SUMMARY

Warning or alarm functions in commercial monitoring equipment generate many false alarms, which restrict their clinical usefulness. Nevertheless, warning functions are indispensable whenever the possibility exists that an unexpected problem escapes our attention.

Anesthesia can be considered as a process of continuous optimization, correcting any disturbance in the desired physiological state. This process requires the anesthetist's continuous alertness. When an initial disturbance escapes our attention, an optimal state is no longer maintained. When the disturbances develop further, management becomes increasingly difficult and eventually permanent damage may result.

It is a difficult task for a human being to keep alert or vigilant continuously, especially when the incidence of unexpected problems is as small as it is in anesthesia.

Monitoring equipment is usually provided with alarm functions to support vigilance. These conventional alarm systems generate an alarm whenever the value of a measured variable exceeds a limit that has been set previously. In this thesis disturbances that are detected with such an alarm system are called 'value events'. The limits are usually set at the physiological limits.

The continuous optimization process of anesthesia occurs almost entirely within the physiological limits. Disturbances which require optimization cannot be detected by a conventional alarm system until abnormal values have occurred. The initiation of disturbances -which requires correction- can only be detected as a change, or more exactly as a difference between present and previous measurements. In this thesis such initial disturbances are called 'change-events'.

A conventional alarm system, being suitable for detection of value-events only, cannot support the continuous optimization process of anesthesia effectively. Therefore, there is a need for a warning system that detects change-events long before values outside the normal range are measured.

Several systems have been described for the detection of changes within the normal range. They compare the variable's present value with a running average, an average of a preceding period. Other methods compare two running averages calculated over a recent period and an earlier period. The disadvantages of these systems are their complete insensitivity for slow changes and the persistent character of their alarm states.

It has been decided to develop a warning system for the detection of change-events, giving a short but clear warning whenever necessary. An important step in this development is to determine which change-events are clinically relevant and worth a warning. Both rapid and slow changes have to be considered, although they require different detection methods. For changes near the physiological limits an enhanced sensitivity is desired since they are considered more relevant than those in the centre of the normal range. Furthermore, the relevance of changes depends on their amplitude and on patient- or anesthetist-related individual factors.

A warning signal is required whenever the degree of change exceeds a certain threshold. The choice of the threshold determines how many warnings are generated. A low threshold produces a high sensitivity, generating many warnings,

of which a large proportion is relatively irrelevant. A high threshold results in a low sensitivity, with the chance that some clinically relevant events pass without generating a warning. Numerically comparable changes are clinically sometimes relevant and sometimes irrelevant depending on secondary factors. The choice of the threshold for the prototype was based on initial experience with the system and is supported by a study of the variability of measured values and their relation to therapeutical intervention.

The numerical methods for the detection of change events are described in a separate chapter. The normalized running average difference (NRAD) is introduced as a qualitative and quantitative representation of the average change occurring in a time window defined by two time-constants. The NRAD is calculated as the product of a correction factor and the difference of two running averages characterized by the two time constants.

Very slow changes can be detected by the Minimax method. It was introduced to detect changes that occur outside the time window defined for the NRAD. The Minimax method compares the present value of a variable with the very largest and the very smallest value that has occurred during the whole observation period.

Furthermore a change-indicator has been introduced. This is the ratio of the NRAD and the appropriate warning threshold. It may be used in the future for mathematical processing of coincidental changes occurring in different variables.

A reset-mechanism has also been introduced. This prevents sustained warning states. As soon as a warning is given -because of a change- a new observation period is started, using the value measured after the change as a new reference value. There is no need for a sustained warning state provided the change occurred inside the normal range. The result of this reset-mechanism is that time is divided into periods that are assumed to be stable, but separated by moments of change. These moments of change are marked by a warning signal.

Carina, the prototype of the new warning system generates warnings according to the methods described above. The warning signal consists of a short melodious tune, completed with a strong optical signal. The latter does not disturb the surgical team but alerts the anesthetist effectively. All measured values can be read from the system's video display. In addition it is indicated which of the variables have recently caused a warning. Trend curves of some of the measured values are shown on the display as well as real time curves of the ECG and the capnogram. Furthermore, the system automatically writes an anesthesia record.

In order to provide the reader with an impression of how the warning system works in practice a single anesthetic is described in detail, with the warnings generated by five different warning systems. Carina's warnings are given for changes that an anesthetist probably recognizes as clinically relevant, while a conventional warning system generates long sustained alarms, once a limit is exceeded. For the purpose of comparison unusually narrow limits were chosen.

For further evaluation five studies have been performed. It is assumed that opiates are given when pain is suggested by an increased heart rate or blood pressure. As an anesthetist gives an opiate when he considers such changes to be relevant, Carina's warnings can be expected to be associated with opiate gifts. In the first study it is demonstrated that hemodynamic changes are associated with opiate gifts. It is concluded that opiate gifts are indeed associated with therapeutically relevant changes. The second study demonstrates that warnings are given for the events that correlate with opiate gifts. However, in this study changes that indicate the necessity of opiate administration cannot be distinguished from changes resulting from opiate therapy. A third study was instigated to investigate if warnings were given for increases in blood pressure, as an example of changes that indicate exclusively the necessity of opiate administration.

The question arises if a comparable correlation between changes and warnings can also be achieved with a conventional alarm system, by choosing unusually narrow alarm limits. Study four demonstrates that such a correlation can indeed be achieved. However, there are theoretical objections against such a system: many false alarms are to be expected, alarm sounds will have a sustained character and not all relevant change-events will be detected. Study five demonstrates that long sustained alarm periods are generated if a conventional alarm system is so adapted. This will obviously cause much irritation and a comparatively small number of useful warnings will be generated.

The occurrence of false alarms is a problem with many warning systems. Therefore, methods were developed for suppression of two frequent causes of false alarms: noise or rapid irregular fluctuations, and spikes or large transient fluctuations. False alarms caused by noise can be suppressed by using a running average over a short period instead of the measured value as such as the input for the detection system. This works as a low-pass filter and is a common method for suppression of noise. It is also used in the prototype.

For the suppression of spikes, a low-pass filter is insufficient because the high amplitude of the spikes cannot be attenuated sufficiently by the filter. A new filter technique was, therefore, introduced. This limits the speed of increase of a variable, before it is fed into the detection system. It largely reduces the amplitude of spikes, but physiological changes will pass such a filter almost unaffected since they occur more slowly than spikes do. The result of such a filtering is called a limited running average (LRA). The normalized limited running average difference (NLRAD) is the normalized difference between two LRA's, and can be used for detection of changes instead of the NRAD.

An example of spike interference is afforded by the disturbances in pulse oximeter readings caused by interruption of the blood flow to the arm when a blood cuff is inflated on the same arm. In a volunteer such disturbances could be suppressed effectively. A decrease in the saturation reading caused by breath holding was used as an example of a clinically relevant change. This relevant change was influenced by this filter technique to a minor degree only.

In the final chapter there is a resume of the main concepts discussed in this thesis. The NLRAD described provides optimal detection of initial changes (change-events) in a definable time window, being insensitive for noise and spikes. Whenever the NLRAD exceeds a certain limit, a short but clear signal is given. A reset machanism is added to prepare the system immediately for detection of subsequent changes compared to the new reference.

The influence that such a warning system has on the daily work of the anesthetist is also described. Previously the anesthetist had the almost impossible task of being alert for beginning changes in the patient's physiological variables and, at the same time, administering medicaments, transfusions and other therapeutic activities. Carina allows him to divide his attention more efficiently, giving a clear signal that indicates any event requiring attention.

Finally, some suggestions are made for future improvements.