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The Antigenic Release of Histamine and SRS-A from Sheep and Calf Lungs¹

by P. Autenried² and P. Eyre³

1. Introduction

Slow-reacting substance of anaphylaxis, (SRS-A), and histamine, (HIS), possess potential biological significance not only for antigen-induced bronchoconstriction but also for other forms of IgE mediated tissue injury. SRS-A has been discovered to be released concomitant with histamine in lung effluent of sensitized guinea-pigs following challenge with specific antigen (*Kellaway and Trethewie, 1940*). Since then, SRS-A has been liberated under similar conditions from other species: in humans by *Orange et al.* (1971); in calves by *Burka and Eyre* (1974); in dogs by *Krell and Chakrin* (1978); in mice by *Murphy et al.* (1979); in rats by *Oerning et al.* (1980); and in pigs by *Paterson et al.* (1981). SRS-A contracts a limited range of isolated smooth muscle in both animals and man. Since SRS-A can cause a strong and well-maintained contraction in isolated human bronchioles (*Ghelani et al.* 1980), it is presumed to play an important role in human asthma. SRS-A offers an explanation of airway responsiveness unexplained by histamine. Human asthma has previously been described as an inappropriate recruitment of body defences (*Kay 1979*).

In calves and sheep experimental anaphylaxis has been described by *Aitken and Sanford* (1969) and *Alexander et al.* (1970). Hypersensitivity to carboxymethylcellulose as a cause of anaphylactic reactions to drugs in cattle has been reported by *Leeman et al.* (1969). Clinical allergies in cattle have been presented by *Campbell* (1970) and the whole complex of bovine hypersensitivity has been reviewed by *Black* (1979 a), *Black* (1979 b), and *Black and Burka* (1979). Not much literature could be found regarding hypersensitivity in sheep.

In the present study sheep and calves were sensitized. The severity of anaphylactic reactions were then estimated by measuring the amount of histamine and SRS-A released into the supernatant of chopped lung tissue challenged *in vitro*, with various concentrations of allergen.

¹ This material is taken from a thesis submitted by Peter Autenried to the Faculty of Graduate Studies of the University of Guelph in partial fulfillment of the requirements for the Master of Science degree.

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2. Methods

The experimental design included four *Ascaris suum* sensitized sheep, four control sheep, four horse plasma sensitized calves, and four control calves.

Sheep were sensitized with 7.5 mg aluminum potassium sulfate precipitated *Ascaris suum* protein. The antigen was injected intraperitoneally at day 0 and 28. The animals were sacrificed for the release of SRS-A and histamine at day 35. Calves were sensitized on day 0 by injecting intravenously 5 ml horse plasma and subcutaneously 5 ml horse plasma with an equal volume of Complete Freund's Adjuvant. The subcutaneous injection was repeated one week later and the animals were euthanized for the release of mediators at day 28.

Lungs were removed with minimum delay and strips were cut from the ventral margin. The floating tissue was chopped into fractions of approximately 5 mm diameter (Burka and Eyre, 1974). In order to optimize the release of SRS-A, a standard Tyrode solution was enriched with 1×10^{-2} M 1-cysteine (Orange and Chang, 1975) and with 3×10^{-6} M indomethacin (Piper et al., 1980). Replicates of lung tissue were challenged with antigen concentrations shown in Table 1. After a 20 minute incubation period supernates were collected and aliquots were frozen instantly in liquid nitrogen.

Samples were quantified by using the guinea-pig ileum assay as it is described by Stechschulte et al. (1967). Samples were measured in a systematic manner. However, isolated guinea-pig ilea only stay alive for an unpredictable length of time. It was found difficult to obtain balanced data. Linear regression, therefore, was applied for the analysis of variance.

Table 1: Allergen Concentrations used to Challenge Lung Tissue

Challenge	Dilution	HP ⁷ mg/ml ⁶	AS ⁸ mg/ml ⁶
CHL 1	∞	nil	nil
CHL 2	1:8	0.75	0.0375
CHL 3	1:4	1.5	0.075
CHL 4	1:2	3.0	0.15
CHL 5	1:1	6.0	0.3

⁶mg protein per ml incubation fluid. ⁷HP = horse plasma, starting material contains 60 mg protein per ml. ⁸AS = *Ascaris suum*-extract, starting material contains 14 mg protein per ml.

3. Results

3.1 Mediator Release in Sheep

Sensitized chopped sheep lung released 7.722 ± 606 Units SRS-A⁴ and 10.1 ± 0.4 μ g histamine per gram lung tissue at the lowest challenge concentration. At the highest challenge concentration, the same animals released 5161 ± 606 Units SRS-A and 11.0 ± 0.4 μ g histamine. Spontaneous mediator release in sensitized sheep amounted to 426 ± 601 Units SRS-A and 0.7 ± 0.4 μ g histamine per gram lung. Non-sensitized chopped sheep lung released 1706 ± 463 Units SRS-A and 2.9 ± 0.7 μ g histamine per gram lung at the lowest challenge concentration and 1483 ± 463 Units SRS-A and 3.5 ± 0.7 μ g histamine at the highest challenge concentration. Spontaneous release was negligible. As shown in Figure 1, considerably more SRS-A than histamine

⁴ One unit SRS-A is defined by Stechschulte et al. (1967) as a contraction of a guinea-pig ileum equal in amplitude to approximately 5 ng histamine base per ml organ bath.

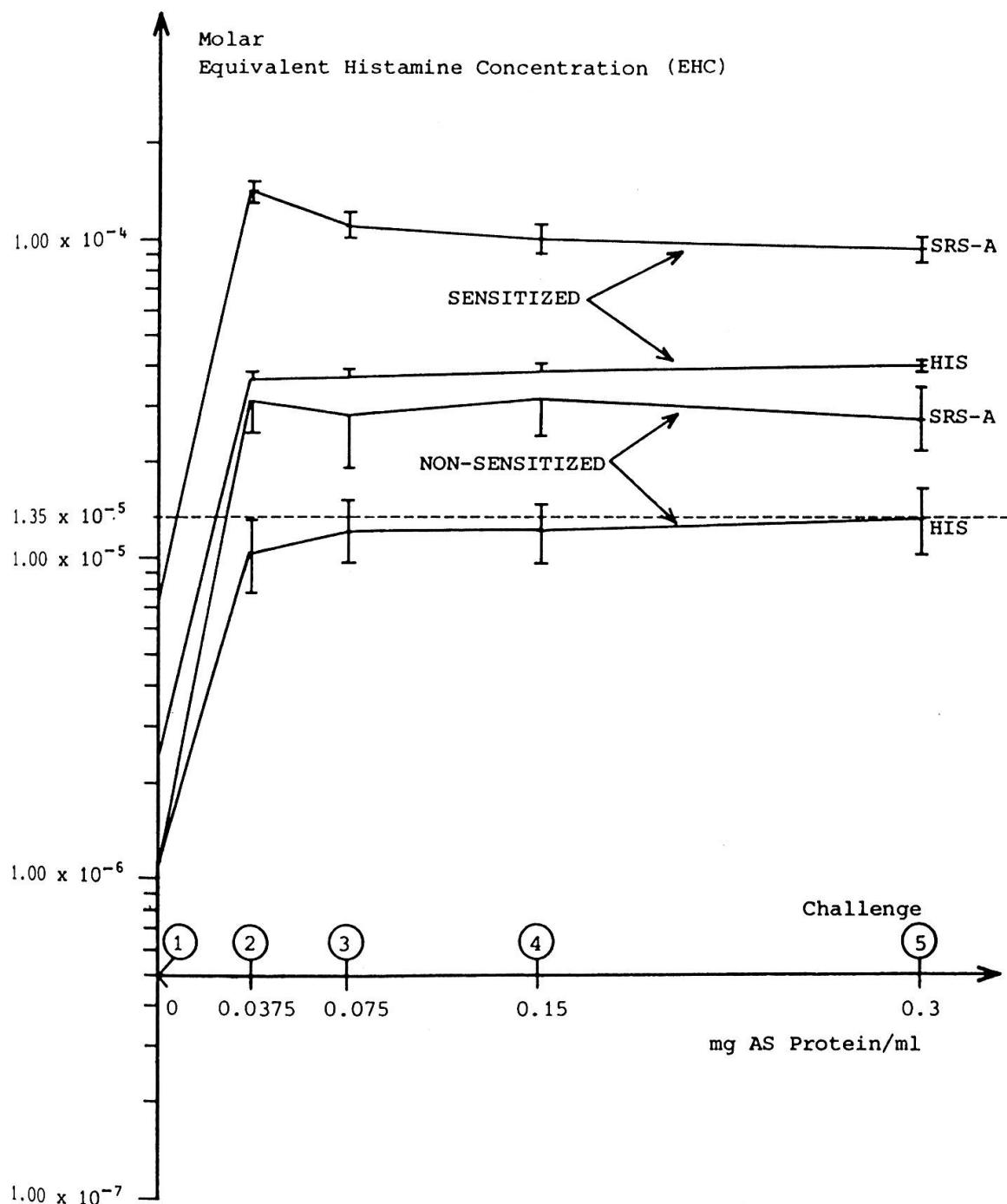


Fig. 1 The Release of Histamine and SRS-A from Sheep Lung

The effect of different challenge concentrations on the release of slow-reacting substance of anaphylaxis (SRS-A) and histamine (HIS) from chopped lungs of sensitized and non-sensitized sheep. The equivalent histamine concentrations (EHC) shown in this Figure depict the amount of histamine and SRS-A found in the incubation fluid (5 ml) of (2 g) chopped lung tissue.

Mediators were quantified by means of a guinea-pig ileum assay. The dotted line at 1.35×10^{-5} M marks the histamine standard solution used for calibrating guinea-pig ilea.

The centres of the vertical bars indicate least square means for the variable challenge. The lengths of the vertical bars indicate standard errors in a group of four ($n = 4$) sheep.

was released from sensitized animals when both mediators were expressed as equivalent histamine concentration (EHC). There was no quantitative correlation between the two mediators. The level of challenge affected the release of SRS-A and histamine to a different degree. In sensitized sheep, smaller challenge concentrations of allergen liberated significantly more SRS-A than higher allergen concentrations. The change in EHC with increasing challenge concentrations was found to be linear and the slope is positive ($p > F = 0.0007$). A trend in the opposite direction, although less pronounced, was observed for the liberation of histamine. The change in EHC with increasing challenge concentrations is also linear and a slope has also been confirmed ($p > F = 0.0013$).

3.2 Mediator Release in Calves

Sensitized chopped calf lung released 4217 ± 611 Units SRS-A and $3.4 \pm 0.2 \mu\text{g}$ histamine per gram lung tissue at the lowest challenge concentration. The same animals at the highest challenge concentration released 9667 ± 611 Units SRS-A and $4.0 \pm 0.2 \mu\text{g}$ histamine. Spontaneous release in sensitized calves was negligible. Non-sensitized chopped calf lung did not release any substantial amounts of either SRS-A or histamine. All applied levels of challenge including spontaneous release revealed no measureable amounts of both mediators. When the release profile of histamine and SRS-A was investigated in relation to different challenge concentrations (Figure 2), it was found that relatively more SRS-A was released than histamine when expressed in equivalent histamine concentrations. This finding was true for all levels of challenge. The relative difference between SRS-A and histamine in the bovine study was larger than in the ovine study. In sensitized calves lower challenge concentrations released less SRS-A than higher challenge concentrations. The change in EHC with increasing challenge concentrations is linear and the slope is positive, ($p > F = 0.0001$). The same trend was observed for the liberation of histamine. The change in EHC with increasing challenge concentrations is also linear and the slope is also positive, ($p > F = 0.0001$).

4. Discussion

4.1 Mediator Identification

Traditionally, the guinea-pig ileum has been used to detect SRS-A and histamine (Brocklehurst 1953). One might argue that substances like acetylcholine, serotonin, dopamine, kinins, and prostaglandins, all known to contract the guinea-pig ileum and all mentioned to be released in anaphylactic reactions, may make the guinea-pig ileum questionable. However, at least for SRS-A, no alternative analytical method was available, and therefore, for reasons of consistency, histamine was also measured by means of the guinea-pig ileum assay. In order to increase the specificity of the assay, selective antagonists were used. All measurements were carried out in the presence of $2.16 \times 10^{-6} \text{ M}$ atropine. When Compound FPL 55712 was added to the organ bath at a final concentration of $5.00 \times 10^{-7} \text{ M}$, contractions to crude extract were indistinguishable from standard histamine contractions. On the other hand, when Compound FPL

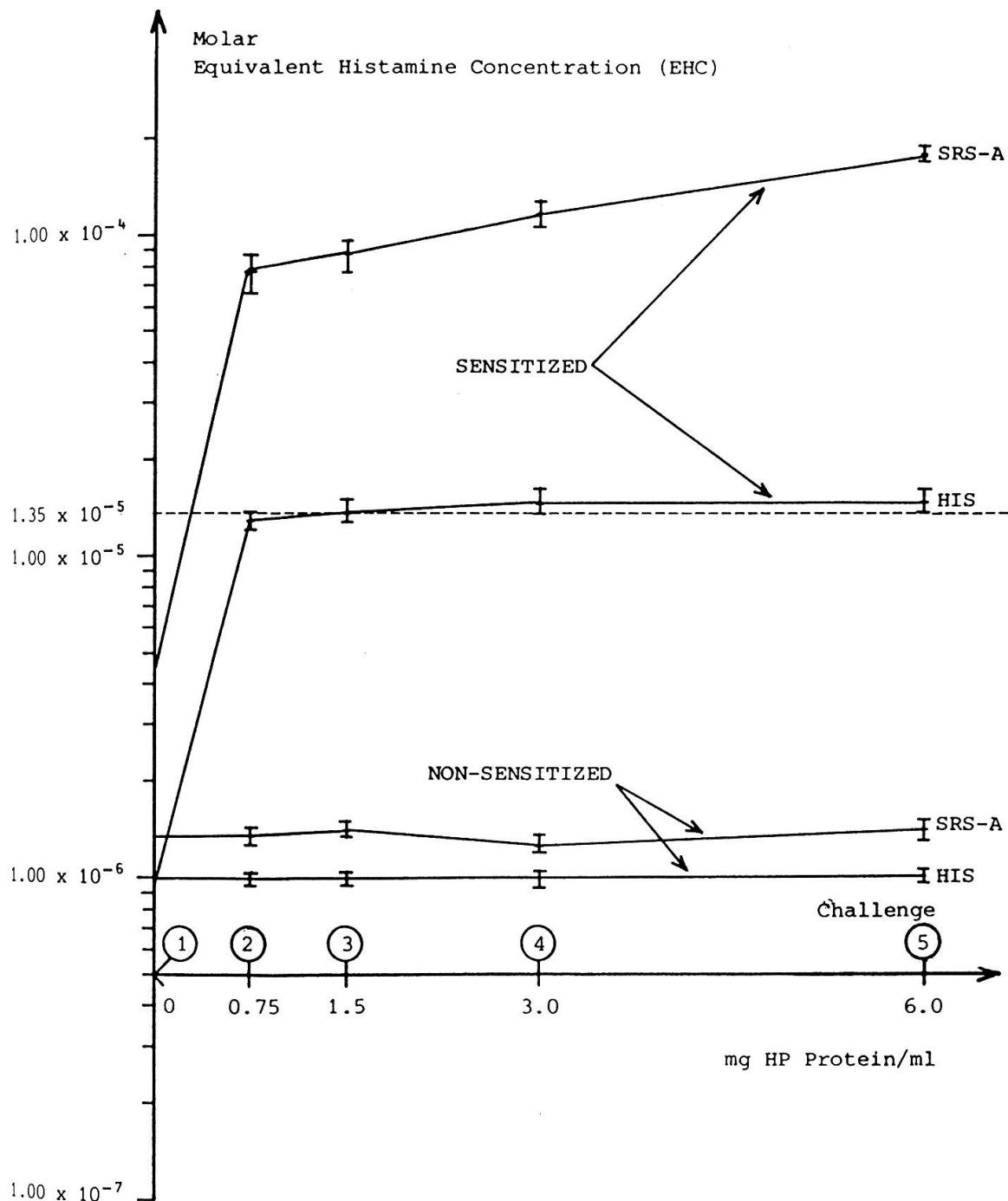


Fig. 2 The Release of Histamine and SRS-A from Calf Lung

The effect of different challenge concentrations on the release of slow-reacting substance of anaphylaxis (SRS-A) and histamine (HIS) from chopped lungs of sensitized and non-sensitized calves. The equivalent histamine concentrations (EHC) shown in this Figure depict the amount of histamine and SRS-A found in the incubation fluid (5 ml) of (2 g) chopped lung tissue.

Mediators were quantified by means of a guinea-pig ileum assay. The dotted line at 1.35×10^{-5} M marks the histamine standard solution used for calibrating guinea-pig ilea.

The centres of the vertical bars indicate least square means for the variable challenge. The lengths of the vertical bars indicate standard errors in a group of four ($n = 4$) calves.

55712 was replaced with the antihistamine tripelennamine, at a final organ bath concentration of 1.00×10^{-7} M, contractions to crude extract had the characteristic of SRS-A as it is described by *Brocklehurst* (1960). The onset of the contraction was usually delayed and the development of the contraction was prolonged. Similarly the relaxation period was extended after the organ baths were drained and refilled. The presence of atropine, tripelennamine, and Compound FPL 55712 effectively suppressed contractile guinea-pig activity to reasonably small volumes of crude extract (5–50 μ l in a 15 ml organ bath). It is possible to conclude from the above observations that: the combination of atropine and Compound FPL 55712 revealed histamine activity; the combination of atropine and tripelennamine revealed SRS-A activity; and that other substances were either absent, or if present, in concentrations not detectable by the way the guinea-pig ileum assay was performed.

Compound FPL 55712 has been described as a specific antagonist for SRS-A (*Augustein et al.* 1973). Compound FPL 55712 also antagonizes the action of leukotrienes on the guinea-pig ileum (*Parker et al.* 1980). There is plenty of evidence to show the link between SRS-A and leukotrienes (*Piper* 1981). Based on that literature and based on Compound FPL 55712 antagonism in this study, it was concluded that sheep- and calf-SRS-A is also a leukotriene, or more likely a mixture of leukotrienes. Further analytical methods would be needed to clarify this conclusion.

4.2 Quantitative Comparisons

Comparison of yields of SRS-A between different studies is difficult, not only because of the different methods applied, but also because of the cumbersome way to express SRS-A-like activity. Many workers use their own arbitrary SRS-A Units (*Fleisch and Haisch* 1980, *Hitchcock* 1980). However, some of the difficulties might be overcome in future as synthetic SRS-A, leukotrienes, will become available more easily.

Comparison of yields of histamine is also unsatisfactory, although the substance is chemically defined and commercially available. A recent quality control study by *Gleich and Hull* (1980) showed that histamine determinations carried out by different laboratories varied remarkably. In addition, many researchers studying histamine release mechanisms express their results as a percentage of total tissue histamine, posing a dilemma for direct quantitative comparisons.

In this study, the amount of SRS-A and histamine released from calf and sheep lungs is comparable to the amount of mediators released by *Brocklehurst* (1960) and *Chakravarty* (1960) from sensitized guinea-pig lungs. The amount of SRS-A released from sensitized bovine lung (e.g. 4215 Units SRS-A per gram lung for the lowest challenge concentration) is more than the quantity which *Burka* (1976) found (850 Units SRS-A per gram lung tissue), but matches closely the amount of SRS-A released from dispersed pig lungs obtained by *Paterson et al.* 1981 (4000 Units SRS-A per gram lung tissue). Histamine release from sensitized bovine lung has previously been reported by *Eyre and Deline* (1971). Their net histamine release from sensitized calf lung averaged at 0.3 μ g histamine per gram sensitized lung tissue, which is about ten times less compared to the amount of histamine released in the present bovine study.

For the first time in literature SRS-A and histamine release has been shown from sensitized sheep lungs. Difficulties were encountered in sensitizing sheep lungs. In a preliminary study (results are not shown) where horse plasma was used as allergen, neither histamine nor SRS-A could be released upon subsequent antigenic challenge. This finding is in agreement with *Eyre and Deline* (1976) who failed to show the antigenic release of histamine from sensitized sheep lung. However, when an extract of *Ascaris suum* was used as allergen, plenty of both mediators could be detected. Nonetheless, the release of SRS-A and histamine from non-sensitized control sheep is remarkable. One could argue that mediator liberation with *Ascaris suum* is a toxic rather than an immunologic phenomenon. This view is supported by *Wanner et al.* (1979) who found that virtually all of his sheep acquired for his experiments showed wheal and flare reactions upon skin injections with the *Ascaris suum* extract. Evidence in the present study suggests that mediator release was of antigenic rather than of toxic nature. Firstly, in the sheep study, the most SRS-A was released at lowest challenge concentration and not at higher concentrations which would be expected in a toxic reaction. Secondly, there was much more mediator released from lungs of sensitized sheep than of non-sensitized controls. Thirdly, in a guinea-pig study (results not shown) where *Ascaris suum* extract was also applied as allergen, no measurable mediator activity could be detected in non-sensitized animals. It is highly suggestive that guinea-pigs raised in a controlled environment had no previous contact with *Ascaris suum* or a cross-reacting allergen. Such an assumption cannot be made in regard to sheep acquired from local farmers.

4.3 Mediator Release Profiles

In this study, the release of SRS-A and histamine was compared with each other in terms of the ability to contract guinea-pig ilea. In both, sensitized sheep and calves, more SRS-A than histamine was found at all levels of challenge. Furthermore, in the sheep study, the observation was made that significantly more SRS-A was liberated at lower challenge concentrations than at higher challenge concentrations, and that less histamine was released at lower challenge concentrations than at higher challenge concentrations. For a long time it has been appreciated that surplus antigen results in suboptimal release of mediators by interfering with the required bridging of adjacent IgE molecules (*Foreman* 1980). Despite the investigated range of challenge being limited, it is interesting in the sheep study to find a decreasing SRS-A release and an increasing histamine release as challenge concentrations rose. Dissociation in the release of SRS-A and histamine has been reported previously (*Orange* 1975, *Fleisch and Haisch* 1980). However, the present study suggests that the events leading to the release of histamine and SRS-A may differ at the level of the initiating immunologic stimuli. It looks as if the balance between the state of sensitivity of the individual animal and the level of allergen exposure determines the amount of SRS-A released independently from the amount of histamine released during an anaphylactic reaction.

In calves, more SRS-A and more histamine are released as challenge concentrations increase. It is probably correct to assume that in the bovine study optimal challenge concentrations were probably still above the applied range of challenge. This finding is

particularly interesting since twenty times more protein was used to sensitize calves than was used to sensitize sheep. There are some indications about the dynamics of the Type I hypersensitivity reaction. Under natural conditions an animal would be exposed to increasing levels of a certain allergen. One might speculate that under such conditions SRS-A would be released first at an optimal rate and that histamine would play a secondary role only during prolonged antigen exposure and/or only during higher levels of an insulting allergen.

This study has confirmed that calves release SRS-A abundantly and histamine less abundantly in an *in vitro* pulmonary anaphylactic reaction. For the first time the same has been shown in sheep. It is quite clear from this study that at least in terms of SRS-A and histamine release, Type I hypersensitivity is by no means an all or none reaction. Crucial is not only the quality of the allergen (horse plasma, *Ascaris suum* extract, etc.) but also the sensitization procedure and the level of challenge. A closer look should be given to the range of challenge between lowest challenge concentration applied in this study and no challenge at all. Furthermore, the reaginic reaction, its regulation, and its integral role as a surface defence mechanism should be further investigated. It will give more insight into why sheep are less susceptible to clinical anaphylaxis as compared to calves.

Summary

Based on Coombs' and Gell's concept of Type I anaphylactic reaction, sheep and calves were sensitized to compare the ability of sensitized and non-sensitized animals to release histamine and SRS-A. Chopped lung was challenged *in vitro* with various levels of the same allergen used for sensitization. The biological activity of the supernatant was quantified using a guinea-pig ileum mounted isotonically in an isolated organ bath. Histamine and SRS-A were identified and distinguished from each other by means of specific antagonism: tripelennamine for histamine and Compound FPL 55712 for SRS-A. In both species, sheep and calves, there was more SRS-A release than histamine release when expressed as equivalent histamine concentration. The amount of mediator released depended on the challenge concentration. In sensitized calves, the higher the challenge concentration was, the higher the amount of mediators released. SRS-A release increased more over the investigated range of challenge than histamine release. In sensitized sheep, on the other hand, SRS-A release decreased with higher challenge concentrations, whereas histamine release increased slightly for the same range of challenge.

The difference in the susceptibility to clinical anaphylaxis between sheep and calves must root in the regulation of the reaginic antibody mediated response rather than in the ability of the release of mediators itself.

Zusammenfassung

Schafe wurden mit einem *Ascaris suum* Extrakt und Kälber wurden mit Pferdeplasma sensibilisiert. Gemäss der Klassifikation von Coombs und Gell (1975), wurde *in vitro* eine anaphylaktische Reaktion vom sofort-Typ eingeleitet. Es wurde untersucht, wieviel Histamin und SRS-A aus sensibilisiertem und nicht sensibilisiertem Lungengewebe freigesetzt werden konnte. Zerhackte Lunge wurde verschiedenen Allergenkonzentrationen ausgesetzt. Histamin und SRS-A wurde anschliessend als isotonische Kontraktionen an isolierten Meerschweinchen-Ilea gemessen. Beide Entzündungsmediatoren wurden mittels spezifischen Antagonisten identifiziert. Um Histamin zu blocken wurde Tripelennamin angewendet und um SRS-A zu blocken wurde die Verbindung FPL 55712 angewendet. Sowohl bei Schafen als auch bei Kälbern wurde mehr SRS-A-Aktivität gemessen als Histamin-

Aktivität. Dies bedeutet, dass entweder mehr SRS-A freigesetzt wurde, oder dass SRS-A das Meerschweinchen-Ileum potenter kontrahiert. Es wurde gezeigt, dass die Menge SRS-A oder Histamin, welche freigesetzt wird, in Abhängigkeit zur Allergenkonzentration steht. In sensibilisierten Kälbern wurde mehr Histamin und bedeutend mehr SRS-A freigesetzt, je höher die Allergenkonzentration war. In sensibilisierten Schafen wurde bei der niedrigsten Allergenkonzentration überraschenderweise am meisten SRS-A freigesetzt. In umgekehrter Weise wurde mit zunehmenden Allergenkonzentrationen geringfügig mehr Histamin freigesetzt.

Schafe im Vergleich zu Kälbern sind weniger anfällig für klinische anaphylaktische Reaktionen. In dieser Studie wurde gezeigt, dass Schafe, vorausgesetzt dass die Tiere richtig sensibilisiert werden, genauso in der Lage sind, Histamin und SRS-A freizusetzen. Es wurde gefolgert, dass die allergische Reaktion in Schafen möglicherweise besser unter Kontrolle gehalten werden kann im Vergleich zu anderen Tierarten.

Résumé

Sensibilisation de moutons avec un extrait d'ascaris suum et de veaux avec du plasma équin. Provocation in vitro d'une réaction anaphylactique de type immédiat (Classification de Coombs et Gell 1975). Recherches sur les quantités d'histamine et de SRS-A pouvant être libérées par un tissu pulmonaire sensibilisé ou non sensibilisé.

Le poumon, haché, fut soumis à des différentes concentrations d'allergènes. Mesure des quantités d'histamine et de SRS-A d'après les contractions isotoniques provoquées sur des ilea isolés de cobaye.

Identification des deux médiateurs d'inflammation à l'aide d'antagonistes spécifiques: pour bloquer l'histamine, utilisation de Tripelennamin et pour le blocage de SRS-A la liaison FLP 55712.

Aussi bien chez les moutons que chez les veaux on obtient une activité de SRS-A supérieure à celle d'histamine. Ce qui signifie, soit que SRS-A est libéré en plus hautes quantités, soit que SRS-A contracte l'ileum de cobaye de manière plus efficace.

Démonstration du fait que la quantité de SRS-A ou d'histamine libérée est en relation avec la concentration d'allergènes. Chez les veaux sensibilisés on remarque, parallèlement à l'augmentation de la concentration d'antigènes, une libération de plus d'histamine et de beaucoup plus de SRS-A.

En ce qui concerne les moutons sensibilisés c'est, fait surprenant, dans le cas de la concentration d'allergènes la plus faible que la quantité de SRS-A est la plus élevée. Au contraire libération légèrement supérieure d'histamine lors d'augmentation de la concentration d'allergènes.

Les moutons sont, comparés aux veaux, moins sujets à des réactions anaphylactiques cliniques. En conclusion, la réaction allergique chez le mouton, peut, vraisemblablement, être mieux contrôlée que chez d'autres espèces animales.

Riassunto

Pecore vennero sensibilizzate con un estratto di Ascaris suum, e vitelli con plasma di cavallo. Secondo la classificazione di Coombs e Gell (1975) venne avviata una reazione anafilattica in vitro, del tipo rapido. Venne ricercato quanta istamina e SRS-A fosse messa in libertà da tessuto polmonare sensibilizzato e non sensibilizzato. Tessuto polmonare sminuzzato venne confrontato con diverse concentrazioni di allergene. In seguito istamina e SRS-A venne misurata quale concentrazione isotonica su ilei isolati da cavie. I due mediatori flogistici vennero identificati per mezzo di antagonisti specifici. Per bloccare l'istamina venne usata tripelamina, mentre per SRS-A venne usata una combinazione FPL 55712. Sia per le pecore, sia per i vitelli venne individuata una maggiore attività SRS-A. Ciò significa che, o viene messa in libertà una quantità maggiore di SRS-A, oppure la SRS-A contrae in forma più massiccia l'ileo della cavia. Venne dimostrato che la quantità di SRS-A o di istamina che viene messa in libertà dipende dalla concentrazione dell'allergene. Nei vitelli sensibilizzati venne messa in libertà più tanto istamina e sensibilmente più SRS-A, quanto più la concentrazione di allergene era alta. In pecore sensibilizzate, nelle concentrazioni più basse di allergene, sorprendentemente venne messa in libertà una quantità maggiore di SRS-A. Al contrario, con un aumento della concentrazione di allergene, venne messa in libertà istamina in modo leggermente aumentato.

Pecore, in contrapposizione a vitelli, sono meno sensibili a reazioni anafilattiche cliniche. In questo studio venne dimostrato che pecore, presupposto che gli animali siano stati correttamente sensibilizzati, sono in grado di liberare istamina e SRS-A. Se ne deduce che la reazione allergica nelle pecore possibilmente è meglio tenibile sotto controllo di quanto avviene per altre specie animali.

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REFERAT

Möglichkeiten und Grenzen des biologischen Landbaus

Zürich (IC). – Der biologische oder alternative Landbau ist eine Bewegung, die schon vor mehr als 50 Jahren entstanden ist. Trotz ihres vielfach erhobenen Anspruches, die allein seligmachende Methode zu sein, hat sie sich nie richtig durchsetzen können: heute werden in der Schweiz um die 500 Landwirtschaftsbetriebe biologisch bewirtschaftet, das sind weniger als 1 Prozent aller Bauernhöfe.

Alternativer und konventioneller Landbau haben vieles gemeinsam, vor allem das angestrebte Ziel, nämlich die Erzeugung von gesunden Nahrungs- und Futtermitteln bei gleichzeitiger Erhaltung der Ertragsfähigkeit des Bodens. Beide berücksichtigen ökologische, ökonomische und soziale Gesichtspunkte. Beide sind Ertrags- und Gewinn-orientiert.

In jüngster Zeit ist das Interesse am alternativen Landbau, nicht zuletzt dank der starken Unterstützung durch die Massenmedien, im Zunehmen begriffen. Wachsende Bedenken werden vor allem von Nicht-Fachleuten laut gegen die angeblichen negativen Auswirkungen der intensiven Produktionsmethoden moderner Bauernbetriebe. Diese Bedenken sind oft stark gefühlsmässig und geprägt vom augenfälligen Unterschied zwischen einem rationalisierten und technisierten Landwirtschaftsbetrieb von heute und der Erinnerung an einen alten Bauernhof – das Urbild zivilisationsmüder Nostalgie nach vergangener heiler Welt.

Gibt es Qualitätsunterschiede?

Gewiss wird derjenige Landwirt, der aus weltanschaulichen Gründen den alternativen Landbau vorzieht, in der Anwendung biologischer Methoden eine qualitative Verbesserung seiner Arbeit sehen. Das ist sein subjektives Empfinden und seine private Angelegenheit. Für die Allgemeinheit interessanter ist die Frage, ob dank der biologischen Methoden eine objektiv nachweisbare Qualitätsverbesserung der Ernteerzeugnisse bewirkt werden kann. Die Antwort ist nein – es gibt keinerlei Beweise für den qualitativen Vorteil alternativer Produkte, weder im Nährwert noch im Geschmack. Die in der öffentlichen Diskussion so hochgespielten Schadstoffe und Rückstände in Nahrungsmitteln spielen in Wirklichkeit kaum eine Rolle – eine gesundheitliche Schädigung von Menschen durch