waking up) of 110 adults (mean value +/- 2 standard deviations). Westermann, J. et al. Clin. Lab. 50, 11–24, 2004.

If patients are exposed to stress (physical and/or psychological) the regulation of cortisol release is suspended, and the cortisol release disturbed. In the first days and weeks it shows a significantly increased cortisol level during the entire course of the day and the circadian rhythm is also disturbed. Such a situation can be interpreted as a response to the acute stress. If the stress lasts very long, the secretion performance of the adrenal gland sinks and can be hardly stimulated by the impulses of pituitary gland with ACTH. Long persisting stress situations could thus lead to chronic fatigue or “burnout”.

\[
y = 1.36x + 2.4 \\
r = 0.97
\]
The secretion of the neurohormone Melatonin

Melatonin is synthesized in the pineal gland from the amino acid tryptophan. The biosynthesis is also subject to a circadian rhythm, whereby very low values are visible during the day because the synthesis is inhibited by the light. At the dawn of the darkness this inhibition is lifted, so that the synthesis and the secretion of melatonin increase. Melatonin is also secreted in the intestines and the retina of the eye. The melatonin concentration increases during the night and reaches in the deep sleep phase around 3 o’clock its maximum, which can reach up to 10 times higher level than values measured during a day (see Figure 3).

Steroid hormones in saliva

An essential advantage of the diagnostics of steroid hormones in the saliva lies in the determination of those biologically active form. Most steroid hormones are bound in blood to certain proteins such as corticosteroid-binding globulin (CBG), sex hormone binding globulin (SHBG) or albumin. Only about 1–3 % of these hormones are present in the blood in free and bioactive form. To estimate a correctly effectiveness of these hormones the blood can be processed very expensively analytic procedures or by can be calculated by special formulas from the total concentration of hormones and their binding proteins. These proteins are due to their molecular size and the salivary secretion mechanisms are not in the saliva and the amount of the hormone corresponds to their active portion. That means, it can be a highly sensitive and specific test procedure for quantitative determination of the most hormones like cortisol, dehydroepiandrosterone, testosterone, estradiol, estrone, estril, progesterone, 17-OH-progesterone and androstenedione, despite their low concentrations in saliva. The determination of this form of steroid hormones is highly recommended and used in the monitoring of transdermal hormone replacement.

Recommended selection of parameters

The saliva analysis of the steroid hormones can be considered as a more effective test and can be used for the following indications:

- determination of physiological state
- detection of deficiencies in the synthesis
- stress monitoring during a day
- clarification of the disbalance between cortisol and DHEA secretion
- clarification of the causes of overweight (night hypercortisolism)
- reduced performance in sport activities (overtraining syndrome)
- determination of the phase of the cycle phase in women
- estrogen status in postmenopausal women
- estrogen dominance in the perimenopausal women
- monitoring of transdermal hormone replacement therapy with bioidentical preparations

Single requests in saliva

- 17-OH progesterone in saliva
- androstenedione in saliva
- cortisol in saliva
- dehydroepiandrosterone in saliva
- melatonin in saliva
- estradiol in saliva
- estril in saliva
- estrone in saliva
- progesterone in saliva
- secretory immunoglobuline A in saliva

Patients who suffer from stress situations, the Melatonin concentration in the evening and at night are significantly lower, so that due to the low level of melatonin sleep disorders can occur. On the other hand, during the winter months, especially in northern countries, the level also increases during the day, so that patients develop a chronic fatigue and can get a winter depression.

Melatonin as an essential neurotransmitter has an influence on hippocampus, which is responsible in the brain for learning and remembering. The action of melatonin increases the synaptic plasticity and thereby improves the performance of the brain. So relaxing sleep is enormous important for learning and memory functions.

The determination of changes in the melatonin rhythm by determination of melatonin in the evening hours and at night can be very be helpful, especially in clarifying:

- sleep disorders
- seasonal affective disorders
- depression
- anorexia nervosa
- disorders of the female menstrual cycle
- jetlag
- difficulty concentrating on learning
Literature


