TABLE OF CONTENTS

The Effect of Context in Healthcare - A Programming Study
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FOREWORD

Therapeutic measures carried out in the healthcare field owe their efficacy to a varying (but generally speaking substantial) extent to what are commonly known as general therapeutic factors, placebo factors or non-specific factors. These are factors that cannot be attributed to the mechanisms of action of specific preparations or procedures, but refer instead to the *context* in which the treatment takes place, and especially the physician-patient relationship. This is why we also sometimes speak of context factors.

The best evidence of the existence of context factors can be found in the history of healthcare. Until the early part of the last century, numerous preparations were being given or procedures applied which we now know cannot possibly have any effect, but which nevertheless did sometimes work. It is worth noting that placebo or context factors need not necessarily be inert substances. Context factors can also have added therapeutic value in relation to "specific" medicines or other specific therapeutic procedures.

In scientific research into the efficacy of specific treatments, placebo or context factors are often regarded simply as an annoyance. If, however, they are viewed from the perspective of medical treatment as a whole, it is extremely important that we try to unravel precisely which mechanisms (to be described in psychological and/or physiological terms) play a role. This field of research is full of pitfalls. That is why the Advisory Council on Health Research has asked NIVEL to conduct what is termed a “programming study”, i.e. to take stock of what is known about context factors with a view to laying down guidelines for possibly meaningful scientific research. The study was financed from the coordination fund of the Consultative Committee of Sector Councils for Research and Development (COS).

The results of this programming study are now available. The RGO is delighted that NIVEL, in the person of Dr A.M. van Dulmen, has discharged its task in an exemplary fashion. On 26 September 2000 an “invitational conference” was devoted to this report, with a view to making recommendations for further scientific research on this basis. For a brief summary see Appendix A.

1 INTRODUCTION

Healthcare in the 20th century is characterised, *inter alia*, by rapid developments in the therapeutic field. Despite the growth in therapeutic possibilities, there does not, in general, appear to be a one-to-one relationship between a medical intervention and its therapeutic effects. This is because, in addition to specific effects of physical or pharmacological interventions and the natural course of complaints and diseases, all kinds of non-specific therapeutic effects also occur within the healing process (Turner *et al.*, 1994; Kleijnen *et al.*, 1994). These effects appear to be responsible for a considerable proportion of the therapeutic effects (White, 1988) and therefore make a positive contribution to the practice of healthcare. Thus it is not only the nature of a medical treatment but also the manner and the setting in which that treatment takes place that impact on the health of the patient concerned. There is unfortunately still a great deal of uncertainty over the mechanisms involved, and the therapeutic value and curative effect of the physician-patient relationship is, in general, underestimated (Sullivan, 1993; van der Geest, 1995; Roberts, 1995). In the interests of the quality of healthcare, however, it is important that we gain a clearer understanding of this issue. Knowledge of this kind can assist us in adjusting treatment programs, in making an adequate assessment of the effects of a given therapeutic agent and also in utilising these factors to their best advantage. This view has already been endorsed in a 1993 advisory report from the Health Council of the Netherlands (p. 208).

1.1 COVER TERM

This report sets out to clarify the nature of the phenomenon and possible research opportunities. It provides an overview of scientific research recently conducted in this field. The first thing we must do is to define our terms: exactly what phenomenon is it that we are trying to get to the bottom of? In considering placebo or non-specific effects, we often think of the effect that is imparted by the ritual of administering a pill. The fact that even patients who know that they are being given a placebo can nevertheless respond positively shows, however, that there are, in addition to that ritual, a range of other factors relating to the patient, the physician and the physician-patient relationship (Park & Covi, 1965; Bergmann *et al.*, 1994). A single factor - such as, for example, the patient's expectations or the status of the physician - is a world within itself. The relative contribution made by each of these factors is unknown. In reality, what we are dealing with is a cover term embracing different elements which point in the

same direction, but which refer to different phenomena and processes and are explained by different theories (Bensing, 2000).

We often speak in this context of non-specific effects or placebo effects. However, it has been pointed out from various quarters that terms such as placebo and non-specific effects have certain shortcomings. Among these is the widespread connotation of the term placebo as being an inactive agent, since this implies that the active mechanism of a verum (i.e. the specific effects) *is* known. Moreover, a distinction between the terms non-specific and specific effects is ambiguous, since this erroneously creates the impression that the activity of a verum would *not* be distorted by non-specific effects (Roberts *et al.*, 1993).

In randomised controlled trials (RCTs), attempts have been made to study the specific effects separately from the natural course and the non-specific effects. However, because non-specific effects also interact with specific factors, the magnitude of the effect of a specific preparation is also ultimately dependent on the influence of non-specific factors (Lindahl & Lindwall, 1982). It is therefore also important to investigate what these non-specific factors are and the extent to which they interact with the specific factors (Kleijnen *et al.*, 1994). The efficacy of *any* medical intervention is therefore dependent on the circumstances or rather the interpersonal *context* in which a medical contact takes place. Consequently, instead of referring to non-specific factors in this report we shall, as far as possible, speak of *"the effect of context in healthcare"*[1]. It is a curiously paradoxical that the more we know about the active components of placebo factors, the more specifically we are able to cite these. The value of the cover term is thereby reduced.

"The Effect of Context in Healthcare" has much in common with a topic that is considered relevant by the Advisory Council for Research on Nature and Environment (RMNO) - namely, "the context effects of the environment". Hence the RMNO is also supporting this study. Following on from this project, the RMNO is planning to conduct a study into the interaction between non-specific environmental factors (nature and the environment) and the perception of sickness and health. The results of the present study may offer some leads in this respect.

1.2 THE EFFECT OF CONTEXT IN PSYCHOTHERAPY

The mechanisms at work in psychotherapy have long been the subject of speculation. The effect of psychotherapy is said to be no more than that of a

placebo treatment, in which the acts of arousing positive expectations, showing interest and recognising an individual as being in need of help are important factors (Prioleau *et al.*, 1983; van Dijck, 1986; Shapiro & Shapiro, 1997). A comparable effect is to be found in hypnotherapy, which is said to function primarily as a method of generating positive expectations (van Dyck & Hoogduin, 1990). Although context effects in psychotherapy lie outside the remit of this report, they may well serve as a guideline for research into the effect of context in healthcare, since there is considerable overlap between the two phenomena. In short, this means that in both psychotherapeutic and medical practice, patients present with symptoms in the expectation that the care provider has a solution to the problem. The position of dependency in which patients find themselves tends to mean that that they are receptive to suggestion, support and attention from the provider. These aspects are significant irrespective of the nature of the psychological or medical intervention.

1.3 THE EFFECT OF CONTEXT IN HEALTHCARE

As with context effects in psychotherapy, the effect of context in healthcare has a bearing on a broad range of factors within medical practice (i.e. factors pertaining to the patient, the physician and the physician-patient relationship) which are not consciously directed at the *nature* of the symptoms, the complaints or the disorder in question. There is, as it were, a continuum of complaint-influencing factors which run the gamut of intentionality, ranging from actions that are less intentional (e.g. patient expectations or the physician's white coat) to those that are more intentional (e.g. showing interest, patient-centredness or influencing behaviour). The nature of a treatment that has been labelled as effective - that is to say a treatment whose therapeutic component is theoretically underpinned (Grünbaum, 1986) - does not, therefore, fall into this category, whereas *the context within which* the treatment is administered does. In the case of disorders for which no effective medical treatment exists (e.g. chronic benign pain (CBP), chronic fatigue syndrome (CFS) or irritable bowel syndrome (IBS)), the fact of actually *deciding against* therapeutic intervention can be interpreted as being a recognised therapeutic. The nature of a disorder can therefore play a role in the effect of context in healthcare. It is, incidentally, also possible for a certain therapeutic procedure to be effective in relation to a particular disorder or patient due to its specific components, whereas in a different disorder or patient, the same procedure is effective primarily as a result of the positive expectations that the procedure arouses. There will, moreover, also be disorders (a fracture, for example) in which context effects play a negligible role. In most cases, neither the physician nor the patient is aware of the context effects.

The complex character of this phenomenon is highlighted in a passage from a recent interdisciplinary exploration of the placebo effect (Harrington (Ed.), 1997):

> "...Placebo effects are influenced by patient-healer interpersonal relationships and are increased in pleasant, non-threatening, efficient clinical settings with doctors who are perceived by patients as warm, likeable, and interested in them. A positive placebo effect occurs more frequently in patients with manifest or free-floating anxiety and with expectation of improvement by patients, doctors, and staff. Expectation of improvement, however, may be independent or overlap with factors such as optimism, enthusiasm, hope, faith, belief, motivation, and conditioning. (Shapiro & Shapiro, p. 30)..."

The influence of context in healthcare is not only manifested in the unconscious positive health effects that may result from a visit to a physician. A medical consultation can also have a less beneficial effect on the patient. The reason for the existence of this so-called “nocebo” effect can be found, *inter alia*, in the phenomenon of reactive or “white-coat” hypertension, which refers to patients whose blood pressure is higher in a physician's consulting room than it is at home.

1.4 PURPOSE

The health effects (both positive and negative) of patient-related and physician-related factors and those of the interaction between physician and patient are central to this study. The question is, precisely which factors pertaining to the patient (such as expectations or confidence), the physician (expectations, status) and the physician-patient interaction (instrumental and affective communication) *contribute* to the efficacy of a medical intervention and how do they do so. We shall be disregarding factors associated with the pharmacokinetics of (placebo) medication, the therapeutic effect of the ritual (impressive instruments, the costs of an intervention) or with the psychophysiological effects of perceptible characteristics of medication (de Craen *et al.*, 1996). Due to the complexity of this phenomenon, factors which presuppose a broader context - such as the influence of the media on the perception of symptoms and the presentation of complaints - will also be disregarded. Nor will this study set out to prove the existence of the placebo effect. The fact that a placebo effect exists is frequently well known, but precisely *why* and *how* it functions is usually more complicated (Roberts, 1995).

As far as possible, the therapeutic effect of context will be viewed in the light of measurable physiological, immunological or psychological changes in the patient. Since it is not clear in advance whether context variables have a specific or general effect on health and moreover since specific physiological parameters are only available for a few disorders (e.g. hypertension, diabetes), both specific physiological (blood pressure or blood glucose) and generic (general state of health, functional status) outcome measures are relevant (Kaplan *et al.*, 1989).

Whilst a great deal of research has already been conducted in the above areas individually, the significance of the frequently inter-related findings in relation to medical practice is generally left undiscussed. In this study we shall be bringing together those investigations that are of relevance to medical practice. Having discussed the literature, we shall provide a summary of possible explanations. This should ultimately result in answers to the question that concerns the RGO, namely whether it is necessary to investigate the effect of context in healthcare and if so, what precisely needs to be investigated and how.

1.5 QUESTIONS

This study is therefore aimed at answering the following questions:
1. What is the relationship[2] between physiological, immunological or psychological outcome measures (blood glucose, blood pressure, immunological parameters, cortisol, general state of health, anxiety) and context factors pertaining to the patient (e.g. expectations, confidence, anxiety), the physician (e.g. expectations, status) and the physician-patient interaction (e.g. the showing of interest, patient-centredness)?
2. What explanations can be given for the phenomena that are identified (e.g. anxiety reduction, stress reduction, the satisfaction of expectations (expectancy), the learning effect (classical conditioning), (psychoneuro)immunology (T cells and natural killer (NK) cells)?
3. How feasible is it to investigate the effect of context in healthcare?
4. If question 3 can be answered in the affirmative, what questions does the research need focus on?

2 METHOD

The questions have been answered by reviewing the literature. Owing to the extent of the material, this did not prove to be an exhaustive review, since the diversity of investigations made even a quantitative meta-analysis impossible. What we have done is to extract from various disciplines those studies that promised to be of relevance to the effect of context in healthcare. On the basis of existing knowledge and additional conversations with experts (see Appendix B), we have endeavoured to produce as complete a picture as possible. In those areas where empirical studies were either unavailable or insufficient, opinion-based articles have been consulted.

We began by conducting a literature search in Medline with which we selected controlled experimental and field studies, reviews and opinion-based articles published between 1990 and 1998 (inclusion criteria). Reviews based on comparative research were used to gain an understanding of the state of affairs within a specific field of research. Letters, editorials and historical articles were disregarded.

Finally, the abstracts were evaluated by two researchers. The following search terms[3] were used:
placebo effect: 431 hits, 60 of which satisfied the inclusion criteria.
White coat: 90 hits, of which 34 satisfied the inclusion criteria.
Nocebo: produced 14 hits.

In order to answer questions 1 and 2, the following combinations of search terms were also used:
Expectancy/expectation*/motivation and stress/anxiety*: 205 hits, 13 selected.
Expectancy/expectation*/motivation and outcome measures*: 1970 hits, 55 selected.
Physician-patient relationship and stress/anxiety: 126 hits, 15 selected.
Physician-patient relationship and outcome measures: 509 hits, 24 selected.
Stress/anxiety and outcome measures: 2686 hits, 142 selected.

Sometimes the same publications were identified via different search terms. Reference lists in the selected publications were screened for potentially relevant cross-references, with articles published before 1990 also being considered at this stage.

3 SUMMARY AND POINTS FOR CONSIDERATION

In view of the extent of the discussion in the literature, it was considered useful first of all to provide a summary of the most significant outcomes and points for consideration. In this chapter we shall therefore begin by systematically reporting the results of the research. A justification of these results can be found in the next chapter. This chapter then goes on to present points for consideration that are relevant to research into the effect of context in healthcare.

3.1 CONTEXT FACTORS AND EXPLANATIONS

3.1.1 CONTEXT FACTORS

This study of the literature has identified a number of factors pertaining to the patient, the physician and the physician-patient interaction which to a greater or lesser extent contribute to the efficacy of a medical intervention. These factors are, of course, also interrelated and to some extent overlap. In the interests of clarity and convenience of comparison, however, they will in this chapter be considered separately. The following are the factors that have come to the fore:

1. *Factors pertaining to the patient*

a. The need to be regarded as likeable and to fulfil the expectations of the physician.
b. The degree of concern and anxiety prior to the consultation.
c. Confidence in the physician and the treatment.
d. Experiences (positive and negative) of previous treatments; in other words, the treatment history.
e. The presence of expectations (positive and negative), fed by these previous experiences or by information from the world around.
f. The degree of self-efficacy; that is to say, the belief that symptoms can be influenced by one's own actions.
g. The degree of perceived control over the situation.
h. The presence of catastrophising cognitions and pessimism.
i. The attribution of complaints to internal or external circumstances.

2. *Factors pertaining to the physician*

a. The expectations (positive or negative) of the physician and his priorities with regard to patient or treatment, which are sometimes unconsciously conveyed to the patient.
b. The (perceived) status of the physician.

3. *Factors pertaining to the physician-patient interaction*

a. The motor activity that is inherent in the verbal expression of the reason for the patient's visit.
b. The emotional charge of the conversation between physician and patient.
c. The giving of (verbal and non-verbal) attention and support to the patient.
d. The extent to which a physician gives a patient the space to advance his own ideas, explanations and emotions in addition to the complaints that he has been experiencing.
e. The extent to which a physician pays attention to how the patient perceives the complaints.
f. Offering an explanation for the symptoms that are presented with reference to a specific diagnosis and related information.
g. Supplying a solution to the complaints in the form of treatment or advice.
h. Recognising and influencing (persistent) misconceptions about complaints, disorders and therapeutic management by the physician.
i. The need to satisfy (or not to satisfy) the expectations of the other party.

A number of these factors - such as confidence and positive expectations, the experience of being in control of the situation, the expression of emotions and receiving attention and support - have a positive effect on health. Other factors - such as anxiety, helplessness and negative experiences and expectations - have an unfavourable effect.

3.1.2 EXPLANATIONS

Several explanations have been advanced for the effect of context factors (see Chapter 5). For three of these explanations, empirical evidence has frequently been adduced, namely explanations based on the conditioning theory, explanations from the field of psychoneuroimmunology and explanations that have emerged from the study of psychotherapy. Classical-conditioning theory offers an explanation for both the positive and the negative context effects. This is because many of the "neutral" factors pertaining to a medical setting - e.g. the physician, the hospital, the physical examination, an injection or the form and colour of drugs - can evoke an association with the effects and experiences of previous treatments. Psychoneuroimmunology shows that all manner of functional connections exist between psychological, neurological and immunological processes, via which these areas "communicate" with each other. Psychoneuroimmunological research not only points to the link between context effects and the response of the immune system, but also to the link between context effects and the resurgence of certain specific disorders, such as Epstein-Barr virus, the common cold and AIDS. Finally, psychotherapy research

underlines the non-specific contribution that is made by an empathic approach on the part of the physician and by encouraging patients to talk about their concerns, preoccupations and anxieties.

3.2 POINTS FOR CONSIDERATION

3.2.1 METHODOLOGY

A research program on the Effect of Context in Healthcare will provide a stepping stone for research which may shed light on one or more facets of this issue. Based on the research that has been included in this programming study, one can draw the following conclusions, which are, at the same time, points for consideration in the context of future research.

- Most of the research has been performed in relatively *small* groups.
- Blood pressure or pain are the most widely used *objectively measurable* outcomes; however, their relationship to a patient's state of health is not always clear.
- Usually there are no *follow-up* measurements, which play an important role in measuring effects on the *general state of health.*
- *Expectations* of the patient prior to a visit to the physician are only sporadically explored.
- *Expectations* of care providers are not generally measured.
- As far as conditioning effects are concerned, it is necessary to take an individual's *treatment history* into consideration.
- The role of *self-efficacy* and *helplessness* continues to be underestimated in connection with research into the impact of stress on health.
- In general, little consideration is given in research to the *cognitions* of patients and physicians.
- There is often no *control group* to monitor the spontaneous recovery from complaints and for the regression towards the mean[4] .
- Research with patients is lagging behind research with trial subjects. It is only patients, however, who experience both the stress and the support of a discussion with a care provider. Research into context effects in a laboratory setting therefore has little relevance.
- It is important to take into account the intermediate role of *mood* and of the patient's *personal characteristics.* Negative (nocebo) context effects are examined far less often than positive (placebo) effects.

3.2.2 OUTCOME MEASURES

Research into the effect of context in healthcare has hitherto focused on a small number of outcome measures, most notably anxiety and blood pressure. As far

as the improvement of objectively measurable health is concerned, physiological outcome measures would appear to be suitable. In addition, subjective (i.e. patient-reported) measures of health (quality of life, compliance, anxiety) are important because the healthcare seeking behaviour and the role of patient are determined more by health as experienced by the patient than by objectively measurable health. If, for example, research is aimed at changing patients' healthcare seeking behaviour, subjective outcome measures would appear to take priority.

3.2.3 Specific disorders

Context factors play a role in a range of disorders, including unexplained somatic complaints such as chronic (benign) or acute pain, hypertension, IBS and chronic fatigue. Context factors also appear to play an important role of chronic, more or less irreversible disorders, such as asthma, diabetes, gastric ulcers, rheumatism and cancer. In all of these disorders it is known that emotional arousal and stress can aggravate the complaints. After all, each disease has its repercussions both on the body and on the mind. Thus every experience that an individual has undergone will impact on his state of health (Jamison, 1996). This explains why the mere fact of talking with a physician about what a patient is feeling and experiencing (emotional disclosure) can have a positive effect on the perception of the disorder. It therefore makes little sense to confine research into context effects to a particular patient group. It is quite possible that for specific disease categories one particular approach will be more successful than another: for example, research among hospitalised medical patients suggests that patients with gastro-intestinal disorders chiefly express psychological problems at an emotional and cognitive level, whereas patients with cancer tend to display vegetative/ somatic symptoms (vonAmmon Cavanaugh & Wettstein, 1989). For these different patient groups, an approach that is aimed at changing cognitions might not be expected to be as successful. Research should therefore preferably be directed at homogeneous groups of patients.

3.2.4 Ethical aspects

One of the factors upon which research into the effect of context in healthcare might possibly be focused is research into (response) expectations and other associated cognitions and emotions on the part of the patient. One important source of expectations lies in the present requirement of informed consent, which means that a patient has to be informed about a proposed therapeutic intervention. Informed consent can be interpreted in two ways. On the one hand, it relates to the Medical Treatment Agreements Act (WGBO), which came into force in 1995. The quality of the contact between physician and patient plays a

central role in this Act. Besides stipulating that a patient has the right to inspect his dossier, the WGBO also obliges a physician to give the patient complete and explicit information about the treatment, including expected side effects and possible alternatives. This obligation is based on the fact that only a well-informed patient can give the legally required consent (informed consent) to medical treatment.
Another form of informed consent relates to the fact that patients must be informed about participation in medical research. The Medical Research Involving Human Subjects Act (WMO) came into force recently. Under this Act, patients must be informed about the research in writing and they must then also give their written consent to participate in the research.

For many of the studies that are proposed here - for example, research into the influence of previous (therapeutic) experiences on health effects - the informed-consent requirement will not present any problems. This is because there is no question of withholding information or an appropriate treatment from someone, but rather of investigating the effects of the patient's subjective experiences being taken into account (or else not being taken into account). In the case of intervention research, the informed-consent requirement could well pose problems. There is, at present, no solution to this problem.

A further problem is the fact that it is difficult to conduct "blind" research into the efficacy of medical interventions other than by prescribing medication. After all, the care provider does not know what procedures he is carrying out. The same problem is encountered in connection with the study of effects in the field of psychiatry (Andrews, 1999). One solution to this problem might be to always have the effects of an intervention measured by an independent reviewer under "blind" conditions.

4 RESULTS

This chapter is directed at the first of the questions posed in this programming study regarding the relationship between physiological, immunological or psychological outcome measures, on the one hand, and factors pertaining to the patient, the physician and the physician-patient interaction, on the other. The results of the identified studies have been grouped according to independent variables and presented in the form of tables.

4.1 PATIENT-RELATED FACTORS

4.1.1 WORRY AND ANXIETY

Regardless of the nature of a medical intervention, it is likely that any form of care will result in a reduction of worry (van de Kar et al., 1992a). As a result, the immune response is boosted and physiological changes take place, which in turn help to alleviate the complaints. It is also possible that the uncertainty surrounding a visit to a physician may itself provoke anxiety, which can have an *unfavourable* effect on the physical complaints. Studies by Gaskin *et al.* (1992), Fowlie *et al.* (1992), Wiebe *et al.* (1994), van Dulmen *et al.* (1995) and Rietveld and Prins (1998) demonstrate the existence of a positive relationship between the degree of anxiety and the experiencing of pain and other physical complaints, including asthmatic and diabetic complaints (Table 4.1.1). It appears that anxiety can lead to a reduction in the activity of NK cells (Fredrikson *et al.*, 1993). There appears to be a correlation between anxiety and the amount of information that a patient is given (Street, 1991): too little information is not good, but neither is too much. The stream of information that is received from the physician can also provoke anxiety (Hadjistavropoulos *et al.*, 1998). Viewed from a physiological and psychological perspective, there is considerable overlap between anxiety and pain (Gross & Collins, 1981). This makes it likely that interventions aimed at reducing anxiety also impact on pain complaints and that the effect of a medical intervention will be reduced if no explicit consideration is given to a patient's worries or anxiety. The only way to reduce anxiety and thus physical complaints would be to offer a solution in the form of medical treatment. It is worth noting that patients' anxiety can also cause them to downplay the seriousness of their complaints when talking to the physician.

Table 4.1.1 *Worry and anxiety in the patient*

Authors	Subjects	Design	Context variable	Outcome measure	Results
Gaskin *et al.*, 1992	60 pain patients	correlational	anxiety	pain complaints	more anxiety, more pain
Fowlie *et al.*, 1992	43 IBS patients	prospective, follow-up	anxiety	abdominal complaints	more anxiety, more complaints
Wiebe *et al.*, 1994	35 diabetes patients	prospective, correlational	anxiety	diabetic complaints	more anxiety, more complaints
van Dulmen *et al.*, 1996a	110 IBS patients	prospective follow-up	anxiety	abdominal complaints	more anxiety, more abdominal complaints
Rietveld & Prins, 1998	40 asthma patients	pre-/post-test, randomised groups	anxiety	asthmatic complaints	more anxiety, more complaints
Fredrikson *et al.*, 1993	27 cancer patients	pre-/post-test, control group	anxiety	NK-cell activity, number of monocytes and T cells	more anxiety, lower resistance
Street, 1991	41 GP patients	observational study	anxiety	medical information	more anxiety, more info.

4.1.2 CONFIDENCE AND HOPE

According to Oh (1991), the factors generated by an empathic physician such as confidence and hope, form the essence of the context effects. Hope and confidence play a role via the expectations on which they are based. Someone can have confidence in the physician, in his diagnosis, in the treatment or in healthcare in general. All sorts of factors can increase confidence, such the provision of a prognosis, affective contact (Morales, 1994), the reputation of the physician and even the way he dresses (McKinstry & Wang, 1991).

In general, the confidence that a person has in his physician is associated with an improvement in the state of health that is reported by the patient (Safran *et al.*, 1998) (Table 4.1.2). Confidence in a positive outcome in response to stressful situations appears to be associated with improvement in immune function

Table 4.1.2 *Confidence on the part of the patient*

Authors	Subjects	Design	Context variable	Outcome measure	Results
Safran *et al.*, 1998	6024 GP patients	cross-sectional	confidence	general states of health	more confidence, better health
Segerstrom *et al.*, 1998	50 healthy patients	prospective cohort	confidence	immune function	confidence promotes immune function
Anderson & Dedrick, 1990	106 NIDDM patients	pre-/post-test	confidence	need for monitoring	confidence reduces need

(Segerstrom *et al.*, 1998). T cells and NK cells, both of which are important in the battle against infectious diseases and cancer, appear to increase in numbers as a result. In a clinical setting, this could mean that whenever a physician arouses positive expectations in a patient, beneficial health effects may also ensue. Both effective reassurance and clear information from the physician can contribute to such expectations (see section 4.3).
Confidence can have negative as well as positive effects, since it can discourage patients from themselves playing an active role. This phenomenon was confirmed in a study by Anderson & Dedrick (1990). In general, the degree of confidence which a patient has in the physician thus gives rise to positive effects. The physician can reinforce this confidence.

It is worth noting that a physician can also reinforce confidence mistakenly. A recent ethnographic study of explanations for misplaced optimism in lung cancer patients receiving palliative treatment reveals what a major impact the way in which physicians impart information can have on patient confidence (The, 1999). The fact that physicians and patients have conflicting points of view and different frames of reference (the physician is concentrating primarily on the effect of the treatment, the patient on getting better) means that information is wrongly interpreted and the patient derives optimism from the physician's words. Disappointing outcomes (relapses) in the course of the disease process come as an even harder blow for these optimistic patients. It also appears that patients frequently do not want to hear the hard truth.

4.1.3 EXPECTATIONS, SUGGESTION AND MOTIVATION

The confidence that a person has in a treatment is closely tied in with his expectations. It is therefore also questionable whether confidence can be investigated in isolation from expectations. Patients' expectations with regard to the nature and the effect of care in general, or of medical intervention in particular, have an important bearing on the effect of a treatment. These expectations can be both positive and negative. As a result, contact with a physician can either have a favourable or an unfavourable effect on health complaints. In general, patients have high expectations of the effect of an invasive therapeutic intervention such as a hysterectomy (Marchant-Haycox *et al.*, 1998). Studies by Luparello *et al.* (1970), Goodenough *et al.* (1997) and Pohl *et al.* (1997) demonstrate that if patients are *expecting* effects, then they will sometimes also experience them (self-fulfilling prophecy) (Table 4.1.3). Isenberg *et al.* (1992) reach the same conclusion on the basis of their literature search in relation to asthmatic patients. Moreover, Jensen & Karoly (1991) have shown that trial subjects who are more motivated to respond experience a greater effect from a placebo pill. Studies by Voudoris *et al.* (1989, 1990) show how important it is, when prescribing a therapeutic drug, to take into account a patient's conditioning history prior to that treatment. A new treatment may be less effective in someone with bad experiences as a result of the conditioned response to context factors that hinder the action of the characteristic component (interaction effect). In order to enhance therapeutic effects, a physician should take note of the experiences of a patient with previous disorders and treatments. In this connection, Bügel and van Everdingen (1998) state the need to know a patient's treatment history. A physician will usually enquire about objective experiences of diseases and treatments when taking a patient's history. However, the patient's experiences of diseases and treatments - such as successful therapies, but also diagnoses that are either too late or are missed - do not, as a rule, come up for discussion. It is precisely these experiences which - whether directly or indirectly, via their influence on expectations and anxiety (based on the principal of conditioning) - are contributory factors in determining the success of a medical intervention. Expectations can also have a negative impact on health, in which case one would speak of a nocebo effect. If, for example, a patient's blood pressure has been extremely high during a previous visit to the physician, then that patient will anticipate this happening again on a subsequent occasion, which will result in increased sympathetic activity and thus higher blood pressure (Janssen & Thien, 1995). Negative expectations can also be generated from what an individual experiences in his immediate environment, what he is told by the media or, in general, as a result of incorrect information (Vermeire, 1995; Hahn,

Table 4.1.3 *Expectations on the part of the patient*

Authors	Subjects	Design	Context variable	Outcome measure	Results
Luparello *et al.*, 1970	20 asthma patients	pre-/post-test, double blind	expectation and suggestion with regard to medication	effects of medication	expectation and suggestion determine effects
Goodenough *et al.*, 1997	117 children	pre-/post-test, control group	expectation regarding analgesic placebo ointment	effects of ointment	ointment with suggestion works better than without
Pohl *et al.*, 1997	40 patients	2x2 balanced placebo	expectation regarding hypoglycaemic symptoms	perceived symptoms	expectation influence perception of symptoms
Jensen & Karoly, 1991	86 healthy patients	RCT, pre-/post-test	motivation and expectation regarding placebo	analgesic effect of placebo	stronger motivation, greater effect
Voudoris *et al.*, 1989	20 healthy patients	RCT, pre-/post-test	expectation regarding effect of analgesic	analgesic effect	placebo response can be conditioned
Voudoris *et al.*, 1990	40 healthy patients	RCT, 2x2 factorial	expectations regarding analgesic placebo	analgesic effect	conditioning more effective than expectation
Jewett *et al.*, 1990	18 allergic patients	post-test, control group	expectation regarding allergic reaction	allergic reaction to active or placebo injection	reaction dictated by expectations, rather than the type of injection
Kvale *et al.*, 1991	31 cancer patients	pre-/post-test	expectation of symptoms	nausea and vomiting	only symptoms if they are expected
Bovbjerg *et al.*, 1990	20 cancer patients	pre-/post-test	expectation of symptoms	immune function and nausea	previous expectations, adverse effects
Kincheloe *et al.*, 1991	77 dental patients	pre-/post-test, control group	suggestion and expectation re-garding placebo ointment	pain from injection	the more pain is expected, the greater the pain

1997; Spiegel, 1997). Such effects may well be described as nocebo effects. Provision of good information is thus, in itself, important to an individual's state of health, since patients will otherwise become caught up in negative expectations.

Studies by Bovbjerg *et al.* (1990), Jewett *et al.* (1990) and Kvale *et al.* (1991) demonstrate that the expectation which a patient already has prior to a visit to a physician is more determinative for the outcome of the contact than the expectation that is aroused by suggestion from the care provider. For the purposes of research into context effects, it would thus appear that it is always important to take into account the expectations that patients have in advance of a medical intervention, either as a result of previous experiences (treatment history) or information from a third party.

4.1.4 SELF EFFICACY AND CONTROL

The perception of symptoms appears to a significant degree to be determined by the extent to which an individual believes he can exert a positive influence over his complaints. It is precisely these so-called self-efficacy expectations that appear to have a positive effect on the perception of complaints, since they influence both a person's emotions and behaviour (Kores *et al.*, 1990). For the patient this means that he not only desires information relating to the explanation of complaints, but also information about the possibilities of adopting effective behaviour in coping with complaints.

Self-efficacy is the extent to which an individual has the feeling of being able to exercise control over a situation. Situations which patients perceive to be uncontrollable have adverse effects on health in terms of blood pressure, cortisol levels (Wittersheim *et al.*, 1985, Nyström *et al.*, 1998, Peters *et al.*, 1998), immune response (Peters *et al.*, 1999) and quality of life (Cunningham *et al.*, 1991) (Table 4.1.4). In general, it is possible that situations in which someone feels himself to be in a dependent position (as, for example, during a visit to the physician) may have adverse effects. Results of a study by Lynch *et al.* (1992) also suggest the importance of taking heed of an individual's personality structure and individual cognitions (e.g. the extent to which an individual considers himself to be in control of his situation). A possible explanation for the mediating effect of control emerges from research by Matthews *et al.* (1980). They investigated how much attention trial subjects paid to predictable and unpredictable events. Unpredictable events appeared to receive greater attention than predictable ones and (as a consequence) resulted in the reporting of more aversive physiological reactions. A feeling of control therefore appears to be important for patients. This

Table 4.1.4 *Self-efficacy and control*

Authors	Subjects	Design	Context variable	Outcome measure	Results
Wittersheim *et al.*, 1985	20 patients	randomised, control group	coping strategies	cortisol	coping strategies are associated with cortisol
Peters *et al.*, 1998	24 patients	2x2 factorial	degree of control	blood pressure and cortisol	less control, higher BP and cortisol
Peters *et al.*, 1999	82 patients	2x2 factorial	degree of control and effort when confronted with stress	immune response and NK-cell activity	effort stimulates, uncontrol-lability reduces response
Cunningham *et al.*, 1991	273 cancer patients	pre-/post-test, correlational	self-efficacy	quality of life	more self efficacy, higher quality

justifies the pursuit of "shared decision-making", whereby a patient maps out a treatment program in conjunction with the physician, instead of simply receiving instructions without discussion.

4.1.5 CATASTROPHISING AND PESSIMISM

Besides favourable cognitions, including self-efficacy and other positive expectations, a patient may also be weighed down with dysfunctional cognitions such as catastrophising thoughts, which can cause and perpetuate physical complaints. Catastrophising cognitions appear to fluctuate much more over time than the above-mentioned self-efficacy cognitions and also to be more susceptible to environmental influences (van Dulmen *et al.*, 1997) (Table 4.1.5). Studies by Affleck *et al.* (1987), Sorbi and Tellegen (1988), Strauman *et al.* (1993), Antoni *et al.* (1994), van Dulmen *et al.* (1996a) and Robinson-Whelen *et al.* (1997), involving a variety of physical complaints and disorders (migraine, rheumatism, CFS, IBS), demonstrate that pessimistic thoughts and feelings of helplessness can have an adverse impact on physical complaints, general state of health, immune function and medicine consumption. This suggests that any attempt by a physician to give a more positive turn to a patient's feelings and beliefs can have the effect of alleviating physical complaints (see section 4.5.3).

Table 4.1.5 *Catastrophising and pessimism*

Authors	Subjects	Design	Context variable	Outcome measure	Results
Sorbi & Tellegen, 1988	29 migraine patients	correlational	catastro-phising cognitions	migraine attacks	more cata-strophising cognitions, more attacks
Affleck *et al.*, 1987	92 rheumatic patients	cross-sectional, correlational	expressions of helplessness	functional problems	more expressions, greater problems
Antoni *et al.*, 1994	65 patients with CFS	cross-sectional, correlational	negative beliefs about complaints	subj. severity of disorder	more negative, severe complaints
van Dulmen *et al.*, 1997	105 IBS patients	prospective, follow-up	catastro-phising cognitions	medical consump-tion and severe abdominal complaints	more cata-strophising, higher consumption and more complaints
Robinson-Whelen *et al.*, 1997	50 healthy patients	prospective, cohort	pessimistic outlook on life	general state of health	more pessimistic, poorer health
Strauman *et al.*, 1993	38 patients	pre-/post-test, control group	negative self-image	immune function	negative self-image, poorer immune function

4.1.6 ATTRIBUTIONS

Attributions are the causes to which an individual attributes events, such as diseases and accidents. They may refer to unchangeable external circumstances, e.g. the consequences of a chemical disaster, or they may be more internally oriented, as when someone knows that his health behaviour leaves something to be desired. The persistent attribution of somatic complaints to physical causes appears to perpetuate those complaints (van Dulmen *et al.*, 1995, Vercoulen *et al.*, 1996) (Table 4.1.6). Aside from the fact that the nature of the attributions determines what steps a person will take to influence his situation (Robbins & Kirmayer, 1991), causal attributions also appear to be capable of exerting direct influence over the immune system (Segerstrom *et al.*, 1996).

Table 4.1.6 *Attributions*

Authors	Subjects	Design	Context variable	Outcome measure	Results
vanDulmen *et al.*, 1995	120 IBS patients	prospective follow-up	somatic attributions	medical con-sumption, course of complaint	attributions have negative effect
Vercoulen *et al.*, 1996	246 CFS patients	prospective follow-up	somatic attributions	fatigue complaints	attributions have negative effect
Segerstrom *et al.*, 1996	86 HIV-positive patients	correlational	internal attributions	decrease in T helper cells	attributions accelerate decrease

This suggests that a physician enquiring about the factors to which a patient attributes his complaints or disorder as well as any consequent influence of these, can help to strengthen the body's natural resistance or elicit an improvement in the complaints experienced.

4.2 PHYSICIAN-RELATED FACTORS

It is likely that factors such as the expectations that a physician has of a given intervention and his confidence in his own actions may impact on the efficacy of an intervention via the patient. However, research into factors pertaining to the physician appears to be scarce.

4.2.1 EXPECTATIONS

Physicians can exert influence over the effect of a given treatment by the way in which they introduce that treatment to a patient. For example, a study into the influence of a physician's expectations on the reduction of pain in 46 chronic-pain patients indicates that the more physicians expect a patient's pain to be relieved, the more this pain does, in fact, diminish (Galer *et al.*, 1997). According to the researchers, these results suggest that physicians in a subtle way transmit their expectations to the patients. Wirth (1995) has even demonstrated that the expectations of the physician are more determinative for health effects in the patient than the expectations of the patient himself. This probably arises from the patient's need to be liked and to satisfy the expectations of the physician. We know of no study that has investigated whether patients report greater

improvement in their complaints when both physician and patient have the same expectations of the intervention.

4.2.2 STATUS

Besides a care provider's expectations, that person's status will also contribute to the effects of a medical treatment. The higher social status of the care provider appears to play an especially important role within alternative medicine. Research into the influence of social status has up until now principally been directed at blood pressure. Blood pressure measured by nurses appears, in general, to be lower than that measured by physicians (Moutsos *et al.*, 1967; Mancia *et al.*, 1987; Veerman & van Montfrans, 1993). Long *et al.* (1982) have also investigated the influence which the status of the care provider has on blood pressure. Using a group of 40 trial subjects, they looked into the way in which blood pressure responded to the presence of a person in a white coat who was introduced as a physician and the same person in casual clothing who was introduced by his first name. All trial subjects were found to have higher blood pressure during the discussion with the person with the white coat than during the same conversation with the person in casual clothing. This finding could provide an explanation for the "white coat" phenomenon (i.e. the fact that blood pressure or blood glucose is higher when measured by a physician than when the measurement is carried out at home by the patient himself). It is possible that the difference in the responsibility of the care provider plays a role here. High blood pressure has greater implications in the presence of a physician than in the presence of a nurse (The, 1999). However, Lynch *et al.* (1980) showed that even in the presence of a clinical trial manager who has the same status as the trial subject, the blood pressure shows a greater increase than in the absence of that trial manager (see also sections 4.3.1 and 4.3.2). An explanation for this is provided by Cacioppo *et al.* (1990), who demonstrated in 27 trial subjects that the mere idea that one is being observed can elicit subtle physiological reactions in the form of a decrease in skin resistance.

It is worth noting that the literature also reports white-coat effects with regard to blood glucose measurements, although these have been far less widely investigated. According to Bodansky (1993), this is usually a case of measurements performed at home (which, unlike automatic 24-hour blood pressure measurements, are reported by the patients themselves) being portrayed in an excessively positive light. However, Campbell *et al.* (1991; 1992) have shown that manipulation of measurements is uncommon and furthermore that it is not a question of measurements being incorrectly performed. The phenomenon may possibly be linked to the fact that stress can also bring about

a rise in blood glucose values. However, this was ruled out by Campbell *et al.* (1992), who, based on the levels of cortisol in the blood of diabetes patients, made a reasonable case for there not being any difference between the levels of stress experienced in hospital and at home. Further research is therefore still needed into whether reactive hyperglycaemia does, in fact, exist and what factors it is influenced by.

4.3 FACTORS IN THE PHYSICIAN-PATIENT INTERACTION

The literature containing research into the psychophysiological effects of the physician-patient interaction is structured according to the continuum mentioned in the Introduction, which ranges from physician actions with a low level of intentionality (verbal activity, topic of discussion) to those with a high level of intentionality (patient-centredness, influencing of cognitions). At the bottom of the continuum are factors that are inextricably connected with medical contact, such as the existence of a social relationship, verbal activity and the topic of discussion. In addition, a consultation may be characterised to a greater or lesser extent by the contribution that is made by the patient and the space allowed for this by the physician. Thus the content of the conversation is further determined by the points that are raised by the patient, meaning that that the role of the physician within the continuum increases accordingly.

4.3.1 SOCIAL RELATIONSHIP

The contact between physician and patient can be viewed as a special form of social relationship in which a variety of aspects such as dependency, interest shown in a patient, empathy, differences in status, control and exchange of information all have a role to play. Social support has an important function in any social relationship. This is all the more applicable in the case of physician-patient interaction, since the degree of social support is related to the course of diseases and disorders (Cohen, 1988).

From this point of view, it is therefore also reasonable to assume that forms of interaction that exist between a physician and a patient can have varying degrees of "healthiness". Research into the effect of social support on health and sickness has up until now principally been directed at cardiovascular activation. From this it appears that the degree of social support has a favourable effect on the blood pressure and other cardiovascular parameters (Kamarck *et al.*, 1998).

4.3.2 VERBAL ACTIVITY

Apart from the content of the discussion between physician and patient, evidence has been found that talking in itself provokes cardiovascular reactions (Lynch *et al.*, 1980; Silverberg & Rosenfeld, 1980; Liehr, 1992; Stein & Boutcher, 1993; le Pailleur & Landais, 1994; le Pailleur *et al.*, 1996) (Table 4.3.2).

Table 4.3.2 *Verbal activity*

Authors	Subjects	Design	Context variable	Outcome measure	Results
Silverberg & Rosenfield, 1980	24 hypertension patients	pre-/post-test	talking	blood pressure	talking increases blood pressure
Liehr, 1992	109 healthy patients	pre-/post-test crossover	talking vs listening	blood pressure	talking increases blood pressure more than listening
Stein & Boutcher, 1993	34 patients	pre-/post-test	talking/ not talking	blood pressure, pulse	talking increases blood pressure
le Pailleur & Landais, 1994	35 hypertension patients	prospective	talking	blood pressure	talking increases blood pressure
le Pailleur *et al.*, 1996	42 hypertension patients	pre-/post-test crossover	talking	blood pressure	blood pressure during talking higher than during silences
le Pailleur *et al.*,1998	50 hypertension patients	pre-/post-test crossover	talking	blood pressure	no blood-pressure increase during silences

These findings suggest that the verbal activity of talking is, in itself, a sufficient explanation of the white-coat phenomenon. It appears that the higher the resting value of the blood pressure, the greater the rise in blood pressure, so that the increase in blood pressure in hypertensive individuals when they are talking is greater than that in normotensive individuals (Lynch *et al.*, 1981). The extent of the reaction is comparable with that of a regular exercise stress test (Thomas *et*

al., 1992), does not change as a result of the use of antihypertensives (Lynch *et al.*, 1982a; Dimsdale *et al.*, 1992) and occurs both in an experimental and a medical setting (Lynch *et al.*, 1982b). It would appear that in hypertensive individuals, the *normal* response of an increase in blood pressure in reaction to everyday situations (such as communication) is exaggerated.

There is evidence that people with cardiovascular disorders such as essential hypertension do, indeed, experience problems with interpersonal communication (Weiner, 1979). Perhaps they experience talking as a stressor *per se*, or else the findings are linked to the fact that the majority of consultations take place between a man and a woman (Millar & Accioly, 1996). It is also possible that the uncontrollability that is experienced may bring about an increase in blood pressure as a result of the dependent position in which a patient finds himself during a visit to the physician (Peters *et al.*, 1998).
It should be noted that Malinow *et al.* (1986) have shown that the blood pressure of deaf people also rises while signing. The rise in blood pressure is therefore not simply connected with the motor activity of talking, but also with the stressful communicative procedure itself. In general however, studies of the reactions to psychological stressors of people with white-coat hypertension do not produce corresponding conclusions. According to some authors, there is no connection (Siegel *et al.*, 1990), while others maintain that such a connection does exist (McGrady & Higgins, 1990; Lantelme *et al.*, 1997).

It has meanwhile become customary in medical practice to remeasure blood pressure after a rest period. A period of four minutes was recently recommended in this context (Bakx *et al.*, 1999). Research confirms that blood pressure does, in point of fact, fall during repeated measurements, perhaps as a result of adaptation to the procedure (Antivalle *et al.*, 1990: Mancia *et al.*, 1991; le Pailleur *et al.*, 1998). Apart from the influence of a medical intervention, variation in blood pressure does, therefore, appear to be inherently associated with visits to a physician.

4.3.3 TOPIC OF DISCUSSION

According to Malinow *et al.* (1986) and Linden (1987), the motor activity involved in talking is not the only factor that is responsible for the increase in the blood pressure. (Table 4.3.3). The content of the words that are spoken (emotional versus neutral) appears to have an even greater effect on the blood pressure, in view of the positive relationship that has been identified between the level of the blood pressure and discussion of stressful events (le Pailleur *et al.*, 1996; Liehr *et al.*,1997; Fontana & McLaughlin,1998). This does not appear to be

explained by the fact that hypertensives, compared with normotensive individuals, are more prone to psychosocial dysfunction (Fark, 1993).

Table 4.3.3 *Topic of discussion*

Authors	Subjects	Design	Context variable	Outcome measure	Results
Linden, 1987	31 patients	pre-/post-test, cross-over	emotional vs neutral discussion	blood pressure	increase in blood pressure in emotional discussion
le Pailleur *et al.*, 1996	42 hypertension	pre-/post-test, cross-over	stressful vs neutral discussion	physical complaints	increase in blood pressure when discussing stressful events
Liehr *et al.*, 1997	60 patients	pre-/post-test	emotional vs neutral discussion	blood pressure	bigger increase during emotional discussion
Fontana & McLaughlin, 1998	33 patients	correla-tional	perception of stress	blood pressure	stress increases blood pressure
Eisenberg *et al.*, 1991	13 hypertension	prospective cohort pilot study	relaxation	blood pressure, anxiety, physical complaints	relaxation reduces anxiety and complaints

An alternative explanation for the rise in blood pressure in reaction to a visit to a physician is offered by Nyklícek *et al.* (1998). Based on an extensive search of the literature, they concluded that hypertensive individuals, due to their defensive coping style, view stressful situations in a less negative light than normotensive individuals, but that they respond with an increase in blood pressure due to conditioning. The assessment of the situation, and possibly also other cognitions, would appear to play an as yet unexplained mediating role here. There is, in fact, evidence to suggest that an anxious and defensive personality structure (King *et al.*, 1990) and likewise strong avoidance behaviour (Kohlmann *et al.*, 1996) are

related to the level of the blood pressure. Nevertheless, relaxation does not appear to automatically lead to a marked reduction in the blood pressure (Eisenberg *et al.*, 1991).

Both the presence and the status of a physician, and the verbal activity and the content of the conversation would thus appear to have a bearing on physiological parameters.

4.3.4 EMOTIONAL DISCLOSURE

As was demonstrated in the previous section, unfavourable changes in blood pressure may be perceived *during* the airing of emotions. This says nothing, however, about the long-term effects of this phenomenon on *health*. The stimulation of verbal disclosure of emotional experiences is widely used in psychotherapy. In this section we shall look at what effects disclosure can have within medical practice.

In view of the association between talking about stressful events and increases in blood pressure, it is likely that talking with a physician about symptoms and their perception will also impact on a person's state of health. It is, after all, a known fact that the suppression of thoughts, feelings and behaviour demands physiological effort. In the short term, that suppression can result in an increase in autonomous activity, and in time it can even come to act as a cumulative stressor, thus increasing the risk of physical complaints (Pennebaker & Susman, 1988). It is possible that the free expression of emotions may have non-specific positive effects, since it gives a person the feeling that he is being looked after. Research shows that the verbalisation of stressful experiences does, indeed, lead to a rise in the blood pressure, but in the long term - probably as a result of increased insight and cognitive changes - results in a better state of health in the form of better immune function, less anxiety and lower $HbA1_c$ and blood pressure (Orth *et al.*, 1987; Pennebaker & Susman, 1988; Kaplan *et al.*, 1989; Pennebaker, 1989; Esterling *et al.*, 1990, 1994) (Table 4.3.4).

It appears from studies in rheumatic patients that both everyday vicissitudes, such as a quarrel or a car accident (Thomason *et al.*, 1992), and traumatic experiences, such as a decision or someone's death (Rimon & Laakso, 1985; Zautra *et al.*, 1989), are related to an objectively measurable resurgence of the complaints. Talking about the emotions that have been experienced possibly has important health promoting effects for these particular patients. This was, in fact, confirmed by Kelley *et al.* (1997).

Table 4.3.4 *Emotional disclosure on the part of the patient*

Authors	Subjects	Design	Context variable	Outcome measure	Results
Orth *et al.*, 1987	170 hypertension patients	correla-tional	extent of disclosure	blood pressure	more disclosure, lower blood pressure
Kaplan *et al.*, 1989	45 gastric-ulcer, 105 hypertension, 59 diabetes, 43 breast-cancer patients	RATS	verbalisa-tion of emotions	general health, blood pressure, blood glucose, symptoms of chemotherapy	verbalisation of emotions benefits outcome measures
Kelley *et al.*, 1997	72 rheumatoid arthritis patients	RCT, follow-up	emotional disclosure	pain, function & condition of joints	emotional disclosure improves function upon follow-up
Esterling *et al.*, 1990	80 patients	pre-/ post-test	emotional disclosure	immune function with regard to Epstein-Barr virus	the more emotions are verbalised, the better the im-mune function
Esterling *et al.*, 1994	57 Epstein-Barr virus-positive patients	RCT	talking vs writing about stress	self-esteem adaptive coping	talking has more beneficial effects than writing

These studies show that it is important in research to give consideration to a follow-up and to the intermediating role of mood. Furthermore, they suggest that the verbalisation of emotional experiences can, in itself, have positive effects on health. It is therefore possible that talking about the perception of a disorder plays a major role in the therapeutic effects achieved in somatic healthcare. More effects on health can possibly be achieved if a care provider also assists a patient in changing his perception of the events (Murray *et al.*, 1989). The health effects

arising from the airing of emotional stress could be directly related to the positive correlation that exists between psychological stress and somatic symptoms (Simon *et al.*, 1996).

The implications of these findings for practitioners are revealed in a study by Bensing *et al.* (1995), which showed that, in general, the more eye contact a GP made with the patient, the more the patient would talk about psychosocial problems. It is possible that, as a result of this increase in emotional disclosure by the patient, non-verbal behaviour may also elicit physiological reactions. After all, cognitive changes, such as a re-evaluation of a particular event, are set in motion as a result of emotional expression and these can ultimately lead to adaptive behaviour. This hypothesis has, to our knowledge, not yet been tested out in practice.

4.4 AFFECTIVE COMMUNICATION

A patient does not tell his personal story just like that. To do so he needs to feel that he is in a trusted environment and be encouraged to do so (Suchman *et al.*, 1997). A good physician-patient relationship is essential in this respect. Such a relationship can be promoted by first putting a patient at his ease. One of the ways of doing this is by making conversation or by making a little joke.

4.4.1 SOCIAL CONVERSATION, HUMOUR

There is evidence to suggest that social conversation contributes to patient satisfaction. It appears to give patients the feeling that they represent more than just their illness (Hall *et al.*, 1998). This greater satisfaction promotes compliance and thus, indirectly, patient health. The extent to which social conversation in itself also has a direct bearing on someone's state of health has not been investigated. Research has, however, been conducted into the effect of humour. From this it appears that humour has a buffering effect on stress (Yovetich *et al.*, 1990; Gaberson, 1991; Abel, 1998) (Table 4.4.1). This relaxing effect can be expected to contribute to the patient's well-being.

4.4.2 EMPATHY , EMOTIONAL SUPPORT

A further important prerequisite when trying to induce a patient to talk is by offering emotional support. Cohen and Wills (1985) showed that the perception of support can protect an individual against the pathological influence of stressful events. Simply the knowledge that there is a physician with whom one can discuss one's problems can therefore have a beneficial effect. This is because the presence of someone who has the *intention* of providing help appears to bring

Table 4.4.1 *Social conversation, humour*

Authors	Subjects	Physicians	Context variable	Outcome measure	Results
Yovetich *et al.*, 1990	53 patients	pre-/post-test, control group	humour	anxiety	humour reduces anxiety
Abel, 1998	131 patients	cross-sectional, correlational	humour	tension	humour reduces tension
Gaberson, 1991	15 surg. patients	post-test	humour vs music	pre-operative anxiety	humour lowers anxiety

about a reduction in anxiety and depression (Foa *et al.*, 1991). It can be assumed, however, that long-term improvement in a patient's state of health demands more than simply "being there" for him. It appears that an empathic interaction, -in the form of reassuring words or affective contact, can lead to a reduction in anxiety, pain and blood pressure (La Monica *et al.*, 1987; Weiss, 1990; Hwang *et al.*, 1998) (Table 4.4.2). It would thus appear to be worthwhile not only from an ethical viewpoint but also in the interests of health promotion for a physician to ensure

Table 4.4.2 *Empathy and emotional support from the physician*

Authors	Subjects	Design	Context variable	Outcome measure	Results
la Monica *et al.*, 1987	656 cancer patients	pre-/post-test control group	empathic discussion	anxiety	less patient anxiety with empathic nursing care
Hwang *et al.*, 1998	60 heart-surg. patients	pre-/post-test control group	reassuring words from the physician vs rest	pain and anxiety	reassuring words reduce pain and anxiety
Weiss, 1990	59 heart patients	within subj. counter-balanced	physical contact vs verbal reassurance	anxiety and blood pressure	physical contact better for anxiety and blood pressure

that a patient feels at his ease during the consultation, which may possibly be acutely stress-inducing. Psychosocial attention, empathy and support appear not only to assist in creating and maintaining an optimal physician-patient relationship, but also to have health-promoting effects.

4.4.3 PATIENT-CENTREDNESS

An effective approach to adopt in medical practice is patient-centred interviewing. We speak of patient-centredness when a physician actively stimulates input from the patient himself by paying explicit attention to the perception of his complaints (in other words, the patient-related factors such as anxiety, expectations and causes that are attributed to the complaints, as discussed in Chapter 4.1) (Weston *et al.*, 1989). Certainly when patients are confronted with a disorder with an uncertain course, the outcome of which is to a great extent determined by the behaviour of the patients themselves (e.g. hypertension, diabetes or coronary heart disease), it is extremely important to explore and discuss the views and motivation of the patient, especially since physicians and patients frequently differ in the value that they attach to personally relevant information (Chaitchik *et al.*, 1992). Furthermore, the patient's views can assist the physician in making a diagnosis (Peppiatt, 1992). Research shows that the extent of a physician's patient-centredness contributes to the improvement of somatic complaints in patients with headaches, rheumatism, gastric ulcer, diabetes and breast cancer (Greenfield *et al.*, 1985; the Headache Study, 1986; Kaplan *et al.*, 1989; Henbest & Stewart, 1990; Rost *et al.*, 1991; Henbest & Fehrsen, 1992; Lorig *et al.*, 1993; Bertakis *et al.*, 1998) (Table 4.4.3).

If, as was suggested earlier, hypertensive individuals do, in fact, experience problems with interpersonal communication (Lynch *et al.*, 1981), paying attention to the significance of certain stressful events in their lives may contribute to the efficacy of the treatment. A study by Lynch *et al.* (1982a) shows, in fact, that blood pressure can be brought under control within fewer than ten therapy sessions by confronting patients with the link between an increase in blood pressure and talking about certain subjects, such as the stress that is caused by anxiety about the high blood pressure, and by these links subsequently being analysed and discussed in conjunction with breathing and relaxation exercises.

In addition to stimulation of input from the patient, attention paid by the physician to the patient's individual perceptions, expectations and needs is also important owing to the fact that a physician can only *effectively* reassure a patient if he knows what is preoccupying him. In their study involving 120 patients with functional abdominal complaints, Van Dulmen *et al.* (1996a) have shown that the

Table 4.4.3 *Patient-centredness on the part of the physician*

Authors	Subjects	Design	Context variable	Outcome measure	Results
The Headache study, 1986	265 headache patients	prospective cohort	"space" for pat. input	pain complaints	more "space", less pain
Henbest & Stewart, 1990	73 GP patients	prospective follow-up	patient-centredness	complaints, anxiety	patient-centredness has beneficial effect
Henbest & Fehrsen, 1992	74 GP patients	prospective follow-up	patient-centredness	complaints, anxiety	patient-centredness has beneficial effect
Greenfield *et al.*, 1985	45 gastric ulcer patients	RCT	information-seeking	functional state of health	active information-seeking improves health
Rost *et al.*, 1991	61 diabetes patients	RCT	patient activation program	blood glucose, physical function	beneficial effects of patient-centred activation
Lorig *et al.*, 1993	224 arthritis patients	pre-/post-test, 4-year follow-up	patient-centred information	pain and medicine consumption	better outcomes
Bertakis *et al.*, 1998	509 patients	RCT	psychosocial attention	gen. state of health	attention to emotions promotes health

more able internists are to correctly assess the significance of patients' complaints, the less frequently patients need to consult the physician again after contact has ended. A primary requirement is that physicians must give patients the "space" to recount what it is concerning them. Recent research shows that physicians actually do this in only 28% of cases (possibly due to lack of time). It is worth noting that when physicians do allow their patients to say what is on their minds, the consultation in question appears only to last an average of six seconds longer (Marvel *et al.*, 1999).

4.5 INSTRUMENTAL COMMUNICATION

4.5.1 PROVIDING INFORMATION

The verbal information which a physician gives a patient will influence the patient's expectations and thus the way he perceives his symptoms. It is even plausible that the mere fact of naming the symptoms or making a medical diagnosis has a therapeutic effect, since it gives a meaning to the complaints and can provide a feeling of reassurance (Brody & Waters, 1980). Furthermore, the formulation of a diagnosis results in the mobilisation of support and also activates possible means of controlling the complaints. This does preassume, however, that the diagnosis fits in with the patient's frame of reference (Bügel & van Everdingen, 1998). The provision of information by recording a consultation on cassette, for example, can also create a feeling of control (even if the patient never actually refers to that information), meaning that patients have a better idea of what to expect (Ong *et al.*, 1995). The mere fact that many patients do actually listen to the recording confirms that a need for information is being satisfied (Johnson & Adelstein, 1991; Deutsch, 1992).

For the patient, the need for information is, in general, an important reason for consulting a physician (van Kar *et al.*, 1992b). The fulfilment of this need will therefore also, in itself, have beneficial effects. Good information also has a bearing on how quickly a patient recovers after an operation (Cupples, 1991).

Giving patients a recording of a discussion with the physician helps them to retain information and also helps to reduce the number of visits to the GP, but does not lead to a reduction in anxiety (Cupples, 1991; Hogbin *et al.*, 1992; Rylance, 1992; McHugh *et al.*, 1995). The stress that is associated with a visit to a physician can even lead to patients having difficulty remembering information (Newcomer *et al.*, 1999) and thus failing to follow a physician's advice properly. Too much cortisol can damage (Bremner, 1999) the hippocampus, an intermediate stage in the long-term storage of declarative knowledge, or else temporarily block it off (Newcomer *et al.*, 1999), with the result that either no information at all is stored, or else only fragmented information. The manner in which information is provided appears to be crucial. In particular, honest, open and personally-tailored communication puts patients at their ease (Sardell & Trierweiler, 1993). A good discussion technique can have positive effects. This is underlined by the research by Hwang *et al.* (1998) that was referred to earlier (section 4.4.2). Patients of physicians trained in imparting information displayed a greater reduction in anxiety than patients of physicians who had received no such training (Rutter *et al.*, 1996). Furthermore, complaints appear in general to show greater improvement when physician and patient identify the same complaints as posing a problem (Starfield *et al.*, 1981).

Table 4.5.1 *Information-giving by the physician*

Authors	Subjects	Design	Context variable	Outcome measure	Results
Cupples, 1991	40 CABG patients	randomised post-test	pre-operative information	anxiety and speed of recovery	information enhances outcome
Hogbin *et al.*, 1992	67 breast cancer patients	randomised pre-/post-test	consultation with physician on cassette	level of patient information and anxiety	better informed as a result of cassette, not less anxious
McHugh *et al.*, 1995	117 cancer patients	prospective RCT, follow-up	information	retention of information and anxiety	repetition of info. promotes retention, not reassurance
Rylance, 1992	286 patients in paediatric sector	post-test	consultation on cassette	retention of information	taping consultation helps
Rutter *et al.*, 1996	36 cancer patients	pre-/post-test, control group	information	anxiety, depression, feeling of control	more info. promotes control, reduces anxiety and depression
Starfield *et al.*, 1981	135 patients in internal or paediatric medicine	correla-tional	agreement between physician and patients	problems presented	greater improve-ment if physician and patients identify same problems
Sox *et al.*, 1981	176 patients with non-specific chest pain	RCT	with/without diagnostic examination	reduction in pain, anxiety	after diagnostic examination, patients have less pain, equally anxious
Glasunov *et al.*, 1973	95 hyper-tensives	prospective cohort	with/without physical examination	blood pressure, cholesterol, glucose	periodic examination reduces outcome

It is worth noting that *not* being able to find a physical explanation also gives meaning to the complaints. Studies by Sox *et al.* (1981) and Glasunov *et al.* (1973) show how this process is influenced by the information that emerges from the physical and diagnostic examination. Further examination results in less pain complaints and lower blood pressure.

Information given by the physician therefore has an influence on patient health.

4.5.2 NEEDS OF THE PATIENT

The same information will not elicit the same effect in every patient simply because patients have different starting situations and not all physicians impart information in the same way. The extent of the information provided by physicians depends in part on the need for information and the concerns of the patient in question (Street, 1991). Research by Miller and Mangan (1983) shows that it is worthwhile in this connection to divide patients into two categories: patients who want as much information as possible about what is wrong with them ("monitors") and patients who want to know as little as possible ("blunters") (Table 4.5.2). If the volume of information does not conform to one of these two coping styles, there appear to be adverse psychophysiological consequences. Personally tailored information can only be given by adopting a patient-centred approach (see section 4.4.3), whereby the physician is mindful of the patient's individual needs. Depending on a person's level of education and coping style, there are patients who find it sufficient to receive information and others who want to be actively involved in the choice of a particular treatment (Margalith & Shapiro, 1997). Thus "monitors" appear to have a greater need for diagnostic tests and information, but at the same time want to play a less active role in their care (Miller *et al.*, 1988). It should be noted that one coping style is not, by definition, any more effective than the other. In fact, this appears to be dependent on the controllability of the disorder, the nature of the outcome measures (proximal or distal) and the stage which the disease has reached (Kiyak *et al.*, 1988).

Patients can themselves exercise control over the nature and amount of information they receive through their individual communication style. This appears to have beneficial effects on health, e.g. via a reduction in HbA1 (Greenfield *et al.*, 1988). However, information alone will not be sufficient to produce beneficial physiological effects. For example, a meta-analysis of interventions in diabetes patients reveals that information alone does not result in better metabolic control. A more individual approach, including attention to psychosocial factors, appears to be much more fruitful in this respect (Padgett et *al.*, 1988). Moreover, the content of the information can have an adverse impact

Table 4.5.2 *Patient needs*

Authors	Subjects	Design	Context variable	Outcome measure	Results
Miller & Mangan, 1983	40 gynaecological patients	randomised, pre-/post-test	information matched to needs	psycho-physiological arousal and anxiety	a better match results in less arousal and anxiety
Greenfield *et al.*, 1988	73 diabetes patients	RCT	patient-centred advance information	HbA1	advance info improves HbA1
Orth *et al.*, 1987	170 hypertensives	correlational	info. from physician, disclosure by patients	blood pressure	discl. and info. reduce blood pressure
Amigo *et al.*, 1993	60 hypertensives, 60 normo-tensives	pre-/post-test, control group	negative, posisitve or neutral suggestion	blood pressure	blood pressure fluctuates according to nature of suggestion
Larsson *et al.*, 1998	53 cancer patients	dyadic, correlational	care matched to patients' needs	anxiety	better match, less anxiety

on health, e.g. by increasing the blood pressure (Orth *et al.*, 1987; Amigo *et al.*, 1993).

It will not always be easy for care providers to correctly assess the emotional and cognitive needs of their patients. Care providers often take a different view of a patient's complaints than the patient himself (Martin *et al.*, 1991; Larsson *et al.*, 1998).

The extent to which a physician takes a patient's needs into account plays a role in the effects which the information given by the physician elicits.

4.5.3 INFLUENCING COGNITIONS

Information given by a physician must be cognitively and emotionally processed by the patient. This processing has an influence on the physiological activity and on the immune system (Brosschot *et al.*, 1991; Lutgendorf *et al.*, 1994). Conversely, cognitions can play a role in perpetuating physical complaints. Negative cognitions (catastrophising, see section 4.1.5) and somatic attributions (see section 4.1.6) appear to be capable of increasing the intensity of pain (Shutty *et al.*, 1990; Summers *et al.*, 1991; Turk & Rudy, 1992; van Dulmen *et al.*, 1997) and perpetuating symptoms of chronic fatigue (Vercoulen *et al.*, 1996) (Table 4.5.3). Changing such cognitions will therefore impact positively on physical complaints (Payne & Blanchard, 1995; van Dulmen *et al.*, 1996b) and even on more serious disorders such as AIDS and cancer (Kiecolt-Glaser & Glaser, 1992). According to Murray (1989), emotional expression alone, is, in point of fact, insufficient to influence unfavourable cognitions. Active intervention on the part of the care provider is needed if disclosure is to have a long-term effect. For example, the provision of clear information and advice to hypertensive patients appears to be capable of reducing misconceptions about a disorder, resulting in better control over blood pressure (Inui *et al.*, 1976).

Both controlled (Bradley *et al.*, 1987; Devine & Spanos, 1990, *inter alia*) and uncontrolled studies (Williams *et al.*, 1993; van Dulmen *et al.*, 1996a, *inter alia*) have been carried out into the effects of interventions aimed at modifying cognitions and emotions in the treatment of physical complaints in medical practice. A meta-analysis of 51 studies into the effect of cognitive coping strategies on the reporting of acute pain demonstrates the value of these strategies in relation to positive expectations (Fernandez & Turk, 1989). This was confirmed by Devine and Spanos (1990). A study by Bradley *et al.* (1987) shows that alongside conventional drug treatment, simple cognitive behaviour-therapy strategies - for example encouraging patients to perform relaxation exercises combined with the restructuring of dysfunctional views - can provide long-term relief of headache complaints. Studies by Wells *et al.* (1986) and Vasterling *et al.* (1993) produce similar results. Advice from the physician, such as "Take it easy" and "Find something to take your mind off it" may possibly have the same effect. O'Leary *et al.* (1988) demonstrate the beneficial effects of cognitive behaviour therapy in which patients receive various cognitive and behavioural tips on coping effectively with a disorder[5].

Successful cognitive interventions have a number of components in common, namely explaining to the patient the connection between the meaning and the perception of his complaints, encouraging physical and psychological relaxation and identifying negative ideas and replacing them with patient-specific positive ideas.

Table 4.5.3 *Influencing of cognitions by the physician*

Authors	Subjects	Physi-cians	Context variable	Outcome measure	Results
Payne & Blanchard, 1995	34 IBS patients	RCT, follow-up	identifying & modifying cognitions	physical complaints and anxiety	intervention has positive effects
van Dulmen *et al.*, 1997	110 IBS patients	prospec-tive follow-up	paying attention to somatic attributions	abdominal-pain symptoms	positive relation-ship between reduction in attributions and complaints
Inui *et al.*, 1976	102 hyper-tensive patients	pre-/post-test, control group	discussing (or not discussing) cogn. and attitudes	knowledge, compliance and blood pressure	lower blood pressure after discussing patients' cognition
Wells *et al.*, 1986	24 surgical patients	RCT, pre-/post-test	changing cogn.	anxiety, pain	less anxiety and pain
Bradley *et al.*, 1987	53 rheum. arthritis patients	RCT	discussing cognitions	pain, anxiety and function	etter outcomes after discussing cognitions
Devine & Spanos, 1990	96 patients	pre-/post-test, control group	cognitive intervention and positive expectations	pain sensations in laboratory	cogn. coping mechanism more effective than pos. expectations
Williams *et al.*, 1993	212 patients with chro-nic pain	pre-/post-test, 6-month follow-up	cognitive skills, relaxation	pain intensity, qual. of life, physical function	positive effects of cognitive behaviour therapy
Vasterling *et al.*, 1993	60 cancer patients	3x2 factorial	cognitive distraction	nausea and blood pressure	cogn. distraction reduces complaints
O'Leary *et al.*, 1988	30 patients with	RCT	information and cognitive	pain, functional state of health,	less pain, better joints, immune function

It is this sort of "non-specific" approach that one usually already finds to a greater or lesser extent in medical practice. After a visit to the doctor, patients frequently modify their ideas about the cause of their complaints and often already feel less concerned once they have heard that they have not contracted a life-threatening disease (van Dulmen *et al.*, 1995). This reassurance can manifest itself in a reduction both in physical complaints and in the accompanying intake of medication (visits to the doctor and use of medication).

Every patient wrestles with thoughts and emotions that are connected to his specific situation at a given moment. By getting these out into the open and explicitly placing them on the agenda - for example, by discussing their validity - one can effectively reassure the patient (van Dulmen *et al.*, 1997). It is therefore important that a physician should form a good picture of what it is that is preoccupying the patient. The fact that physician and patient are in agreement about the reason why the patient is feeling unwell plays an important role in the improvement of complaints (Bügel & van Everdingen, 1998).

5 SUMMARY OF UNDERLYING MECHANISMS

The second of the questions underlying this study relates to explanations for the effect of context in healthcare. Many explanations have been given for the effect of context in healthcare. For example, health effects that occur as a result of a hospital visit in the absence of any specific therapeutic measures may possibly be explained on the basis of theories involving the relationship between the soma and the psyche, such as psychophysiological and psychoneuroimmunological explanations. Furthermore, classical conditioning theory may explain how apparently neutral factors can assume importance.

In this chapter we shall discuss the most important explanations. Global mechanisms such as anxiety reduction or the release of endogenous opiates have an impact on the entire body. Other mechanisms such as conditioning or the effects of expectations, on the other hand, relate only to specific parts of the body. Research by Montgomery and Kirsch (1996) is inconsistent with the existence of global mechanisms. Anxiety reduction could just as easily be an aspect as a cause of context effects (Wall, 1993).

5.1 STRESS REDUCTION

Stress plays an important role in the development and course of disorders and in connection with therapeutic effects (Maes *et al.*, 1987). Because secretion of cortisol rises in situations of increased stress, the hormone cortisol is considered to be the indicator of stress (Francis, 1979). Research into this physiological measure of stress was for a long time hampered by the need to identify the cortisol concentrations in the blood, and blood-tests are, in themselves, already a stress-increasing, unnatural situation, the effect of which may possibly interact with the effect of a particular intervention. This situation has improved now that research has shown that cortisol can also be reliably measured in saliva (Vining *et al.*, 1983; Burke *et al.*, 1985; Tarui *et al.*, 1987). As a result, fresh light has been shed on the individual variability in reactions to psychological stress.

Research conducted in 24 female trial subjects by Bohnen *et al.* (1991) demonstrates that the increase in cortisol in response to a psychological stressor in which trial subjects were confronted with an uncontrollable situation is dependent upon an individual's cognitive coping style. Cognitive re-evaluation and the ability to put the situation into perspective appear to lead to a less marked cortisol response. It is worth noting that the relationship between chronic stress and cortisol does not appear to be so clear-cut as that between acute stress and cortisol. Chronic stress does not result in either an increase or a decrease in cortisol production. If account is taken of the extent to which an individual is able

to control the chronic stressor in question, then the relationship becomes clearer (Vingerhoets & Assies, 1991). Furthermore, as far as immunological parameters are concerned, it appears that the more chronic stress a person experiences in his daily life, the greater is his immunological response to acute stressors in terms of reduced NK cells and lymphocytes (Brosschot *et al.*, 1994). Cortisol therefore also has an influence on the immune system (Nomoto *et al.*, 1994).

An important problem in research with physiological parameters as a measure of stress is the apparent lack of any conclusive relationship between these objectively measurable outcomes and the subjectively experienced outcomes. Thus a person may feel more relaxed in response to a particular intervention and yet still have a higher cortisol level (Manyande *et al.*, 1992) and the relationship between stress and physiological measures of stress also appears to be related to an individual's inclination to report physical symptoms (Vingerhoets *et al.*, 1996). Even though physiological measures of stress are therefore not ideal at an *individual* diagnostic level, related research in *groups* of patients would appear to be worthwhile, since these individual variations will then be averaged out.

5.2 CLASSICAL CONDITIONING, THE LEARNING EFFECT

According to the theory of conditioning, context effects are conditioned responses to stimuli which are present in the therapeutic (or experimental) setting. - Neutral, unconditioned stimuli that occur concurrently with the treatment, such as a physician, a physical examination, a hospital, an injection or a tablet, are associated with a reduction in negative symptoms and are thus positively conditioned as far as recovery and anxiety reduction are concerned. As a result of that association, improvement can already begin to occur in response to neutral stimuli in the absence of an active intervention. This argument is supported, *inter alia*, by research indicating that the effects of placebo medication are more marked if, during a previous phase, an active substance has been taken (Suchman & Ader, 1992). Similarly, experience of ineffective treatments will be contributory to a negative response to follow-up treatments. Voudouris *et al.* (1985) were the first to conduct research into the conditioning effect in human beings. They investigated what analgesic effect an inert ointment had on the experience of pain impulses among 32 healthy trial subjects. In half of the trial subjects, the pain impulses were experimentally increased following administration of the ointment, while in the other half they were reduced. Individual pain thresholds were established in advance for all trial subjects and they were "taught" that the ointment had an effect by varying the intensity of pain after administering the ointment (whereas the trial subjects were led to believe that the stimulation

remained the same). The results confirm that the reaction to the ointment can be conditioned both in a negative and positive direction. In their follow-up studies, Voudouris *et al.* (1989, 1990) show that the expectations of patients alone are insufficient to explain this conditioning effect. Öhman and Soares (1998) have also recently demonstrated that expectations are not related to the conditioned response. These studies suggest that in order to determine the effect of a treatment, it is important to examine how previous treatments have been experienced by the patient concerned. The previously cited studies by Bovbjerg *et al.* (1990) and Kvale *et al.* (1991) also demonstrate that the association of certain stimuli (hospital, smell and taste of chemotherapy) with aversive effects (nausea and anxiety) can trigger effects of this type. Moreover, comparable research in 27 cancer patients (Fredrikson *et al.*, 1993) suggests that the reduced resistance that is associated with a high level of anxiety in these patients can result in the occurrence of a conditioned decline in the natural defence mechanism (see section 5.4). Blood glucose concentrations also appear to be conditionable (Fehm-Wolfsdorf *et al.*, 1993; Stockhorst *et al.*, 1999).

Conditioning effects thus appear to play an important role in context effects. Physicians can enhance these effects by the way in which they approach their patients. Although classical conditioning provides a good explanation for the context effects, it cannot be the only explanation, since extinction would have to occur after repeated association. In the case of expectations, however, no extinction takes place (Kirsch, 1997). One reason for this could be that the result, i.e. symptom reduction, is an extremely strong reinforcer: once a response expectation has proved to be correct, it will confirm itself even without any renewed reinforcement by an unconditioned stimulus. It therefore seems likely that the expectations that are formed by conditioning which patients have from their care have an important role to play in explaining context effects.

5.3 EXPECTANCY, EXPECTATIONS

Response expectations are not only developed through conditioning, but can also be triggered by the information that a person receives. As a result of conditioning, a person may well expect that one particular event will follow another, but this remains dependent on the information that the conditioned stimulus gives about the unconditioned stimulus. Various aspects within the physician-patient contact, such as the physician-patient relationship, confidence, reduction in anxiety, etc, help to boost those expectations. Ultimately it is the response expectations that are determinative for the effect of a therapeutic

measure, not the strength of the association that underlies those expectations or the way in which those expectations have been formed (Kirsch, 1997).
Several hypotheses have been formulated to explain the connection between expectations and a (positive or negative) therapeutic effect. Thus the expectation that a treatment will be effective will reduce anxiety and hence symptoms, the patient develops a more positive attitude, and as a result regards symptoms as being more controllable, or starts to be less avoidant of certain activities. The question as to which of these mechanisms are effective cannot be answered on the basis of the empirical studies that were discussed earlier.

5.4 PSYCHONEUROIMMUNOLOGY

Psychoneuroimmunology aims to study the reciprocal relationship between the central nervous system and the immune system. Susceptibility (incidence, duration and severity) to various disorders, such as influenza, colds, TB, allergies and autoimmune disorders appears to be related to psychological factors such as emotional stress (Glaser *et al.*, 1992; Glaser *et al.*, 1999). There is evidence to suggest that during periods of extreme (chronic) stress the immune system is weakened through a decline in multiplication and activity of antibodies (white blood cells such as lymphocytes and NK cells), which are needed in order to combat exogenous micro-organisms (antigens such as bacteria, parasites and viruses). Thus diseases (infectious diseases, HIV and cancer) are afforded greater opportunities (Martin, 1987; Kiecolt-Glaser & Glaser, 1995; Cohen & Herbert, 1996). *Acute*, short-term stress actually appears to activate the immune system, probably as a result of an acute arousal response (Naliboff *et al.*, 1991; Gerritsen *et al.*, 1996). Furthermore, a decrease in antibodies appears to take place principally where an individual thinks he has no *control* over his situation and loses the capacity to successfully avoid stressors (Pettingdale *et al.*, 1981; Brosschot *et al.*, 1991, 1998). Certain hormones such as ACTH, insulin, endorphin, adrenaline and cortisol, the release of which is influenced by stress, appear to interact with the immune system. The discovery of the same peptide receptors in the brain and other organs also demonstrates that there is a direct connection between the mind and the body. The complexity of psychoneuroimmunology is also evident from the findings that immune responses can be conditioned (Bovbjerg *et al.*, 1990; Buske-Kirschbaum *et al.*, 1992; Ader & Cohen, 1993).
The relationship between stress and immunological reactions is mediated by cognitions. This was demonstrated in a study by Wiedenfeld *et al.* (1990) in 20 phobic patients whose immune response, measured by the number of lymphocytes and T cells, increases as they experience greater self-efficacy, or in

other words, the more convinced they are of their own ability to control the phobic stressor. Comparable outcomes emerge from a study by Wallbott and Scherer (1991) in 60 trial subjects, which demonstrates that physiological reactions to mental stressors are dependent on how an individual copes with the stressor. In a study of 62 HIV-infected men, Goodkin *et al.* (1992) also found a positive relationship between the number of NK cells and an active coping style, with positive reinterpretation, acceptance and active seeking of help being key factors. This ties in with the outcomes of research by Manuck *et al.* (1991) in 25 trial subjects, which reveals that the influence of psychological stress on the immune system is related to an individual's cardiovascular reactions to stress. The immune system of people who were more inclined to respond to stress with an increase in blood pressure and pulse proved to be more susceptible to a decline in defence mechanisms than that of individuals who lack such a rapid response. It is possible that coping styles such as avoidance and resistance also play a role here. It is worth noting that immunological effects of stress appear to be most clearly reflected in changes in the number of NK cells (Brosschot *et al.*, 1992).

As far as the clinical implications of such experimentally proven immunological changes are concerned, it would appear to be important to measure not only the patient's immunological parameters, but also the presence of cognitive coping styles and the degree of cardiovascular reactivity.

5.5 CONCLUSION

It is not possible to offer a single explanation for the effect of context in healthcare. Countless interactions are taking place inside the body between the different systems that are responsible for hormonal, immunological and cardiovascular responses (Sgoutas-Emch *et al.*, 1994; Benschop *et al.*, 1998). It would appear important to have an understanding of an individual's conditioning history as far as a particular treatment is concerned, since the effect of a given treatment and the immune response are both dependent on the stimuli to which a body has been exposed hitherto. In general, cognitions of physicians and patients alike appear to play a major role in the interpretation of physiological processes and of the effects of therapeutic measures.

NOTES

1 Because the terms "placebo" and "placebo effect" are still widely used, it is possible that they will also appear in this report. Where the term *placebo* effect is used, it refers to the positive or healing effect of the entire context within which a physician-patient contact takes place; *nocebo* refers to the negative effect of this context.

2 The mediating role of such factors as stress, anxiety and coping strategies will only be considered indirectly in this study.

3 Where no hits were found for a search term in a title, the abstract was screened for the indexed term.

4 "Regression towards the mean" in this case means that patients are inclined to consult a physician when their complaints are most severe and will also diminish without intervention.

5 The impression may exist that the influencing of cognitions by a physician is actually tantamout to pracising cognitive therapy. This might result in questions being raised as to the extent to which one can still speak of context effects in this connection. Treatment is termed cognitive therapy if this is all it comprises. If, however, physician-patient contact also includes discussion and the influencing of cognitions and emotions, then it is not interpreted in this way.

Sector Councils (*Sectorraden*) are independent bodies comprising representatives of the research community, the general public, trade and industry, and government (as an advisory member). Sector Councils are, first and foremost, engaged in identifying developments within society and, on this basis, any gaps in knowledge that might have implications for publicly financed research. In addition, Sector Councils are also geared towards analysing trends in science and technology and their implications for society as a whole.

Under the Sector Councils Framework Act on Research and Development, a system of Sector Councils operates in the following areas: healthcare, nature and the environment, spatial planning, the agronomic sector and development cooperation.

Being an umbrella organisation, the Consultative Committee of Sector Councils for Research and Development (COS) provides a platform for consultation on issues of collective interest and the organisation of projects and conferences on such topics as the formulation of questions and the development of methodologies. The COS also looks after the interests of the sector councils on the basis of common standpoints. Under the Framework Act, bodies that are not actually sector councils but operate in a similar fashion may be advisory members of the COS - e.g. the Study Centre for Technology Trends (STT).

The COS has at its disposal a budget fixed by the Ministry of Education, Culture and Science (OC&W) for the funding of programming studies (the coordination fund).

NIVEL (National Institute for Research into Healthcare) is an independent national research institute that conducts research within the healthcare field. The aim of this study is to acquire and disseminate knowledge and an understanding of the structure and functioning of healthcare and social services, also in relation to other sectors of society. In this respect, NIVEL is aimed both at care users and care providers as well as national policy-making organs. Scientific quality is guaranteed by external certification (ISO standard 9001), and by the fact that the research is performed at two graduate schools accredited by KNAW (the Royal Netherlands Academy of Arts and Sciences) - CaRe and Psychology & Health.

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APPENDIX A: INVITATIONAL CONFERENCE ON RESEARCH INTO THE EFFECT OF CONTEXT IN HEALTH CARE

As a result of the programming study entitled "The Effect of Context in Health Care"
the Advisory Council on Health Research (RGO) organised a conference aimed at establishing whether it is possible to carry out research into context factors, and if so, how this might be accomplished. Held in Utrecht on 26th September 2000, the conference was divided into the following three parts: discussion of the report and of the methodological and psychoimmunological problems associated with research into context factors; scientific papers concerning the opportunities for research; and a general discussion.

Following an introductory address by the Chairman of the RGO, Professor H.G.M. Rooijmans, Dr A.M. van Dulmen of the Netherlands Institute for Research into Health Care (NIVEL) presented the report and provided some explanatory comments about the questions underlying the research and the findings. The literature study provides an overview of context factors, for which three explanatory mechanisms are cited: stress reduction, classical conditioning and psychoneuroimmunological mechanisms.

Dr. A.J.M. de Craen (Clinical Epidemiology, LUMC[1]) looked at the methodological problems surrounding research into context factors. There is a publication bias because virtually only positive findings appear in the literature. To prevent any distortion in the research results, investigators generally adopt randomisation and blinding techniques. This widely used methodology is inadequate in the case of research into context effects, while the alternatives (Zelen design and pre-randomisation) are not acceptable. De Craen views the provision of informed consent prior to randomisation as one possibility. The patient then needs to be informed of the fact that it is important, for study purposes, that he is not aware of the exact questions which the investigators are seeking to answer. He also needs to be made aware of the fact that the study has the approval of the Medical Ethics Committee. In the past, a proposal for such

[1] University of Leiden Medical Centre

a study design was approved by the former Central Committee on Medical Research Ethics (KEMO, which is now known as the CCMO[2]).

Professor C.J. Heijnen (Wilhelmina Children's Hospital, Utrecht) gave a paper on psychoneuroimmunological aspects of context effects. A great deal of research has been conducted into acute effects of context on various neuroimmunological parameters (as is evident from the literature study), but very little work has been done on the influence which context has upon the clinical course of the disease in question. Animal-based experimental research into the influence of chronic stress indicates that there is a relationship between individual coping strategy and the possibility of certain disorders being induced. Context factors may possibly lead to changes in the balance of the immune system (Th1 versus Th2 cells) which influence the clinical course.

Three speakers then outlined their visions of the possibilities for research into context factors.

Professor R. van Dyck (Department of Psychiatry, VUMC[3]) proposed, as a first step, that a systematic review should be conducted among patients (and possibly also, at a later stage, among care providers) with a view to gauging the effect of each individual factor. Research into the role of patient preference is one example. In the case of anxiety disorders, the non-preferred treatment appears to be just as effective as the preferred approach. Van Dyck expected that a number of the factors mentioned in the study actually have a negligible effect. Only the most influential factors should be considered for further investigation. Furthermore, he found that "bedside manner" deserves to receive more attention. Finally, cognitive behavioural therapy is, to some extent, composed of non-specific factors. Research should enable this technique to be applied more efficiently.

Professor F.J.H. Tilders (Department of Pharmacology, VUMC) emphasised the intended goal of the research: the importance for science and health care. The goal must be clear in order to determine the research strategy. Tilders focusses on two areas: research into the efficacy of drugs and research into context effects in health care. Drug trials are usually expressly designed to eliminate the impact

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[2] Central Committee on Medical Research Involving Human Subjects

[3] Free University (of Amsterdam) Medical Centre

of context factors as far as possible. We might ask ourselves, however, whether the effect of context and the specific effects of a given substance are not additive, and whether we should not actually be striving for precisely that additive effect. As far as health care is concerned, there is sufficient evidence to suggest that context factors do play a role. In order to identify those factors, one might investigate whether there are relevant differences between the treatment outcomes that are achieved by different physicians. If this is the case, then adoption of an open search strategy in exploring the background to that variation might enable us to identify the crucial factors.

Professor C. van Weel (Department of Family, Social and Nursing-Home Medicine, KUN[4]) approached the subject from the perspective of the general practitioner, asking what "context" a GP has to deal with. He looked at the need for research into context effects and made it clear that a research program would have to be based on medical practice. One possibility would be to study the discrepancy between "efficacy" and "effectiveness". Van Weel cited the following four research priorities as far as family medicine is concerned: context effects and the effectiveness of deciding against treatment (whether this be desired or required); empowering strategies for the treatment of patients with chronic complaints (requests for a changeover from a casuistic to a systematic approach); critical assessment of context effects in connection with marginally effective interventions; and the relationship between context and the desired results of the treatment in question.

The discussion focussed on the question of whether research into context effects is worthwhile and if so, what avenues need to be pursued.

The conclusion that was reached in the debate about the first question was a cautious "yes". Research was considered to be possible with regard to hypertension, diabetes mellitus, asthma, anxiety and depression. Research was also regarded as being both feasible and relevant in connection with syndromes of as yet unknown pathogenesis (e.g. whiplash, chronic fatigue syndrome, irritable bowel syndrome). Sick leave and quality of life are outcome measures that might possibly be employed.

Van Dyck wondered whether it might be possible to miss out the observational phase of the research. The potential factors have, after all, already been

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[4] Catholic University of Nijmegen

identified. He emphasised once again the need to look for the most influential factors (i.e. factors whose effect exceeds the natural variation in clinical course). These factors alone should be subjected to mechanistic research.

Rooijmans foresaw problems as far as the manipulation of context factors is concerned. How do you isolate a single factor from the other factors, and how do you tell the patient what you are going to do?

The discussion was then directed at the influence of attributions (whereby a patient ascribes a symptom or complaint to a specific cause). Cancer patients were cited as an example of a patient group with a strong tendency towards attributions. The conclusion was reached that it is possible to carry out research into attributions in the case of both chronic and acute conditions. Attributions have implications for the patient himself and can be modified. It emerged that there may possibly be differences between GPs (who ask about attributions almost as a matter of course) and specialists (who are possibly less inclined to ask such questions), and that the very manner in which questions about attributions are asked is a topic suitable for research.

A number of comments were made as a result of this discussion. First of all, when considering the doctor-patient relationship it is important not to lose sight of the influence of context factors in a broader context. Consideration must be given to the patient's social environment and what impact this has. Furthermore, the term "manipulation" has negative connotations. The terms that are to be used need to be carefully chosen and explained. Finally, when designing the research it is necessary to take cultural differences into account (consideration of ethnic minority groups).

Professor J.M. Bensing (NIVEL) and Professor H.G.M. Rooijmans rounded off the conference by concluding that there are sufficient grounds for continuing along the path that has already been embarked upon and for seeking opportunities to flesh out the research that is being conducted in this area.

Note added in proof: The fact that there is interest in this subject at international level as well as in the Netherlands is evident from the conference entitled "The Science of the Placebo: Toward an Interdisciplinary Research Agenda", which was held at the National Institutes of Health in Bethesda, USA, from 19-21 November 2000.

APPENDIX B CONSULTED EXPERTS

As part of this study, contact has been established with various experts who in their work have had some form of involvement with placebo or context effects. Their ideas and views have been incorporated in this report.

- Dr AJM de Craen,
  Clinical Epidemiology, Leiden.
  Placebos and placebo effects in clinical trials

- Professor R van Dyck,
  Valerius Clinic, Amsterdam.
  Placebo and suggestion in psychotherapy and hypnotherapy

- Professor L van Doornen,
  Healthcare Psychology, Utrecht.
  Psychophysiology, stress and health

- Professor J Kleijnen,
  NHS Centre for Reviews and Dissemination, York.
  Field of research: Context effects in physician-patient contacts