Cow - Calf /Feedlot Split Session II

Dr. Larry Rice, *presiding*

A Review of Bovine Respiratory Disease*

Robert A. Smith, *D.V.M., M.S.*
Department of Medicine and Surgery
College of Veterinary Medicine
Oklahoma State University
Stillwater, Oklahoma 74078

A Critical Evaluation of Preconditioning

Preconditioning (PC) is a management system designed to immunize calves and reduce stressors prior to shipment to a stocker or feeder operation. Although the program varies somewhat from state to state, calves are weaned, castrated, dehorned, vaccinated, treated for parasites, trained to eat, and identified three to four weeks prior to sale or shipment. One must be cautious that preconditioning programs are not confused with backgrounding. Preconditioning refers to a management procedure on the farm of origin while backgrounding is done by assembling calves from various sources rather than a single cow-calf operation. The term preweaning (PW) refers to calves which are weaned and fed as in preconditioning but vaccination and treatments for parasitism are not done.

Testimonials and uncontrolled surveys have suggested that preconditioning of feeder calves will do the following:

1. Increase on-farm weight gain.
2. Reduce market-transit shrink.
3. Improve feedlot performance.
4. Reduce feedlot morbidity and mortality.
5. Increase profits for producer and feeder.

Controlled studies of the effect of PC or PW are rather limited and have been reviewed by Cole (1983).

Farm Weight Gain and Market Transit Shrink: When considering the effect of PW and feeding on calf weight gains, PW calves gained about the same weight as calves left with their dams with a range of 5 kg more to 8 kg less than unweaned controls. When comparing weight gains of PW calves with unweaned calves left with their dams, PW calves required about 52 kg of feed dry matter for each kg increase in weight gain over unweaned calves (Table 1).

When unweaned control calves and PW calves were subjected to the same marketing channels, weight losses were similar (Table 2). Other trials indicated that PW calves consume more feed at the orderbuyer facility than freshly weaned calves and lose less weight during marketing. During transit, however, PW calves lose more weight.

Feedlot Performance and Health: Early in the feeding period PW calves consumed more feed and gained more weight than controls, but by 100 days control and PW calves have similar average daily gains. Similarly PW calves lost the advantage of improved feed efficiency when on feed for greater than 100 days (Table 3).

In the seven trials reviewed, preconditioning reduced feedlot morbidity about 6 percentage units or about 23% compared to controls (Table 4). Preconditioning reduced feedlot mortality about 0.7 percentage units. It should be noted that when calves are preconditioned the cow-calf producer will have more health problems than when handling them in the conventional manner (Table 5).

Economics: A list of costs to precondition a calf is presented in Table 6. Of the total cost of $38.76, 50% is feed and 20% is labor. If the producer weans his calves early he will require a bonus price of $9.69/cwt to break even. If he holds his calves an extra 28 days (18 kg heavier calf) he will need a bonus price of $2.51/cwt to break even (Table 7).

Since PC would reduce feed and medicine costs only minimally and the higher purchase price and increased interest cost would increase the investment in the calf, a higher selling price for both stockers and feeders would be required to break even (Tables 8, 9).

In conclusion, PW or PC calves have shown no distinct advantage over controls when considering on-farm gains, market-transit shrink, ADG, feed efficiency or economics. PW and PC calves did, however, have slightly lowered morbidity and mortality rates.

**A review of selected papers presented at the North American Symposium on Bovine Respiratory Disease, Amarillo, Texas, September 7-9, 1983. Much of the information here is abstracted directly from the proceedings. The reader is invited to consult the references listed at the end of this paper for further information.*

TABLE 1. Feed/Gain of Preweaned Calves at Farm of Origin.

Reference	Total		Extra[a]	
	Gain, kg	Feed/Gain	Gain, kg	Feed/Gain
Wieringa et al., 1974*	10	11.4	—3	—
Pate and Crockett, 1978*	10	11.6	0	—
Cole et al., 1979	20	6.8	5	27.2
Cole et al., 1982	34	3.5	5	23.6
Hutcheson et al., unpublished*	17	8.0	3	45.7
Five Trial average	18.2	8.26	2.4	51.7

[a] Increase in gain over calves left with their dams.
* Totally preconditioned. References without asterisk are preweaned only. Cole, 1983

TABLE 2. Effects of Preweaning or Preconditioning on Market-Transit Weight Losses.

Reference	Hr. in transit	Weight loss			
		Control		Treated	
		kg	%	kg	%
Knight et al., 1972*	3[a]	—	5.7	—	4.4
Wieringa et al., 1976*	128[b]	24	11.4	24	11.4
Pate and Crockett, 1978*	30	21	10.0	28	12.4
Pate and Crockett, 1978*	3	6	2.7	12	5.4
Cole et al., 1979	26	23	10.8	25	11.4
Cole et al., 1982	26	29	13.0	27	12.5
Cole et al., unpublished	26	32	14.3	29	13.7
Strohbehn et al., 1981*	3[a]	7	2.9	8	3.3
Hutcheson et al., unpublished*	28	—	6.7	—	6.2
7 or 9 Trial Average		20	8.6	22	9.0

[a] Estimated from length of haul.
[b] Calves were fed and watered 3 times while in transit.
* Totally preconditioned. References without asterisk are preweaned only.
Cole, 1983

Feedlot Health Management

Information presented in this section represents management procedures used in a commercial feed yard. Procedures are based on the results it has provided but controlled studies have not been done.

Newly arrived cattle are processed within 24 hours. Processing includes:

1. IBR/BVD/PI_3/Lepto-P.
2. Clostridial bacterin.
3. Levasole® injectable dewormer.
4. Ralgro implant.
5. Dipped in GX-118®.
6. Eartagged.

Long stem hay is provided on arrival and Purina Receiving Chow® is fed twice daily until calves are consuming 3% of their body weight. Cattle are checked twice daily for 30 days and sick cattle are placed in hospital pens for the treatment period.

Antibiotics used, in order of preference, are oxytetracycline, erythromycin, sulfadimethoxine, penicillin and tylan.

TABLE 3. Influence of Preweaning or Preconditioning on Feedlot Performance.

Reference	Days fed	Daily gain, kg		F/G[a]	
		C[b]	T[b]	C[b]	T[b]
Meyer et al., 1971*	252	.97	.97	7.85	8.00
Knight et al., 1972*	204	1.15	1.15	—	—
Woods et all., 1973*[b]	130	.50	.54	—	—
McArthur, 1973	210	1.09	1.12	—	—
Wieringa et al., 1974*	30	.98	.95	—	—
Pate and Crockett, 1978*	200	.92	.97	8.31	8.34
Cole et al., 1979	211	1.15	1.10	5.89	6.40
Cole et al., 1982	186	.98	.97	8.10	8.50
Cole et al., unpublished	184	1.10	1.10	6.90	7.50
Strohbehn, 1981*	90	.94	1.00	8.94	8.68
Hutcheson et al., unpublished*	56	1.13	1.22	6.80	6.50
7-11 Trial Average		.99	1.01	7.54	7.70
Less than 100 days		.89	1.00	7.87	7.59
More than 100 days		.98	.99	7.41	7.75
Preconditioned*		.94	.97	7.98	7.88
Preweaned		1.08	1.07	6.96	7.47

[a] kg of feed dry matter per kg weight gain.
[b] C = control, T = preweaned or preconditioned.
* Totally preconditioned. References without asterisk are preweaned only.
Cole, 1983

TABLE 4. Influence of Preweaning or Preconditioning on Feedlot Morbidity (%).

Reference	Control	Treated
Knight et al., 1972[a]*	16.4	20.2
Knight et al., 1972[b]*	16.4	9.6
Woods et al., 1973[a]*	23.8	21.5
Woods et al., 1973[b]*	73.0	63.0
Wieringa et al., 1976*	12.0	4.0
Pate and Crockett, 1978*	23.0	7.0
Cole et al., 1979	53.3	51.1
Cole et al., 1982	53.7	51.6
Cole et al., unpulished	51.1	28.9
Hutcheson et al., unpublished*	20.9	17.2
Stronbehn, 1981*	NR[c]	NR
10 Trial Average	34.4	27.4 (—20%)
Preconditioned (7)*	26.5	20.4 (—23%)
Preweaned (3)	52.7	43.9 (—17%)

[a] Vaccinated at weaning.
[b] Vaccinated 30 days before weaning.
[c] Not reported but no difference between controls and preconditioned calves (Strohbehn, personal communication).
* Totally preconditioned. References without asterisk are preweaned only.
Cole, 1983

Antihistamines are administered the first two to three days. Antibiotics are changed if no favorable response is noted.

The general appearance of cattle in the pen, per morbidity and feed consumption is closely monitored. If one or more of these criteria become unacceptable, the entire pen is returned to the processing area and medicated. One of the following mass medication is administered:

1. LA 200®.
2. Benzathine penicillin G procaine in aqueous solution.

3. IM IBR vaccine and one of the above antibiotics.
4. Levasole® injectable and one of the above antibiotics.

The regimen selected depends on recorded temperatures and responses to antibiotics in the hospital pens. High temperatures dictate IM IBR vaccine and an antibiotic. Temperatures of 103-105°F along with poor appearance and/or poor feed consumption dictates Levasole® injectable and an antibiotic.

The observations and responses of six pens of cattle are summarized in Graphs I–VI. The author indicated that the use of a 50% dose of Levasole® (Graph V) did not give as dramatic a response as the full dose normally did.

TABLE 5. Influence of Preweaning or Preconditioning on Calf Mortality (%).

		Preweaned/preconditioned		
Reference	Control	Farm	Feedlot	Total
Knight et al., 1972[a]*	2.5	—	0.0	0.0
Knight et al., 1972[b]*	2.5	—	1.9	1.9
Woods et al., 1973[a]*	1.4	—	0.8	0.8
Woods et al., 1973[b]*	0.0	—	1.3	1.3
Wieringa et al., 1976*	0.0	—	0.0	0.0
Pate and Crockett, 1978*	2.5	1.0[c]	0.0	1.0
Cole et al., 1979	3.3	0.0	2.2	2.2
Cole et al., 1982	1.1	0.0	1.1	1.1
Cole et al., unpublished	0.0	0.0	0.0	0.0
Strohbehn, 1981*	NR[d]	1.9[c]	NR[d]	NR
Hutcheson et al., unpublished*	1.2	0.0	1.2	1.2
Trial Average	1.45	(0.26)	0.85	0.95
Preconditioned	1.44	(0.36)	0.74	0.88
Preweaned	1.47	0.0	1.10	1.10

[a] Vaccinated 30 days before weaning.
[b] Vaccinated at weaning.
[c] Deaths due to bloat, acidosis, or surgical infection.
[d] Not reported, but no difference between controls and preconditioned calves (Strohbehn, personal communication).
* Totally preconditioned. References without asterisks are preweaned only.
Cole, 1983

Physiology of the Bovine Lung

Anatomy: For its size, the cow has a small lung, yet its resting oxygen consumption and alveolar surface area are similar to mammals of equal size. In order to obtain an adequate surface area for gas exchange in a small lung, cattle have relatively small diameter alveoli. The alveoli have few communications with neighboring alveoli. There is a paucity of interalveolar pores of Kohn and interlobular septa completely subdivide the lung into secondary lobules.

The bronchial anatomy and lobulation of cattle lungs is different from many other species. Like other species, cattle have four lobes (cranial, middle, caudal, and accessory) on the right side, and two lobes (cranial and caudal) on the left side. Because of the location of the bronchial opening of the right cranial lobe, there may be drainage of secretions into the bronchus tending to make the right cranial lobe

TABLE 6. Estimated Cost to Precondition a Calf for 30 Days Excluding Facility Costs.

Item	Amt/Head	$/Unit	$/Head
Feed	127 kg	0.165 ($150/ton)	20.96
Vaccines	—	—	3.00
Wormer	1 dose	1.20	1.20
Grubacide	1 dose	0.50	0.50
Labor	2 hr[a]	4.00	8.00
Veterinarian	.05 hr[a]	50.00	2.50
Antibiotic	10%	10.00/head	1.00
Death loss	0.4%	70.00/cwt.	1.12
Interest	15%	—	.48
			38.76

[a] Meyer et al., 1971. Cole, 1983

TABLE 7. Economics of Preconditioning Calves: Cow-Calf Producer.

		Value or cost, $	
Item	Unit price, $	Early weaned	Normally weaned
Calf, 182 kg	1.54	280.28	280.28
Preconditioning	—	38.76	38.76
Total cost, $	—	319.04	319.04
Sold: 182 kg calf	1.54	280.28	—
Sold: 200 kg calf[a]	1.54	—	308.00
Difference[b], $	—	38.76	11.04
Bonus $/kg[b]	—	0.213	0.055
($/cwt)[b]	—	(9.69)	(2.51)

[a] Gain of 18 kg over 28 days (Table 2).
[b] Bonus required for cow-calf producer to break-even financially.
Cole, 1983

TABLE 8. Economics to the Feeder of Feeding Preconditioned Calves to 500 kg[ab].

	Normal	Preconditioned	
Item	182 kg	182 kg	200 kg
Calf cost	280.28	280.28	308.00
Bonus paid	0.00	38.76	11.04
Subtotal, $	280.28	319.04	319.04
Feed cost	418.71	413.46	390.06
Medicine	3.98	3.06	3.06
Death loss	4.06	2.73	2.73
Interest	63.65	68.56	67.04
Subtotal, $	490.40	487.81	462.89
Total costs, $	770.68	806.85	781.93
Increase over controls, $	—	36.17	11.25

[a] Cost figure: calf-$1.54/kg ($70/cwt); feed-$0.165/kg $150/ton); medicine-$15/head treated; interest-15% on 100% of cattle and 50% of feed.
[b] Control calves: daily gain = 0.94 kg; F/G = 7.98; morbidity = 26.5%; mortality = 1.44%. Preconditioned calves: daily gain = 0.97 kg; F/G = 7.88; morbidity = 20.4%; mortality = 0.74%.
Cole, 1983

TABLE 9. Economics of Using Preconditioned Calves in a 120-Day Stocker Program.

Item	Normal 182 kg	Preconditioned 182 kg	Preconditioned 200 kg
Calf cost	280.28	280.28	308.00
Bonus	0.00	38.76	11.04
Subtotal, $	280.28	319.04	319.04
Pasture	40.00	40.00	40.00
Medicine	3.98	3.06	3.06
Death loss	4.06	2.73	2.73
Interest	15.02	16.93	16.93
Supplement	12.00	12.00	12.00
Subtotal, $	75.06	74.72	74.72
Total cost, $	355.34	393.76	393.76
Final wt, kg[a](lb.)	295 (649)	302 (664)	320 (704)
Break-even price: $/kg[b]	1.20	1.30	1.23
($/cwt)	(54.75)	(59.27)	(55.93)
Increase over controls:			
($/cwt)		4.52	1.18
Total, $		30.01	8.31

[a] Daily gains of .94 and 1.0 kg for normal and preconditioned calves, respectively.

[b] Price required by stocker to break-even.

Cole, 1983

susceptible to infections.

Cattle have relatively muscular pulmonary arteries which is thought to contribute to vascular hyperreactivity that is not as dramatic in other species. The vigorous response to hypoxia, for example, leads to pulmonary hypertension and right heart failure in cattle pastured at high altitudes and hypoxia may also be the cause of very high pulmonary arterial pressures observed in calves with chronic lung disease.

Physiology: The major function, gas exchange, is accomplished by bringing air and blood together in the peripheral gas exchange portion of the lung. Delivery of air depends on the respiratory muscles generating sufficient force to overcome both the elastic recoil of the lung and the frictional resistance of the airways. The elastic properties of the lungs are reflected in measurements of lung compliance while the resistive properties of airways are indicated by measurements of pulmonary resistance. Lung diseases generally decrease compliance and/or increase resistance, both of which increase the work of breathing and require additional energy use by respiratory muscles.

Delivery of blood to the lung is determined by the work of the heart and the flow resistance of pulmonary vessels. Because the total cardiac output passes through the lungs, constriction of pulmonary vessels by hypoxia, for example, increases the work of the right heart and elevates pulmonary arterial pressure. Hypoxemia occurs when regions of lung receive blood flow but too little ventilation as a result of atelectasis, consolidation or airway obstruction.

Ventilation: The maximal oxygen consumption which can be achieved by cattle during exercise is less than one-third of that which can be achieved by a horse of similar size. The cow reaches maximal oxygen consumption at a speed of 4 m/sec whereas a horse must go 10 m/sec. This limited maximal oxygen consumption which is reflected in the relatively small alveolar surface area available for diffusion means that cattle must utilize anaerobic metabolism with its resultant metabolic acidosis when herded or when severely stressed. Metabolic acidosis has been reported to suppress bacterial clearance from the lung.

Of the total ventilation entering the lung only part participates in gas exchange (alveolar ventilation). The remainder ventilates dead space, i.e. the trachea and bronchi or poorly perfused regions of the lung. In calves, 42% of the minute ventilation is dead space ventilation. Dead space ventilation increases with age and by 10½ months accounts for 68.5% of minute ventilation. Heat stress increases minute ventilation but 79% is dead space ventilation because cattle begin to pant. Cold stress increases metabolic rate with a resulting increase in oxygen requirements. This is met by an increase in alveolar ventilation accomplished by increasing tidal volume and decreasing both respiratory rate and dead space ventilation.

Mechanics of Ventilation: The calf is like other neonates in that it has a compliant thorax and a lung with a relatively low compliance. The low lung compliance is probably due to closure of peripheral airways at relatively high lung volumes. If airways close during tidal breathing ventilation perfusion mismatching occurs and hypoxemia can result. Another potential consequence of airway closure is atelectasis distal to the point of closure. The compliant thorax of the calf may facilitate the development of atelectasis by failing to support underlying lung tissue which is beginning to collapse.

Matching of Ventilation and Blood Flow: During respiratory disease, atelectasis, consolidation and airway obstruction result in regions of lung which are poorly ventilated but continue to receive blood flow.

Lungs possess several mechanisms to match ventilation and blood flow. These mechanisms include 1) collateral ventilation between adjacent regions of lung, 2) interdependence between adjacent regions of lung, 3) hypoxic constriction of pulmonary arteries and 4) hypocapnic constriction of airways.

The complete separation of secondary lobules by loose connective tissue prevents collateral ventilation in cattle. Following obstruction of an airway, there are no alternate pathways available for ventilation of the obstructed regions. Since air cannot enter the obstructed region, coughing is ineffectual in removing any mucus which may be causing the obstruction. Alveoli distal to the obstruction become hypoxemic and atelectasis develops. Hypoxia suppresses macrophage function which may allow infections to persist.

It is well accepted that the extensive interlobular connective tissue of cattle and pig lungs results in almost no interdependence between adjacent lobules in excised lungs at low lung volumes. With the thorax intact, interdependence between adjacent regions of lung is increased but there

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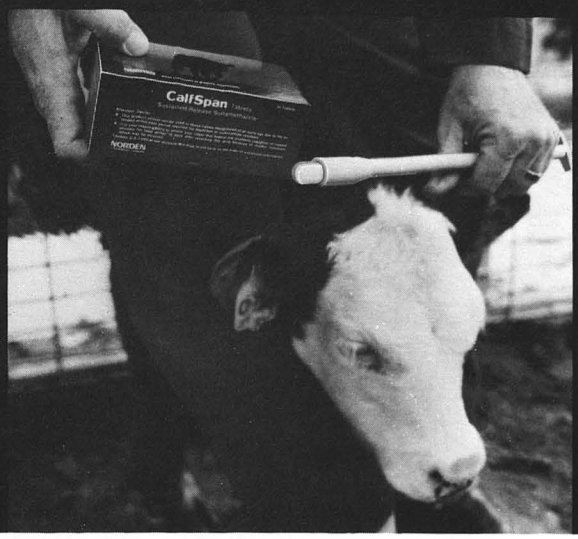

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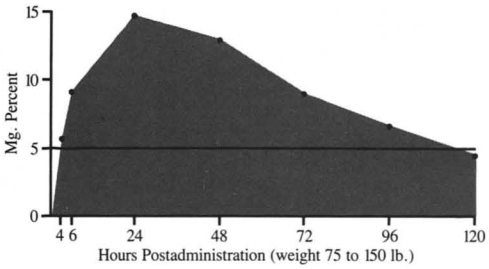
Summary of sulfamethazine plasma levels for all experiments in which calves were dosed with a minimum of 160 mg/lb and a maximum of 200 mg/lb sulfamethazine as 'CalfSpan'



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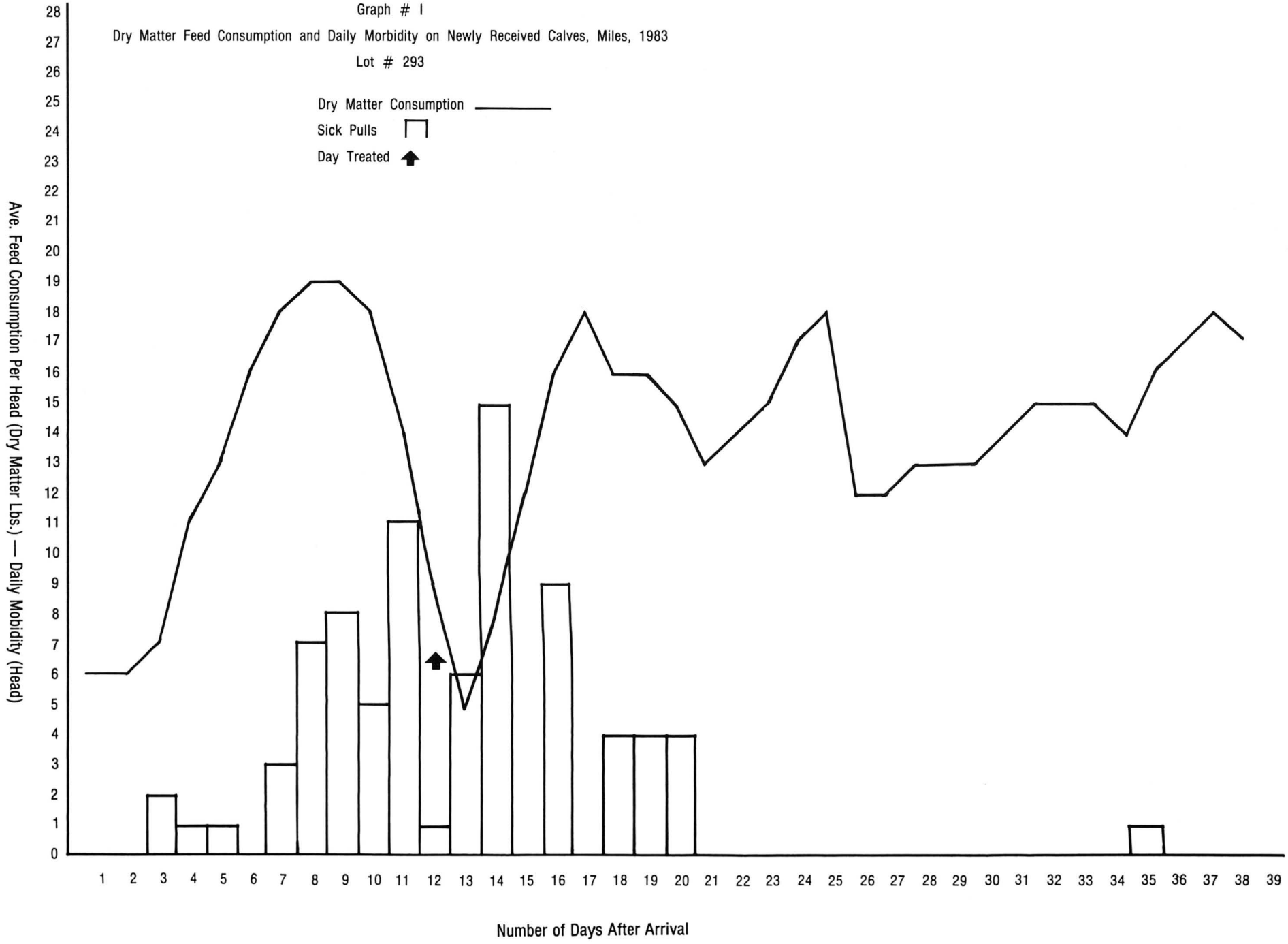
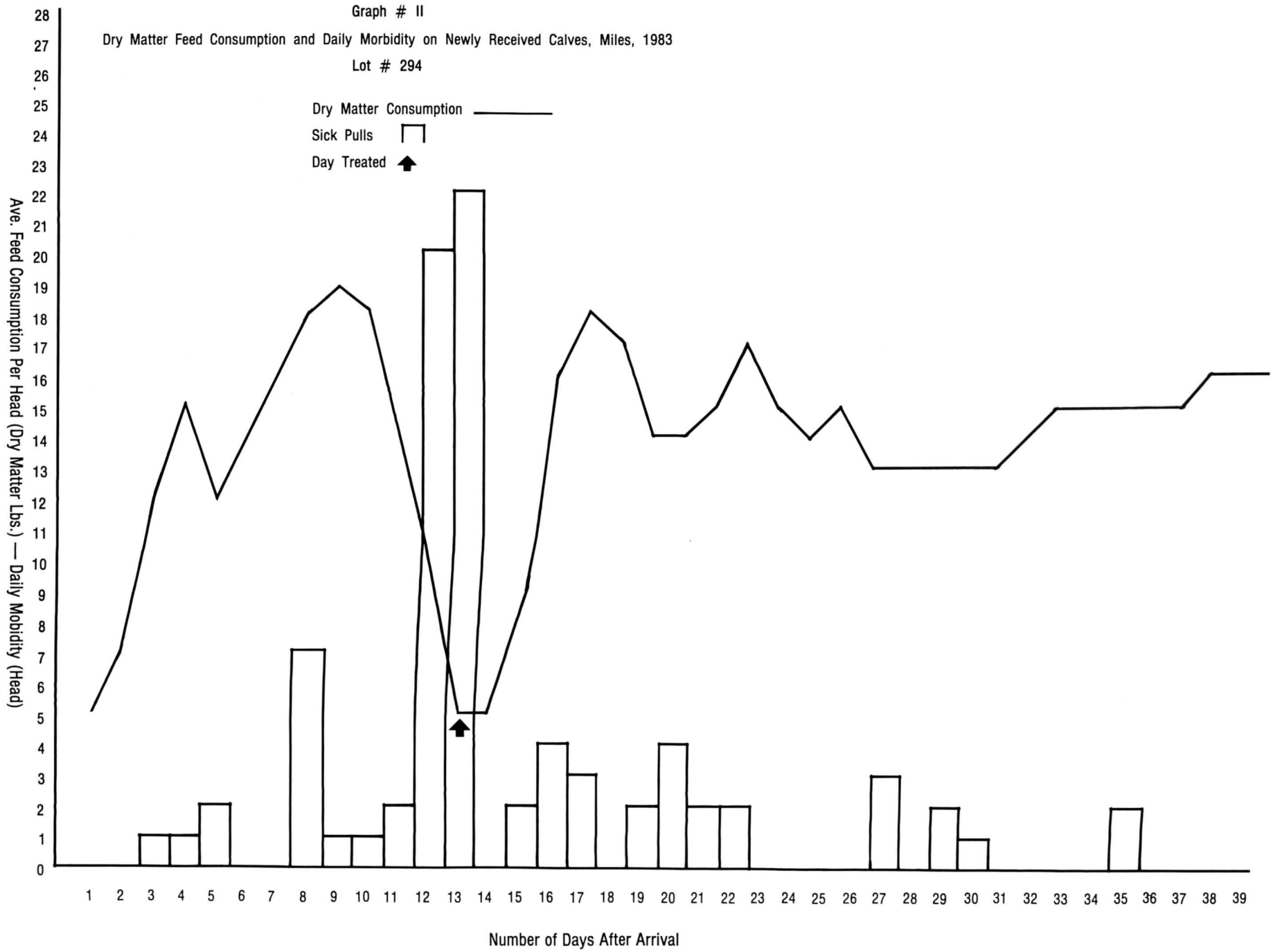
Graph # 1

Dry Matter Feed Consumption and Daily Morbidity on Newly Received Calves, Miles, 1983

Lot # 293





Graph # III

Dry Matter Feed Consumption and Daily Morbidity on Newly Received Calves, Miles, 1983

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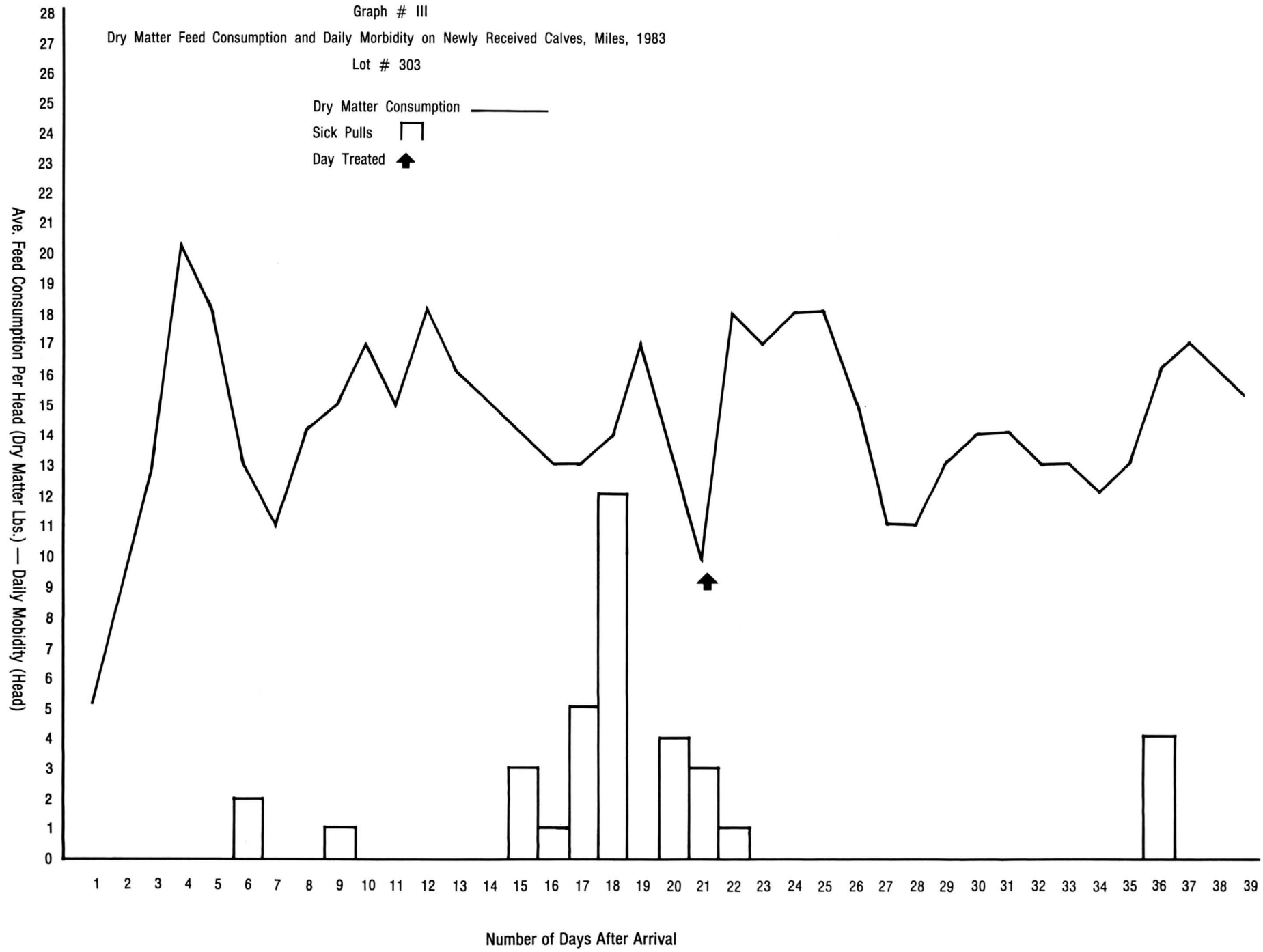
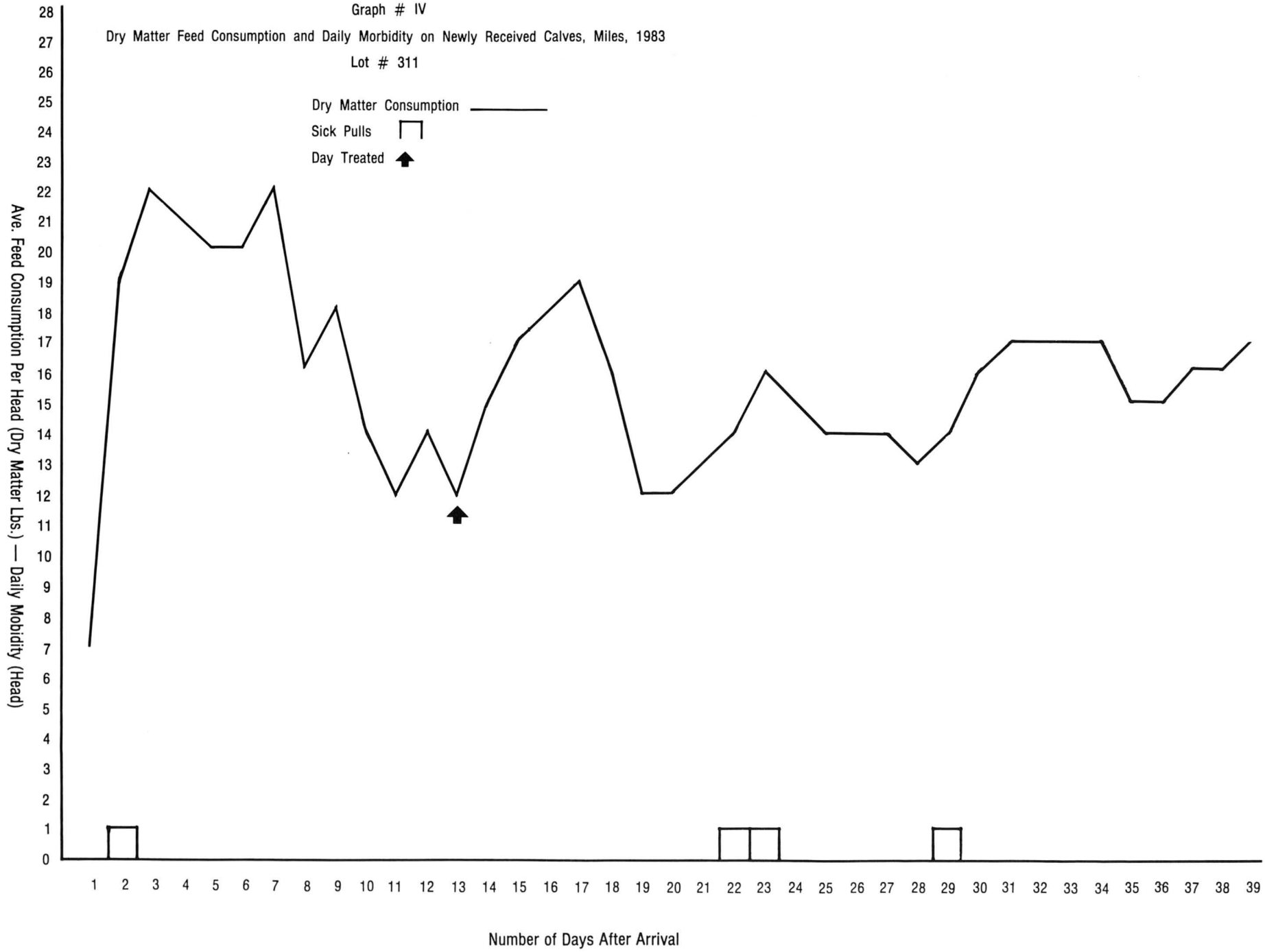
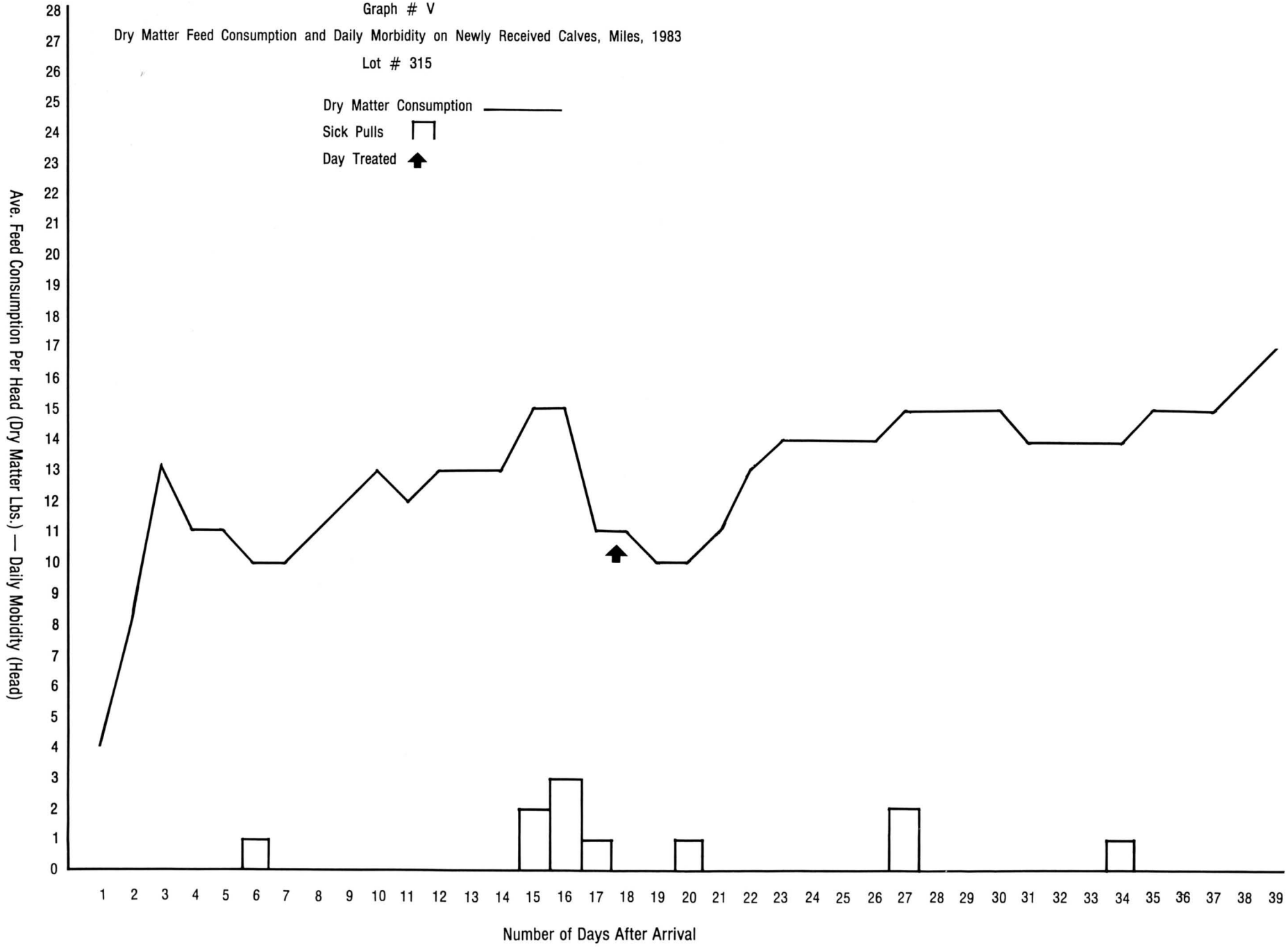




Graph # V

Dry Matter Feed Consumption and Daily Morbidity on Newly Received Calves, Miles, 1983

Lot # 315



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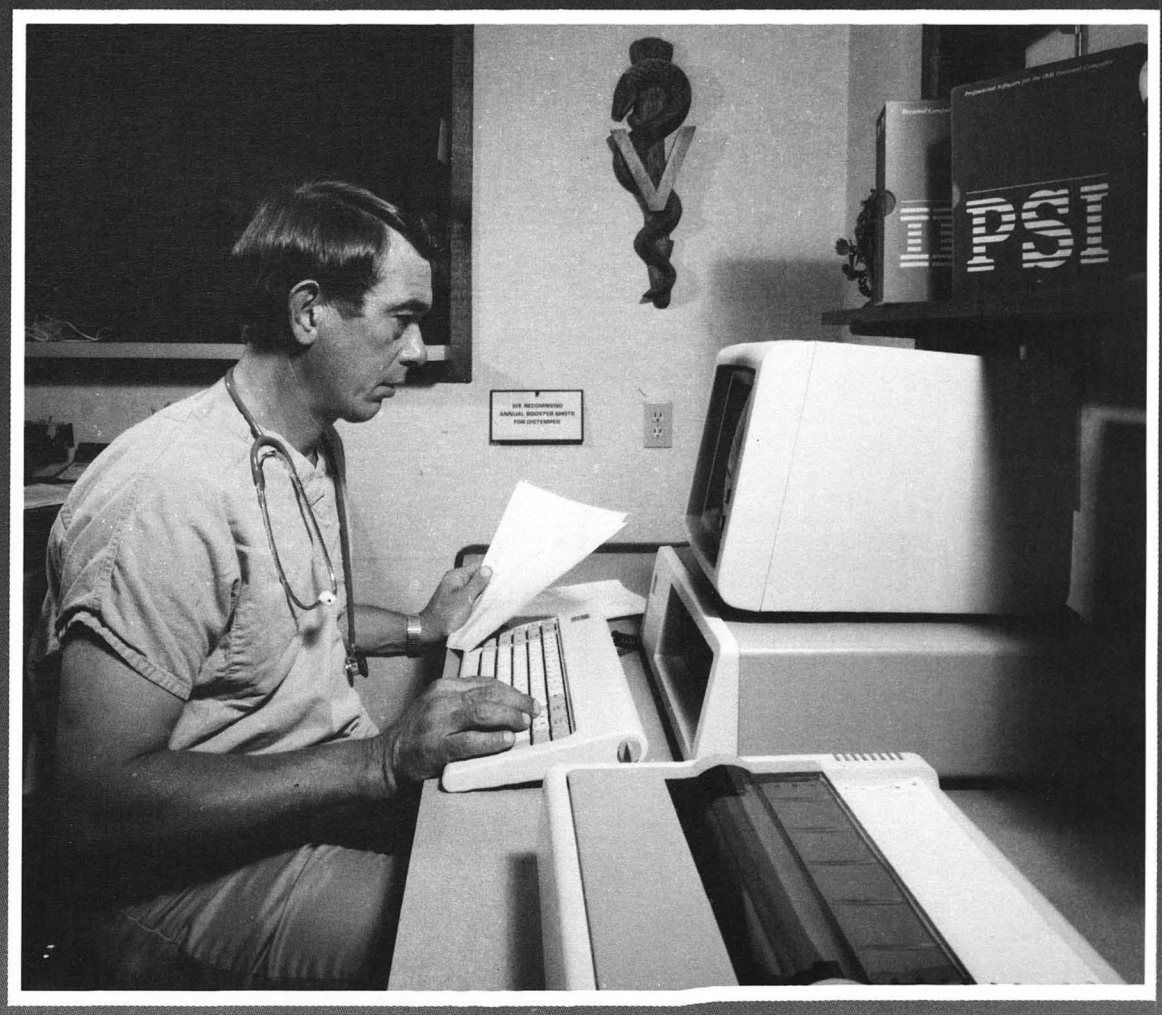

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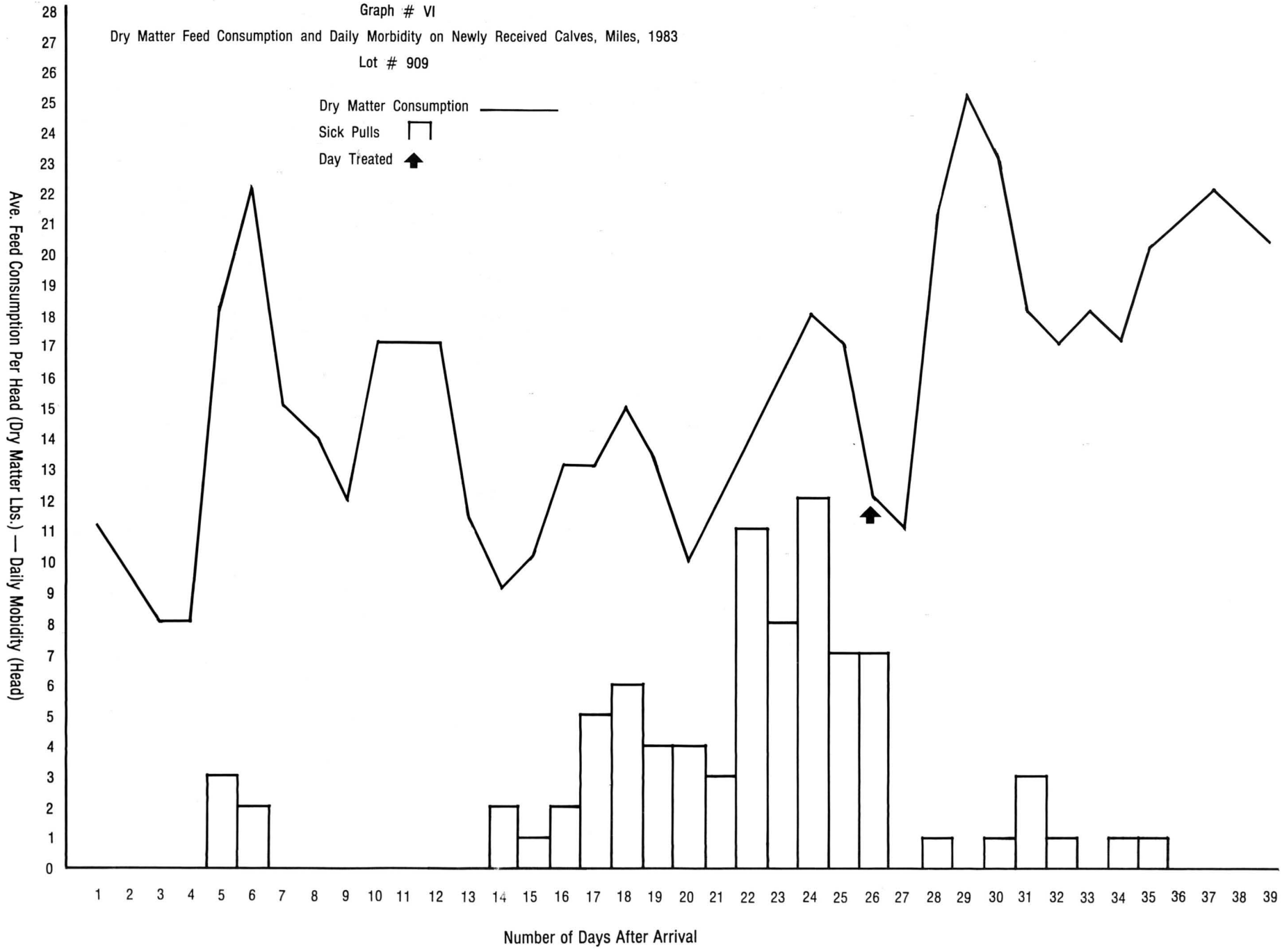
Graph # VI

Dry Matter Feed Consumption and Daily Morbidity on Newly Received Calves, Miles, 1983

Lot # 909



is still less interdependence in lobulated than nonlobulated lungs (e.g. dog). This limited interdependence of cattle lungs may be another factor making cattle susceptible to atelectasis and regional alveolar hypoxia following airway obstruction. It should be noted that lung thorax interdependence cannot restore ventilation to a region of cattle lung supplied by a completely obstructed airway because cattle lack interlobular collateral pathways. Lung thorax interdependence can only attempt to maintain ventilation in the face of incomplete airway obstruction.

Because of the lack of collateral ventilation, regions of lung supplied by obstructed airways cannot function as gas exchangers. It is therefore appropriate to reduce the blood flow to these regions and redirect blood to the better ventilated regions of lung. The pulmonary arteries of cattle constrict vigorously in response to hypoxia and this may facilitate the redirection of blood flow away from poorly ventilated regions. The adequacy of this mechanism in maintaining normal ventilation/perfusion does not appear to be very good. In acute pneumonia and allergic lung disease the hypoxic constrictor response appears to be overridden probably by mediators of inflammation. Blood flow to diseased portions of lung is not reduced and hypoxemia results.

Distribution of Lesions of Pneumonia: It is generally thought that the preferential distribution of pneumonic lesions in the anteroventral regions of the lung is because the orientation of these regions in the gravitational field results in fluid accumulation. Other possible causes include 1) limited defence mechanisms in these regions, 2) regional variations in mechanics of ventilation which cause preferential inhalation of microorganisms and 3) regional differences in interdependence. A further review of the literature has failed to prove these causes. It is still possible that the typical distribution of pneumonic lesions results from regional mechanical factors and not just because fluids run downhill.

Lung Function in Infectious Bovine Respiratory Disease: Infectious bovine rhinotracheitis (IBR) produced changes in respiratory function compatible with obstruction of the upper airway and trachea. Pulmonary resistance is determined to a large extent by the resistance of the upper airway, trachea, and bronchi. An increase in pulmonary resistance can be caused either by obstruction of these large airways or by diffuse obstruction of peripheral airways. In the case of airway obstruction distal to the carina, an increase in pulmonary resistance is usually accompanied by a decrease in dynamic compliance because the obstruction causes inequalities in regional time constants. Calves infected with IBR had no change in dynamic compliance suggesting airway obstruction was restricted to the upper airway and trachea.

In contrast to IBR, which presents functionally as an obstruction of large airways, pasteurellosis is a disease of lung parenchyma. Following intratrachael inoculation of *Pasteurella hemolytica,* PaO_2 decreased significantly by 2 hours. The decrease was not due to alveolar hypoventilation because $PaCO_2$ remained constant but was the result of an increased alveolar-arterial oxygen difference indicating ventilation perfusion mismatching. Over the next ten hours, hypoxemia became more severe. Further evidence of damage to the lung parenchyma was a decrease in dynamic compliance occurring three to six hours after inoculation. This decrease in compliance was unaccompanied by an increase in pulmonary resistance and therefore indicates either stiffening of the lung by exudates, edema, or fibrosis or diffuse obstruction of peripheral airways. Twleve hours after inoculation there was an increase in pulmonary resistance which resulted in hypoventilation (increased $PaCO_2$).

The sequence of functional changes following Pasteurella challenge i.e. hypoxemia, decreased compliance, increased resistance and hypoventilation is compatible with a disease process beginning in the lung parenchyma and extending into the peripheral airways. This was confirmed at necropsy when disease was limited to alveoli and bronchioles.

One of the interesting observations in both IBR and Pasteurella infected calves was tachypnea which developed one hour after inoculation with Pasteurella and was present three to four days after IBR inoculation. Tachypnea was not in response to hypoxemia or hypercapnia because blood gas tenions were not abnormal when tachypnea occurred. Perhaps infectious agents also stimulate intrapulmonary receptors either directly or by modifying their response to other stimuli such as stretching, edema accumulation or chemical mediators.

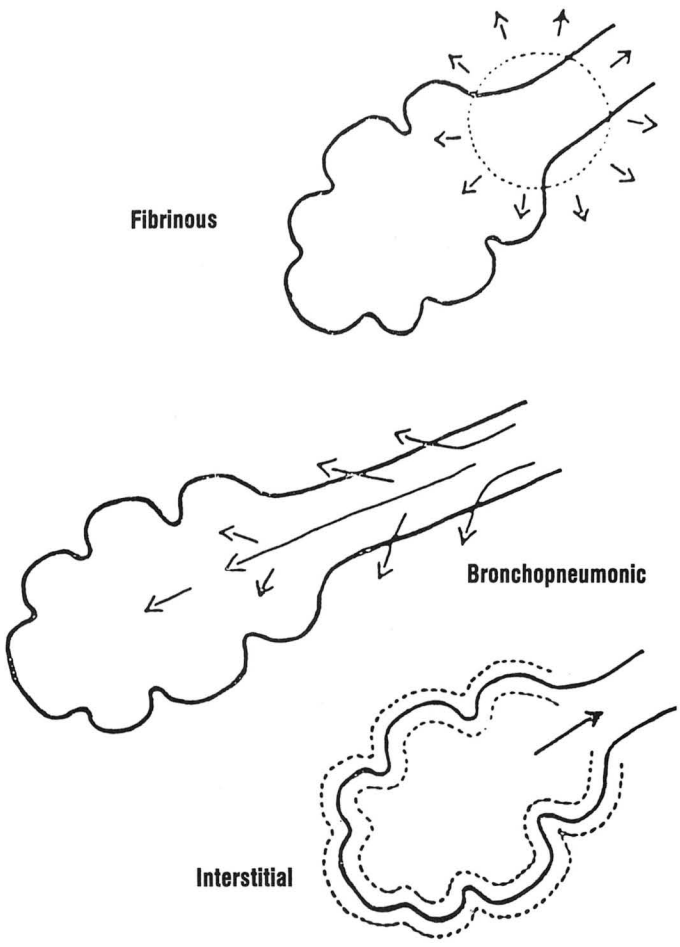
The tachypnea of calves with pasteurellosis occurred with no decrease in tidal volume resulting in a large increase in minute ventilation. Alveolar ventilation was unchanged and most of the extra ventilation was deadspace ventilation. This deadspace ventilation could not be explained by the combination of increased frequency and a fixed anatomic deadspace. It therefore had to result from ventilation of poorly perfused regions of lung such as would result if much of the pulmonary blood flow was directed away from normal regions toward pasteurella infected regions of lung.

There is no data available on changes in lung perfusion following challenge by infectious agents. Robinson has measured pulmonary artery pressure in a calf with chronic pneumonia. Pulmonary arterial pressure equalled systemic pressure. When the calf was ventilated and hypoxemia was relieved, pulmonary arterial pressure decreased to normal levels. If pulmonary artery constriction occurs with lung disease, the work load of the right-heart will be greatly increased.

Pathogenesis of Pneumonia in Feedlot Cattle

Jubb and Kennedy present a very practical description of the three main morphological types of lung lesions in cattle. Figure 2 conveys the essence of each in general terms. **Bronchopneumonia** is an anteroventral dark, firm, lobular lesion which involves inflammation of and within bronchi,

Figure 1. Diagrammatic representation of the three main morphological types of pneumonia in cattle.



bronchioles and alveoli. **Fibrinous pneumonia** is an anteroventral dark, hard, swollen, lobar lesion involving inflammation primarily in terminal airways, alveoli and interlobular tissue. The presence of fibrin indicates severe vascular damage with much edema, hemorrhage and exudation. There has literally been an explosion deep in the lung parenchyma. **Interstitial pneumonia** is generalized in the lung, tan to pink to red, rubbery and wet, often with noticeable separation of lobules by edema, with the main lesion being in the alveolar walls which are thickened. The acute lesions of each type are very characteristic (Table 10).

The most important pneumonia caused by microbiological agents is the fulminating acute fibrinous pneumonia caused by *Pasteurella hemolytica* and which is highly fatal. The distinctive feature of these lesions is the pattern of coagulation necrosis of the lung parenchyma. Such acute lesions are probably of three or four days duration. Affected animals are difficult to identify clinically in time for therapy to be effective.

Acute bronchopneumonias have less or no fibrin, less or no coagulation necrosis, more fluid in the exudate and are likely to have mixtures of *P. hemolytica* and *P. multocida,* with the latter predominating, possibly with evidence of viral infection.

Toxic agents arriving in the lung via the blood damage alveolar capillaries and alveolar lining cells resulting in hypercellular alveolar walls which results in interstitial pneumonias, such as "acute atypical interstitial pneumonia of cattle". The acute lesions of the latter disease are very characteristic.

The lesions of acute fibrinous or fibrinous bronchopneumonia of a week or more duration usually appear as bronchopneumonia, often with areas of coagulation necrosis (sequestration) present as raised, hard, irregular areas. These are often confused with abscesses. Lesions which have had significant viral component may show chronic bronchiolitis including obliterative and/or peribronchial fibrosis with nonspecific alveolar exudation.

It is rare to see specific evidence of virus infection, such as inclusion bodies, in acute lesions of fatal cases of fibrinous pneumonia. Rarely parainfluenza-3 viral inclusions can be observed. If necrotizing bronchiolitis is present, infectious bovine rhinotracheitis viral inclusions may be seen. Usually they are no longer visible in naturally occurring cases at the time of death. The significance of recognizing the lesions of IBR viral-induced necrotizing bronchiolitis is often not appreciated. When this lesion is dominant in the lungs, that specific IBR viral problem must be recognized and dealt with. Specific morphological evidence of lesions of mycoplasma, bovine virus diarrhea (BVD) virus, adenovirus, chlamydia or respiratory syncytial virus are very rarely recognized or confirmed.

P. hemolytica is a cause of acute fatal cases of severe fibrinous pneumonia. Viruses may assist by weakening the antibacterial defenses but are not necessary for these lesions. Several laboratories are now concentrating on the toxin produced by *P. hemolytica* as the factor which injures the lung and causes the fibrinous pneumonia. *P. hemolytica* is part of the normal nasal flora in cattle.

A study by Thomson is described where their laboratory tries to determine what happens in cattle that develop respiratory disease under natural conditions. Cattle were classified as sick (S) or well (W) based on the level of body temperature and plasma fibrinogen. Levels of serum antibody, lung scores, nasal flora (quantitative and qualitative) were compared between S and W groups. None were treated. In general, sick animals had lower serum antibody to *P. hemolytica* and high levels of *P. hemolytica* in nasal flora on arrival, whereas there was little difference between S and W in serum antibody levels to PI-3 virus. They concluded that S animals were more susceptible to the effects of *P. hemolytica* and had much higher levels of *P. hemolytica* in their nasal flora.

It was necessary to determine if there was a relationship between the high levels of *P. hemolytica* on the nasal mucosa and the numbers being breathed into the lung from the nasal mucosa. Using an Anderson air sampler in an isolated environment, animals with high numbers on their nasal mucosa did breath them into the lung, generally in

TABLE 10. Accute Gross Pneumonic Lesions in Feedlot Cattle.

	Type of Pneumonia				
Features	**Fibrinous**	**Fibrinous-broncho**	**Bronchopneumonia**	**Necrotizing Bronchiolitis**	**Interstitial**
Location	Anteroventral	Anteroventral	Anteroventral	Anteroventral	Entire lung
Color	Dark red	Dark red	Dark	Dark	Reddish-tan
Fibrin	Present	Present - variable	Absent	Absent	Absent
-surface	Present				
-interlobular	Present				
Size	Swollen	Swollen or normal	Normal	Normal or swollen	Swollen
Texture	Hard	Firm	Rubbery to firm	Rubbery to firm	Rubbery
Cut surface	Dry, marbled	Marbled, wet, red	Wet, red	Dark with pale bronchiolar pattern	Wet, lobules separated
Trachea	Normal or froth	Normal or froth	Normal or froth	Froth and necrotic debris	Froth
Bronchioles	Froth	Froth and exudate	Exudate	Necrotic debris	No lesions
Coagulation necrosis	Present	Variable	Absent	Usually absent	Absent
Cause	**Past. hemolytica**	**Past. hemolytica** ± multocida ± virus	**Past. multocida** ± virus	IBR Virus **Past. multocida** **Past. hemolytica**	Toxicity

Thomson, 1983

relationship to the numbers present in the nasal mucosa. Numbers of organism and particle size were determined in tracheal air. The organisms were constant in the oral cavity but were not breathed out in expired air.

Another study investigated the normal clearance of bacteria from the lungs of cattle and also whether viruses could influence normal bacterial clearance. Parainfluenza-3 (PI-3) virus did impair the bacterial pulmonary clearance of *P. hemolytica* in calves 7 days after the viral infection and the defect corrected after 11 days.

The focus keeps coming back to *P. hemolytica* as the most significant organism in causing the acute fatal fibrinous pneumonia in feedlot cattle. *P. multocida* is not likely primary but will be present secondarily, either in viral induced lesions or in some *P. hemolytica* induced lesions. In field cases of acute fibrinous pneumonia *P. hemolytica* is present in pure culture. However, in cases where evidence of viral infections are present, particularly in bronchioles, *P. multocida* dominates.

Another reference sheds some interesting light on the relationship of the environment within the host to the establishment of residence by the bacterial pathogen. Bacteria on mucosal surfaces exist in a very complex ecosystem. Different species associate with each other in a fluid mosaic of glycocalyx and the relationships of organisms change with their various growth phases. Microcalories exist in the glycocalyx. The glycocalyx can exclude phages, sera, antibody macrophages and clearance mechanisms. Pure cultures on mucosal surfaces are an artifact. Virus infection, stress and antibiotics alter the relationships of organisms to each other and to the cells near them. Most bacteria must attach to a cell to cause it harm. Bacteria attach to the cells by specific host receptor sites called adhesins. Such attachments are genetically determined and this accounts for the apparent specificity of certain infections of certain tissues in certain species. Many of the disease causing bacteria are part of normal flora. Thus the tissue specificity of infection resides in attachments which are called adhesins on the fimbria of Gram negative bacteria and fibrillae of Gram positive bacteria.

Another major factor in pathogenesis is to determine the influence of management practices on the pneumonias. The Bruce County Beef Project has assisted in evaluation of certain influences. Mixing groups of animals, vaccinating on arrival, and feeding corn silage increased the risk of disease, and when all three occurred in the same groups of animals, the incidence and risk of respiratory disease was increased considerably.

In summary, the agents which cause the respiratory disease in feedlots are known, the general circumstances and management practices which allow the agents to cause respiratory disease are known, and good management practices which can largely prevent major respiratory disease problems are known. The problems are in the execution of good management practices, including accurate records, in establishing early accurate clinical and pathological diagnoses of what is happening in sick and dead cattle and in developing effective prevention procedures.

Respiratory System Humoral and Cell Mediated Resistance Mechanisms of Cattle

Resistance to Respiratory Infection:

1. Nonspecific Resistance Mechanisms. Agents of relative low virulence or of subvirulent dose may be adequately controlled as a result of nonspecific mechanisms operating within the upper and lower respiratory tract. Clearance of particles from the respiratory system is mediated by ciliary action above the alveoli which elevates material within fluid secretions to be swallowed or expectorated and by phagocytosis in the alveolus, especially by lung macrophages. The site of particle deposition is a function of particle size, the larger particles (>10μm) impinging upon nasal mucosa while smaller particles (0.5 – 3μm) reach the lung. Bovine lung clearance of *Pasteurella hemolytica* may reach 90% or more of the delivered dose by four hours post inoculation and bacterial clearance is impaired at 7 days post infection with PI-3 virus. Both PI-3 virus and bovine herpes virus-1 (BHV-1) have been shown to enhance susceptibility to pneumonic pasteurellosis induced by *P. hemolytica* given by aerosol at discrete time intervals of 3-10 days for PI-3 and greater than 4 days for BHV-1.

The alveolar macrophage, the most numerous cell type in bovine lung lavage fluids may well be the principal mediator of nonspecific resistance in the lung. *P. hemolytica* has been shown to produce a potent cytotoxin which is active against ruminant leukocytes, including alveolar macrophages, both impairing phagocytosis and killing the leukocyte. Cytotoxin neutralizing antibody has been shown to correlate positively with resistance to pneumonic pasteurellosis in feedlot cattle. In addition, *P. hemolytica* has been shown to inhibit production of leukocyte chemotactic factors, an important component of nonspecific resistance, by bovine alveolar macrophages. The observed dose relatedness of *P. hemolytica* induced bovine pneumonia as well as the increase of *P. hemolytica* nasal colony counts in shipped calves judged to be unhealthy suggests that in nonimmune cattle nonspecific respiratory system resistance is overcome by increasing numbers of *P. hemolytica* entering the lung with inspired air.

Nonspecific resistance mechanisms operating in the bovine respiratory tract may well include nonspecific opsonization by IgG and IgM or complement as has been reported in other species and the contribution of lysozyme, lactoferrin or other antibacterial substances, as described in other species, may also be significant in cattle but are presently undescribed. The resistance afforded by macrophage, and likely also neutrophil function, is apparently substantial.

2. *Immunologically Specific Resistance Mechanisms:* Products of specific antibody or cell mediated immune response are complementary to pre-existing nonspecific resistance and clearance mechanisms.

The following general concepts apply to the respiratory immune response:

- The respiratory system is relatively compartmentalized from blood and blood-derived immune response, particularly in the upper areas but less so in lung.
- The respiratory system is itself compartmentalized immunologically into upper, mid and lower areas with apparent functional differences occurring by area.
- Both antibody and cell mediated immune response occur within the respiratory system.
- Surface respiratory system immune mediators can be induced by surface or by parenteral immunization and surface mediators are better correlated with resistance than are serum mediators. Respiratory immune response varies qualitatively and quantitatively in relation to route and method of its initiation.
- Mechanisms of immunologically mediated respiratory resistance are similar to those operating in other sites and are subject to the same limitations imposed by immunoglobulin isotype-related function as well as availability of immunoglobulin and cells.
- Presence of respiratory surface immune mediators is transient in the absence of ongoing stimulation by antigen.
- Memory can be established and measured in relation to surface immunization of the respiratory system.

a) *Antibody Mediated Immune Response.*

Regional differences exist in secreted immunoglobulin isotypes with the ratio of IgA:IgG favoring IgA in nasal secretions while approaching unity in lung lavage fluids and strongly favoring IgG in serum.

The presence of complement components in secretions of the bovine respiratory system has not actually been confirmed but by extrapolation from other species it seems likely that a functional complement system should exist, at least in alveolar fluids. Complement is important in opsonization of bacteria for phagocytosis by lung macrophages and in lung clearance of bacteria in mice and rabbits.

Lung fluids obtained from calves immunized by subcutaneous injection of killed adjuvanted *P. hemolytica* rarely impaired phagocytosis in contrast to fluids from animals exposed to the bacterium by the respiratory route. The opposing effects occurred in spite of similar bacterial agglutinating antibody activity in opsonizing and phagocytosis inhibiting lung fluids. Although immunoglobulin isotypes were not fractionated from the lung fluids used in these experiments the authors speculated that the observed phagocytosis inhibitory effect may have been due to a preponderance of antibody in the IgA class following respiratory immunization. This isotype is nonopsonizing and may block phagocytosis. Since phagocytic uptake of *P. hemolytica* leads to macrophage killing, parenteral immunization with this organism may be detrimental if the immunogen fails to induce cytotoxin neutralizing antibody. Surface immunization with propensity to induce nonopsonizing IgA antibody may be less detrimental and beneficial if toxin neutralization occurs. For organisms which do not possess macrophage injuring ability, or which

do not survive within phagocytic cells, induction of respiratory IgG antibody by parenteral immunization may be advantageous.

Secreted immunoglobulin may arize by secretion from plasma cells immediately beneath the epithelium of the respiratory system or from tissue fluids by transudation. Neonatal calves have much higher concentrations of IgM and IgG in nasal secretions than do older animals in which IgA is present in higher concentration. These changes likely reflect early secretion of colostrum-derived Ig into respiratory secretions and a gradual increase of endogenous epithelium associated production of IgA. In small airways associated lymphoid cells of normal calves IgA producers predominate but with development of pneumonia the proportion of IgGl producing cells increase. Physiologically delayed onset of respiratory immunoglobulin synthesis may be important in predisposition to neonatal respiratory disease by analogy with the calf intestine in which local antibody production is also delayed.

Induction of antibody within bovine respiratory tract secretions can be accomplished by local or parenteral administration of antigen. Antibody readily appears in lung washing fluids following parenteral immunization but induction of nasal secretion antibody apparently requires more rigorous immunization with adjuvanted or replicating agents. In parenterally immunized calves lung washing contain antibody only transiently and without apparent relationship to serum antibody titer. The best correlate of resistance in calves challenged with *P. hemolytica* was nasal antibody present after exposure to the live organism and nasal antibody was found to be associated with reduced nasal *P. hemolytica* colony counts. Nasal antibody was not increased in calves immunized subcutaneously with adjuvanted killed *P. hemolytica.* Following intramuscular vaccination with attenuated BHV-1 virus, 2 of 4 cattle had nasal antibody only in association with IgG while intranasal vaccination resulted in more virus neutralizing IgA than IgG at 14 days and the reverse by 28 days after vaccination. Serum antibody was detected at 14 days after intramuscular vaccination and at higher titer than after intranasal vaccination which resulted in detectable antibody by day 21. Anamnesis was induced by both routes since serum antibody increased by 5 days after challenge to a higher titer than in controls which did not produce detectable antibody until day 12. Both nasal and serum antibody occurred in calves vaccinated intranasally or intramuscularly with modified live PI-3 virus vaccines although nasal vaccination produced higher nasal antibody titers.

b) *Cell Mediated Immune Response (CMI).*

CMI occurs within the lung of several species and is partially compartmentalized from parenteral CMI as is true for antibody mediated respiratory immune response. Compartmentalization can be eroded by rigorous immunization. Limited information is available concerning CMI within populations of bovine respiratory systems cells.

c) *Protective Effect of Bovine Respiratory Immune Response.*

The protective potential of the respiratory immune system varies by region, there being apparently more effective resistance in lung than nose where antibody is more likely to be IgA with attendant limitations in antimicrobial mechanisms, possibly enhancing the likelihood of the carrier state. Agents which remain upon the surface of epithelia at any level of the respiratory system are subject to a more restricted inventory of immunological control mechanisms than are those that penetrate and spread beyond the portal of entry. The most pertinent question is therefore the effect of immune mediators upon agents prior to their entry to epithelia, however, experiments reported to date are frequently such that this distinction cannot be made. Prevention of infection may be the most important objective so that the disadvantages of persistent foci of infection and serological positivity, common features of BHV-1, PI-3 and *P. hemolytica* infection, may be avoided. Surface resistance may be needed to provide this.

Although respiratory protection is generally best correlated with immune mediators within the secretions of the respiratory system, advantage does not clearly result from local rather than parenteral administration of modified live PI-3 virus, BHV-1 or live *P. hemolytica* when compared in terms of induced protection against homologous respiratory challenge. Parenteral vaccination with BHV-1 modified live virus may result in fewer post-vaccinal clinical signs than respiratory vaccination. Parenteral vaccination with formalin killed *P. hemolytica* however failed to protect calves and was associated with more severe reaction to homologous respiratory challenge. While the exact pathogenesis of this response has not been elucidated it is thought to be due to inappropriate specificity of immune response for surface antigens rather than cytotoxin or other virulence factors induced as well as possibly inappropriate class bias of lung antibody. Similar antigen given locally does not induce adverse reaction but fails to protect against challenge.

Vaccination with live *P. hemolytica* by aerosol or by subcutaneous injection induced resistance to homologous challenge by direct injection into the lung. Protection was associated with enhanced phagocytosis of the bacterium *in vivo* and reduced extent of pneumonic lesions and no mortality. Subcutaneous vaccination resulted in more intact intracellular bacteria than did aerosol vaccination.

Viral Bacterial Interactions in Respiratory Tract Infections

Pulmonary Antibacterial Defenses: Although bacteria enter the lungs daily by inhalation of small droplets or by aspiration of fluid from the upper respiratory tract, the distal airways and alveoli are normally sterile. This is because the normal lung has the inordinate capacity to inactivate bacteria. Bacteria deposited in the lung parenchyma are rapidly engulfed and inactivated by the phagocytic cells of

the lungs. The rate of intrapulmonary killing greatly exceeds the rate of physical translocation so that in terms of successful resistance against bacterial infections, *in situ* bactericidal mechanisms are more important than transport mechanisms out of the lung.

The resident phagocytes of the lung, the alveolar macrophages, play the pivotal defensive role against bacterial infection. However, when inflammatory processes are established, the polymorphonuclear leukocytes (PMNs) from the circulation immigrate into the lungs. This leukocytic response brings auxiliary defense capabilities to the lungs and indicates that rather than being wholly dependent on alveolar macrophages, pulmonary antibacterial defense is dependent on a dual phagocytic system that involves both alveolar macrophages and PMNs.

Environmental manipulations or alterations of the host can modulate pulmonary antibacterial defenses. Conditions known to decrease intrapulmonary killing of bacteria include alveolar hypoxia, pulmonary edema, acidosis, certain pharmacologic agents, stress, inhalation of atmospheric pollutants, pulmonary virus infections and a number of other influences. On the other hand, immune mechanisms enhance the intrapulmonary killing of bacteria. Immune enhancement of pulmonary bactericidal activity varies with different bacterial species.

At the cellular level the bactericidal armamentarium of the pulmonary phagocytes rapidly inactivates and degrades inhaled and aspirated microorganisms within hours of their entrance into the alveolar region. Phagocytes are attached to bacteria by chemotactic factors. Engulfment is triggered by the attachment of the bacteria to specific immunologic and nonspecific receptors on the macrophage cell membrane. Once ingested, the bacteria are internally isolated in phagosomes. Lysosomes, sequestering microbicidal and degradative enzymes, then fuse with the phagosome to form the phagolysosome in which intracellular processing of the bacteria occurs.

The mechanism of recruitment of PMNs to the alveoli to provide auxiliary phagycytic defenses is not completely understood. Explanations would include that the alveolar macrophages secrete chemotactic factors specific for the recruitment of PMNs. Alternatively, the microbes against which PMNs provide auxiliary phagocytic defenses are primarily gram negative organisms that contain endotoxin. Endotoxin is known to activate complement of which the C^5 component has been demonstrated to be chemotactic for PMNs.

Pathogenesis of Uncomplicated Viral Pneumonia: During the acute stages of the infection the ciliated epithelial cells of the conducting airways are the principal sites of viral replication. In the affected areas the ciliated epithelium degenerates and desquamates, leaving only a thin layer of basal replacement cells. By one week, the affected areas of the lung parenchyma are characterized by hyperemia and thickening of the alveolar walls with interstitial infiltration with leukocytes and capillary thrombosis. The alveoli are congested and edematous and contain leukocytic exudates. Concurrently, the luminal side of the affected airways may be partially or completely occluded by the sloughing of degenerated epithelial cells and the influx of inflammatory cells, whereas the peribronchial areas are intensely infiltrated with mononuclear cells. The virus-induced lesion begins to resolve by the ninth day of the infection.

Host defenses against the virus infection include interferon and the specific antiviral immune response. Interferon concentrations in the lung are usually at their highest levels on approximately the fifth day of infection and then decline as the virus disappears. Specific antiviral immunoglobulins have been detected in the lungs by the third day of infection, and by day 8 locally synthesized antibodies are present in bronchial washings; serum antibodies usually appear by day 8 also. In addition to the humoral immune response, cytotoxic T lymphocytes sensitized to viral antigen also appear in the lungs during the third day of infection. This response peaks at approximately day 7 and thereafter rapidly declines.

Current concepts of antiviral immunity indicate that the host response controls the infection by halting the spread of the virus to extrapulmonary sites and by destroying virus-infected cells. Both humoral and cellular immune responses can participate in the destruction, antibody with the aid of complement and T lymphocytes through their direct cytotoxic activity.

Virus-Induced Pulmonary Bactericidal Dysfunction: During the acute phase of the viral infection the bactericidal mechanisms of the lung become progressively depressed, with maximal suppression occurring approximately a week after viral inoculation. Thereafter, the antibacterial defenses of the lung become reestablished, being essentially normal by the second week of infection. The extent of the virus-induced suppression of pulmonary bactericidal activity at day 7 is dependent on the amount of virus used for infection.

Virus-Induced Phagocytic Dysfunctions: Recent studies have questioned the significance of the viral lesion as the primary mechanism responsible for pulmonary antibacterial dysfunction since bacterial multiplication associated with virus infection of lungs is related to defects in *in situ* bactericidal (phagocytic) mechanisms rather than transport mechanisms of the lung. Studies on the functional activity of alveolar macrophages lavaged from virus infected lungs during the time of maximum virus-induced suppression of pulmonary bactericidal activity have demonstrated dysfunctions in:

a) immunologic and nonimmunologic membrane receptor binding activity;
b) immunologic and nonspecific receptor-mediated phagocytic ingestion;
c) phagosome-lysosome fusion;
d) intracellular killing; and
e) bacterial degradation. In addition, alveolar macrophages from

virus infected lungs have abnormally low levels of lysosomal enzymes. These combined observations clearly demonstrate

that pulmonary virus infections induce a functional paralysis of the alveolar macrophage phagocytic system. In contrast to alveolar macrophages, little is known about the effect of viral infection on the phagocytic function of monocytes and PMNs.

To date, the available data demonstrate that virus infection induces a paralysis in lung phagocyte function at a time that coincides with the greatest susceptibility to secondary bacterial pneumonias. The impaired function of the lung phagocytes remains the primary reason most often proposed for the occurrence of bacterial complications after pulmonary virus infection.

The Involvement of the Antiviral Immune Response in Phagocyte Dysfunction:

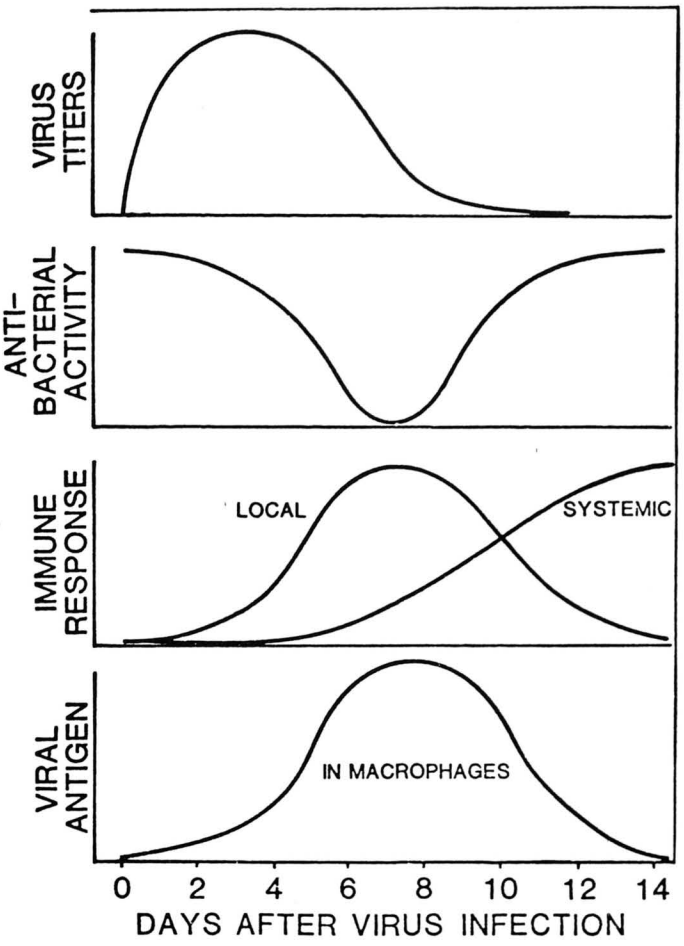
The growth of virus in the lungs is not immediately accompanied by the transient suppression of pulmonary bactericidal activity (Figure 2). Instead, the impairment of phagocyte function is some time after peak lung titers of infectious virus are obtained. This temporal relationship suggests that macrophage dysfunction does not result from a direct effect of the virus on the phagocyte.

The rapid decrease of infectious virus titers occurs concomitantly with the appearance of the antiviral immune mechanisms, consisting of both antiviral antibody and a specific cytotoxic lymphocyte response, are maximal in the lungs at approximately a week after viral infection. An apparent paradoxical association is that during the period of time of decreasing virus titers and increasing immune responsiveness in the lungs, the phagocytic capabilities are maximally suppressed. These simultaneous occurrences indicate that components of the host's antiviral immune response may be involved in producing the phagocytic defect.

The mechanism by which antiviral immune mechanisms participate in the virus-induced derangement of alveolar macrophage phagocytosis remains to be elucidated. All enveloped RNA viruses (including influenza and parainfluenza) which acquire an outer lipid envelope by budding from the host cell membrane express viral antigen on the cell surface. Antiviral antibody and specifically sensitized lymphocytes are known to interact with such virus infected cells resulting in pertubation of cell function, or even cell death. Therefore, explanations for the involvement of the antiviral immune mechanisms in the phagocyte derangement could include that the alveolar macrophages become target cells for the antiviral immune response. This is a desirable response because it eliminates virus-bearing cell. It is detrimental to the host because it transiently reduces the phagocytic capacity of the macrophages and thereby the antibacterial defenses of the lung.

Contributing Factors and Other Considerations: The data detailed above demonstrate that virus-induced suppression of pulmonary antibacterial defenses are mediated through defects of the alveolar macrophage phagocytic system and provide strong support that the induction of phagocyte dysfunction is mediated, in part, by the antiviral immune

Figure 2. Diagrammatic summary of the temporal events during virus pneumonia. Correlation between pulmonary virus titers, virus-induced suppression of pulmonary antibacterial activity, the antiviral immune response and viral antigen in alveolar macrophages. (Jakab, 1983)



response. However, a number of additional effects are induced during the viral infection which alter the millieu of the lung and undoubtedly also play a role in increasing susceptibility to bacterial superinfection.

First, it has been proposed that as an initial step in bacterial infections, the organisms adhere to the cells of the respiratory tract. This adherence, in turn, enhances bacterial colonization, which could proceed to bacterial infection and disease. Upper respiratory tract colonization with increased numbers of bacteria may increase the chances of bacterial infection of the lung through either the presence of the microbes in the respiratory tract or, upon aspiration, a bolus containing a larger number of organisms is delivered to the lung.

Second, in the viral lesion in the lung parenchyma, the type 2 alveolar pneumocytes are destroyed. These cells synthesize and secrete surfactant, the level of which is decreased in the consolidated but not in the unconsolidated areas of virus-infected lungs. Since a component of surfactant is considered to play an important role in the phagocytosis of bacteria by alveolar macrophages, its

decreased presence may be an additional factor involved in macrophage malfunction. In addition, alveolar macrophages are aerobic cells whose phagocytic capacity is suppressed by hypoxic conditions; anaerobic conditions brought about by atelectasis and edema would be expected to affect their phagocytic capacity.

Third, maximal virus-induced inhibition of phagocyte function coincides with the time that the greatest number of alveolar macrophages contain viral antigen. The source of antigen is most likely a combination of intracellular viral multiplication and ingestion of cellular debris from the sloughed bronchial epithelium, the site of earlier virus proliferation.

It is known that ingestion of large amounts of material will block subsequent phagocyte function. Thus, the lung macrophages that are actively processing ingested cellular debris may have a reduced capacity to ingest additional material (i.e., bacteria). Those affected macrophages that ingest microorganisms, albeit fewer or at a slower rate, may not have the resources to process the additional load intracellularly.

Finally, evidence is accumulating that, in certain instances, the bacterium itself may play a role in diminishing macrophage phagocytosis. *Pasteurella hemolytica* and culture supernatants of the organism are cytotoxic to bovine alveolar macrophages and peripheral leukocytes. This observation would suggest that if the bacteria gained a foothold in the lung through virus-induced macrophage dysfunction, the organism could perpetuate itself through its own toxic mechanism.

The Role of Antiviral and Antibacterial Immunity: The magnitude of the virus-induced suppression of pulmonary bactericidal mechanisms is related to the disease-inducing potential of the virus. Specific antiviral immunity prevents viral infection and thereby the ensuing decrease in pulmonary antibacterial defenses. Specific antiviral immunity however, does not preclude infection with a heterologous virus, which would again increase host susceptibility to secondary bacterial complications.

The efficacy of antibacterial immunity in preventing bacterial superinfections appears to depend on the organism.

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