

A PRACTICAL UNDERSTANDING OF ROSACEA

PART 1:
HEAT REGULATION AND THE
WARM ROOM FLUSH PHENOMENON

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CONTENTS

CHAPTER 1: ABOUT THE BOOKLET	2
CHAPTER 2: ROSACEA MECHANICS	3
CHAPTER 3: UNDERSTANDING THE WARM ROOM FLUSH	9
CHAPTER 4: OVERCOMING THE WARM ROOM FLUSH	12

CHAPTER 1: ABOUT THE BOOKLET

This booklet has been written for rosacea sufferers who are struggling to understand their condition and are looking for new ways to overcome the facial flushing and facial redness aspects of rosacea.

The booklet uses the warm room flush phenomenon to explain what is going on when the body regulates heat and ways you can reduce this form of facial flushing.

The simplified biological mechanics of rosacea have been explained in the booklet. Minimal medical terms have been used and may be further referenced online. I believe that a basic understanding of how the body deals with heat regulation and dilation of blood vessels is needed if you want to begin reversing this and other forms of facial flushing associated with rosacea.

It is not the intention of this booklet to name or deal with specific chemicals. The reason for this is simple, once you have excessive blood vessels and nerves in your skin, you will have an excess of numerous inflammatory chemicals. It is the intention of this booklet to highlight the systems involved, so that these systems can be used in your favor.

To enable a continual reversal of rosacea, the majority of people with rosacea will need to steadily manage their condition. This may simply involve being aware of what biological systems are currently in play, such as heat regulation or skin sensitivity, but keeping it under control is very achievable.

I hope the contents of this booklet help you to better understand rosacea and assist you in dealing with rosacea.

CHAPTER 2: ROSACEA MECHANICS

To a certain point the phenomenon known as the warm room flush, where someone with rosacea enters a warm room and promptly experiences a facial flush, is a normal process.

If someone without rosacea gets too hot, that is their internal thermostat is high, then their body will trigger events to normalize their temperature. These events primarily involve sweating to cool the body and dilating cutaneous (skin) blood vessels to release heat from the body. Someone with rosacea will do the same, because this is a normal process.

What is happening? To put it simply, nerves are being activated to perform some special functions. A function we are concerned with here is vasodilation. Cutaneous nerves are triggered and the nerves release chemicals to dilate blood vessels as well as activate other nerves. As more blood flows through the blood vessels, the blood vessels themselves release more chemicals to keep vasodilation going.

The blood vessels further respond to this extra blood flow by initiating angiogenesis (the growth of blood vessels) and nerves respond by initiating axonogenesis (the growth of nerves). The body thinks there is a good reason behind this activity, so new infrastructure is prepared for this extra blood flow and nerve activity. Again, this is a normal process that occurs in everyone. Without it we wouldn't be able to regulate our body temperature, fight off infection or repair tissue after injury.

However, if the nerve-mediated vasodilation occurs too frequently and too rigorously, then frequent and considerable angiogenesis and axonogenesis will result. This is in-effect the process behind the progression of rosacea.

It is only to be expected that if you have more blood vessels and more nerves in your skin, that you will have more dilation of blood vessels and more facial flushing when your body initiates the heat release process.

ROSACEA INFRASTRUCTURE

It often takes many years of cumulative angiogenesis and axonogenesis before rosacea begins to be seen as apparent or a problem. The good news is that this process is reversible, as will be discussed in the next section.

In rosacea, there is a lot more infrastructure in the skin to release heat. Both nerves and blood vessels are increased. If you only see rosacea as a skin disorder or even a blood vessel disorder you will struggle to control it because there is more to this biological system.

The common red butterfly pattern across the cheeks and nose can be explained by special infrastructure the body uses to release heat. The head and face are important areas, as well as the inner hands and feet. These areas have special nerves to dilate blood vessels and special blood vessels to release the heat carried in the blood.

The nerves involved in these areas are sympathetic nerves. They can act to dilate special blood vessels (arteriovenous anastomoses), which open up and shunt blood into the blood vessels of your skin, creating the phenomenon we know as the flush. This also explains why many people have intense flushing confined to certain regions of the face.

Did you know that blood vessels in your skin don't actually have a colour. It is the redness of the blood flowing through that gives a red appearance.



Figure 1: This figure is a representation of the head and neck arteries of the human body. Imagine the incredible volume of blood that the special blood vessels (arteriovenous anastomoses) can shunt from arteries into the small capillaries of your flush zones. The flush zone capillaries therefore take on a more heat regulatory function than a nutritive role. ©iStockphoto.com / London England.

Another important type of nerve involved in rosacea is the sensory nerve. Unlike sympathetic nerves that are triggered centrally in the brain, sensory nerves are important local mediators of vasodilation.

Sensory nerves can directly initiate vasodilation by local activation through such triggers as sunlight or irritating chemicals applied to the skin. In many cases of rosacea the sensory nerves can play a role in all flushing episodes. This scenario involves the dilation of blood vessels by any means, which in turn creates localised inflammation that activates sensory nerves in that region, creating the burning sensation often associated with flushing.

A major problem involved with the continual activation of sensory nerves is hyper-sensitization. As rosacea progresses through regular flushing, nerves not only undergo axonogenesis but they can become sensitized. This can cause flushes to become more intense and painful.

In advanced rosacea, the extensive nerve and blood vessel infrastructure is so sensitized that even a small increase in blood flow will result in significant flushing episodes.

CHEMICALS

There are hundreds of known chemicals involved with nerves and blood vessels. This section raises some important chemical groups released by cutaneous nerves and blood vessels, such as neurotransmitters, neuropeptides and growth factors.

Neurotransmitters can simply be seen as chemicals that transmit a nerve signal to other nerves as well as other tissues, such as blood vessels. Neuropeptides have a similar function to neurotransmitters but often act longer and are more potent.

These chemicals can activate or deactivate nerves, or act to dilate or constrict blood vessels. An important concept that will be discussed in this book is that of neuropeptide depletion and storage.

Australian Sciences has conducted several years of neuropeptide rosacea research. An early goal was to determine the role of neuropeptides released by cutaneous nerves in various forms of flushing. The findings of this research, which involves neuropeptide storage and depletion, led to a new approach for rosacea management. This will be discussed in depth in the following sections.

Nerves and blood vessels both need growth factors. Growth factors help to maintain blood vessels and nerve structures and to enable their further growth. Skin cells release growth factors, which results in nerve and blood vessel innervation of the skin. Nerve activation also increases growth factors as part of a chemical cascade. Certain nerve growth factors are also involved in nerve sensitization. Nerve growth factors and blood vessel growth factors have also been found to be interchangeable.

The main goal of this section is to make you aware that the human body has an established system in place to perform heat regulation that leads to vasodilation and may lead to facial flushing. Nerves and chemicals are involved and there are consequences such as nerve and blood vessel growth as well as sensitization. These concepts will be used in the next section to help build an understanding of the warm room flush that is often seen in rosacea.

Abundant reading on neuropeptides and growth factors are available on-line. I recommend you do further reading, without focusing on anyone particular neuropeptide, growth factor or chemical.



Figure 2: This figure is a representation of nerve conduction. The electrical connections result from the release of numerous neurotransmitters (short acting) and neuropeptides (long acting) crossing the nerve junctions. More inflammatory neurotransmitters and neuropeptides means more nerve activation. For flush zones of your skin this may mean more dilation of blood vessels and greater flushing. *@iStockphoto.com / ktsimage.*

CHAPTER 3: UNDERSTANDING THE WARM ROOM FLUSH

We previously glanced over the general heat regulation process when someone is too hot. Now let's look at heat regulation a little more in-depth and through the eyes of someone with rosacea who experiences a facial flush when entering a warm room.

The scenario of entering a warm room implies that you are entering from a cooler environment. We must first understand what is happening in this cooler environment before we can understand what then happens when in the warm room.

HEAT CONSERVATION

The body has a system of releasing excess heat when too hot, but it also has a system to conserve heat when cold. The systems are very much intertwined. In the cooler environment, the body will constrict cutaneous blood vessels because heat is carried in the blood. Less blood getting to the surface of the skin, means less heat escaping from your body.

Those with rosacea often experience colder cheeks and hands in cool or even slightly cool environments. This phenomenon is a result of the excess heat regulation infrastructure in the flush zones of the skin. In cool environments the extra blood vessels could potentially release too much heat. However, due to the extra nerve infrastructure, the nerves begin to constrict blood vessels in the flush zones of the skin much earlier than other areas. This results in cooler areas of skin.

When blood vessels get too cold they begin to automatically dilate because the blood vessels lose their ability to constrict, causing redness of the skin.

NEUROPEPTIDE STORAGE

In cooler environments, chemicals the body uses to dilate blood vessels are no longer getting released in significance. If the person is in a cool environment for a long period of time, then these dilating chemicals such as neuropeptides, begin to build up.

As previously discussed, many neuropeptides are major dilating chemicals released by the body. Many of the inflammatory neuropeptides we are interested in can only be made in small amounts by the body everyday. So the nerves have a way of storing these chemicals to use when needed. Similarly, other dilating chemicals are also building up their availability.

Australian Sciences has conducted tests that not only show more neuropeptides are released in rosacea skin during flushes, but that the regeneration of neuropeptides happens faster. This may be another consequence of more nerve and blood vessels in the skin.

ENTERING THE WARM ROOM

Lets now return to the warm room example. First lets assume someone with rosacea has remained in a slightly cool environment for several hours. Due to their excessive heat regulation infrastructure (more blood vessels and nerves), their body over compensates by constricting cutaneous vessels. This results in the accumulation of inflammatory chemicals such as neuropeptides, which have built up their capacity.

The person then enters the warm room and their internal thermostat begins to increase. The body quickly responds by initiating the release of heat. Nerves are activated in the skin to dilate blood vessels as well as trigger other nerves. It is at this point where the previous exposure to the cool

environment makes an impact. The nerves release their abundant neuropeptides in what seems an ongoing burst. Vasodilation begins and further nerve activation occurs, resulting in a facial flush.

The process may be so great that the flush continues even when you go back to the cooler environment. This is in part due to the ongoing nerve mediated burst as well as the downstream inflammatory consequences, such as the flow of extra blood through blood vessels causing sheer stress within the vessels and the release of further chemicals to continue the dilation.

After some time, for no apparent reason the flush abruptly ceases. This abrupt end to the flushing phenomenon can be partially explained by neuropeptide depletion.

As previously discussed, many inflammatory neuropeptides are only produced in a limited amount and once depleted they take time to regenerate their stores. From a biological view, the sudden end to an intense flush somewhat resembles the neuropeptide depletion induced by capsaicin (the active chemical found in red peppers).

In summary, this section tells us that heat regulation, both cooling and heating, is likely to be excessive when there is excessive heat regulation infrastructure in the skin. More nerves and blood vessels in the flush zones of skin cause constriction of blood vessels even in slightly cool environments. This results in a build up in the availability of inflammatory compounds such as neuropeptides, which can later be released in large amount when the body goes into heat release mode.

The extent of this excessive heat regulation and how you can assess your own heat regulation activity is discussed further in the next section.

CHAPTER 4: OVERCOMING THE WARM ROOM FLUSH

Before we discuss how overcoming the warm room flush is possible, I would first like to discuss an efficient and practical way of reducing the excessive heat regulation infrastructure within rosacea skin and also discuss effective ways of reducing excessive skin activity thereby reducing the need for excessive blood vessels and nerve infrastructure.

IPL – INTENSE PULSED LIGHT

If you have persistent facial redness then you have an excessive blood vessel structure in your facial skin and you are perfectly positioned to benefit from a reduction of this excessive infrastructure by a simple treatment known as IPL. There is a direct relationship between the amount of blood vessels and inflammation/flushing. Reducing the excessive blood vessels in your flush zones is a major step towards reducing flushing.

The best way to reduce the excessive blood vessels is through Intense Pulsed Light (IPL) therapy. IPL will reduce cutaneous blood vessels, but how much will depend on: (1) the IPL procedure (2) the individual.

IPL works by sending energy (in the form of light) into the skin. The red colour of the blood attracts the energy that ultimately damages the blood vessels and results in their removal. However, it is common for IPL practitioner's to firmly press the IPL head down on the skin prior to releasing the light. This may allow deeper vessels to be treated but the superficial vessels are having the blood squeezed out of them. This is a problem because unless blood vessels contain blood, they don't have any colour and won't absorb as much of the light energy.

We recommend a multiple pass procedure that involves both firmly applying the IPL head to the skin (to treat deep vessels) and then lightly applying the IPL head to the skin (to treat superficial vessels).

IPL is good but it isn't perfect. The process of sending energy to destroy blood vessels also causes the regeneration of blood vessels (known as angiogenesis). This can lead to different treatment outcomes. Some people may reduce their facial redness by 90% while others may see a 50% reduction after several IPL treatment sessions. People with rosacea also have a tendency for greater angiogenesis.

IPL TIPS:

You don't need high IPL energies to damage blood vessels. Find an IPL Practitioner who understands this and uses multiple pass procedures. Don't apply too much water to your face for several hours after the IPL session. The water is easily absorbed and can increase the swelling. If you get to the point where you no longer reduce facial redness through IPL, then focus on reducing flushing to continue your reduction in facial redness and rosacea.

One of the aims of this booklet is to let you know that IPL is likely to reduce cutaneous blood vessels and directly assist in reducing facial flushing as well as make the other flush reducing recommendations in this booklet feasible or achievable. I believe IPL is the best first line treatment of facial redness and flushing. IPL can be further referenced online or discussed with your doctor.

Your aim should not be to reduce your facial redness to zero with IPL. Instead look to make a major reduction in redness and follow up with flush reduction methods over the long term that will allow you to reverse the excessive skin infrastructure and sensitization.

REDUCING SKIN ACTIVITY

Even after successfully reducing facial redness with IPL, the problem of skin sensitivity may persist and may contribute to the progression of rosacea. Reducing this problem can greatly assist in reversal of rosacea symptoms. This is just common sense. Even if you do not use irritating cosmetics on your flush zones, a reduction in skin activity is recommended.

If you reduce the over activity of the skin, you reduce the infrastructure required to maintain it. Less nutrients will be needed for supply, so less blood vessels are needed to get them there. Just as the body has a system to increase blood vessels and nerves in your skin to correlate with their activity, the body also has a system to reduce blood vessels and nerves in your skin when they are less active. The body uses growth factor regulation as one method of achieving this balance. This is why reducing flushing and skin irritation is so important.

Australian Sciences is developing a range of effective products aimed at assisting in the reduction of excessive skin cell activity due to environmental factors such as sun exposure. Australian Sciences has conducted extensive research into the normalization of inflammatory skin cells with natural compounds such as silymarin, egcg, vitamin B12 and many others. Independent research has also showed these compounds to be effective for other inflammatory skin disorders such as atopic dermatitis and psoriasis. We believe these products can help normalize skin cells and assist in the long-term reversal of excessive skin infrastructure.

Further benefits can be achieved through reducing the exposure of skin cells to environmental factors. A major contributor to excessive skin cell activity is sunlight. Not only is the ultraviolet radiation a major contributor, but the excessive heat energy delivered to skin cells is enough on its own to cause problems for those with rosacea.

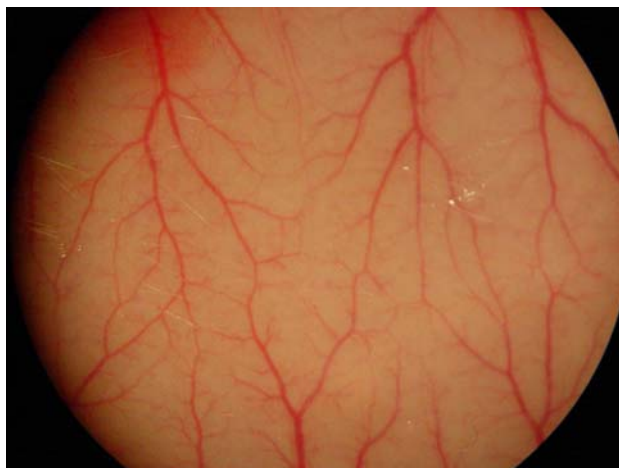


Figure 3: This picture shows the dramatic effect of UV (ultraviolet) light on the skin of mice. 4 MED (minimal erythema dose) was administered to mice over a period of 30 minutes. 20 hours after the UV exposure significant vasodilation and growth of blood vessels can be seen. Picture supplied by Australian Sciences.



Figure 4: 4 MED was again administered to mice over a period of 30 minutes. However these mice were pre-treated with topical Silymarin & EGCG. You can see the potent inhibitory action of this combination on the UV induced vasodilation and growth of blood vessels. Picture supplied by Australian Sciences.

ENTERING THE WARM ROOM WITHOUT FLUSHING

Early on in my own rosacea experience I believed that heat exposure and getting hot was the problem, because it would ultimately cause me to flush. So I tried to stay cool. But I found that I was not getting better. I even seemed to be experiencing more intense flushes. At the time I didn't understand what was going on or what I could do about it.

I pressed on with the rosacea research. The research had now taken me to China where I spent several months conducting experimentation. When I got back to Sydney I noticed that my facial redness was reduced. What happened during this time to cause this reduction? In addition to trying to reduce flushing triggers and sun exposure, which I always try to do, one thing immediately struck me. Due to the opposite seasons of Australia and China I went through a year without experiencing winter.

Putting some of the rosacea neuropeptide research I learned into practice, the coming winter I did an experiment to try to continually release neuropeptides thereby not enabling a build up of these chemicals by the nerves in my skin. After all, what is the facial flush? It's not caused by a gentle release of inflammatory chemicals produced by the body, but caused by a massive release of these chemicals! In effect I was creating a summer-like environment by using heaters to prevent my face and body from getting cool (without getting too hot). I got through the winter and saw further improvement in erythema and flushing.

I continued the experiment in the summer, but this time the cool environment was inside due to air conditioning or insulation. The warm room was now outdoor exposure to hot weather. I again tried to continually release neuropeptides throughout the day. I did use air conditioning sparingly during the summer only to reduce very warm environments like hot cars. But did not focus cool air directly on my face (flush zones) and did not get cool. Again I noticed a great reduction in overall flushing and my facial redness was further improved. Over time I noticed a greater tolerance to warm environments.

There does seem to be a correlation between cooler environments and rosacea. In tropical southern China there is little rosacea found, but as you travel north towards areas that experience cold winters, rosacea is very common.

Over the previous 18 months I had experienced significant continual improvement in erythema and flushing. I planned to continue the same regime and monitor the outcome. However, I needed to return to China to perform research on another project for Australian Sciences. When I arrived in China it was approaching winter. I was spending eight hours a day in a cold lab that was only 15 degrees Celsius. After just a few days I began to experience something that hadn't happened for more than a year, I began to experience warm room flushing again!

The experimentation finished after just 3 weeks and I was able to work in a heated room for the rest of my stay in China. Needless to say the warm room flushing abruptly ceased. Even short periods in below zero weather did not cause the warm room flushing to re-appear.

Could the build up of neuropeptides and other inflammatory chemicals cause of all my rosacea flushing? Unfortunately the answer is no. However, this build up did play a major role in warm room flushing and warm environment flushing, both very common flushing triggers.

The term 'inflammatory cycle' has previously been used to describe a state of rosacea that leads to the continual progression of the condition. The heat regulation process may have much to do with this 'inflammatory cycle'. This is likely due to the fragile balance of heat conservation and heat release systems seen in those with rosacea.

Even slightly cool environments will kick off the heat conservation phase in flush zones enabling greater stores of neuropeptides, which when released in large amounts are likely to result in a flush.

Many with rosacea even try to remain in cool environments for long periods in an attempt to reduce facial flushes from occurring. However, this is counter productive because it can result in significant inflammatory neuropeptide storage. When the person eventually enters a warm environment they have a build up of neuropeptides ready for release. In this situation a large flush will be difficult to prevent.

An aim of this booklet is to let you know that even slightly cool environments may cause neuropeptide storage to begin in your flush zones, as these areas begin to conserve heat very early. The impact of this neuropeptide storage may result in an increase in the number of warm room flushes and an increase in the severity in warm room flushes.

WHAT IS COOL AND WHAT IS WARM?

So how can you tell what is a cool environment and what is a warm environment? The answer lies in your flush zones.

If the flush zones of your face (cheeks, etc) are cool to the touch, then it is very likely that the availability of inflammatory chemicals such as neuropeptides are building up. Your flush zones don't have to be red hot for these chemicals to be released. If you want to continually release neuropeptides gradually, then you want to have neutral to slightly warm skin (not hot and not cold).

By ensuring your environmental temperature is biased towards warm, then your flush zones will be biased towards neuropeptide depletion rather than neuropeptide build up. I also believe that it is not the actual temperature that is important but more of a question of time. The longer you stay in a heat conservation phase (your flush zone is cold) then the longer the neuropeptide build up continues.

If you continually experience flushed skin in warm environments, and you just get hotter during flushes, then you need to reduce the excessive infrastructure in your skin before you can attempt to modulate your environmental temperature and avoid neuropeptide build up. First try IPL to reduce some of the extra blood vessels in your skin.

This final chapter has highlighted ways that will assist you in overcoming warm room flushes. An important initial step is to reduce some of the excessive heat regulation infrastructure (blood vessels) in your skin by IPL. Other important steps involve reducing skin cell activity by limiting sun exposure and to attempt flush reduction methods to change the natural bias of your flush zone towards blood vessel and nerve regression. This chapter has focused on reducing warm room flushing and neuropeptide build ups by adjusting your environmental temperature and therefore your flush zone skin temperature.

A key objective of this booklet is to let you know that even slightly cool environments will set your flush zones into heat conservation mode and neuropeptide build up, and that slightly warm environments are enough to enable continual neuropeptide release in flush zones.

To enable a continual reversal of rosacea, the majority of people with rosacea will need to steadily manage their condition. This may simply involve being aware of biological systems such as heat regulation or skin cell activity. By following the recommendations in this booklet I have found that keeping rosacea under control and the long term reversal of rosacea is very achievable.

I sincerely wish you success in reversing rosacea. This is the first rosacea booklet produced by Australian Sciences and the topic of this booklet was chosen because we believe this topic will be of greatest benefit to rosacea readers. I hope you have enjoyed reading this booklet and I hope it has given you a new perspective on warm room flushing phenomenon and rosacea.